Saturday, July 21

8:15 AM

Predictive Analysis of the 12-Week Dosing Status at Week 48 for Patients Receiving Brolucizumab in the HAWK and HARRIER Studies

- David M. Brown, MD
- Pravin U. Dugel, MD
- Gabriele Lang, MD
- Sam Razavi
- Andreas Weichselberger, PhD
- Yuichiro Ogura, MD

OBJECTIVE Identification of 12-week dosing suitability for patients treated with brolucizumab in HAWK and HARRIER

PURPOSE Brolucizumab is a novel single-chain antibody fragment with potent anti-vascular endothelial growth factor attributes. HAWK and HARRIER are prospective, phase III studies where the majority of patients receiving brolucizumab 6mg were maintained on an exclusive 12-week (q12w) interval at Week 48. The predictive role of the first q12 interval on identification of q12 dosing suitability is presented.

METHODS Patients were randomized 1:1:1 to brolucizumab 3mg (n=358), brolucizumab 6mg (n=360) or aflibercept 2mg (n=360) (HAWK), or 1:1 with either brolucizumab 6mg (n=370) or aflibercept 2mg (n=369) (HARRIER). One eye of each patient was designated as the study eye. After three loading doses, brolucizumab patients were

treated every q12w, with the option of 8-week dosing (q8w) during the first q12 interval and at each scheduled q12 treatment visit; aflibercept was dosed in a fixed q8w, as per label. Key endpoints included the proportion of patients on the q12w treatment regimen at Week 48 and the predictive value of the first q12w treatment interval for maintenance of a q12w regimen up to Week 48.

RESULTS For the brolucizumab 6mg arm, 57% and 52% of patients, in HAWK and HARRIER respectively, were maintained on a q12w interval up to Week 48. The majority of patients with a need for q8 dosing were identified during the first q12 interval (80% and 78% of brolucizumab 6mg patients in HAWK and HARRIER, respectively). Patients receiving brolucizumab 6mg who successfully completed the first q12w interval had an 87.4% and an 82.5% probability of remaining on q12w treatment until Week 48 in HAWK and HARRIER, respectively [82.6% probability for the 3mg brolucizumab arm (HAWK)].

CONCLUSION Brolucizumab patients identified to be suitable for the q12w interval dosing in the first q12w interval, were likely to remain on q12w treatment for the remainder of the study. Learning from the first q12 interval can have an essential role in defining suitable treatment intervals for patients and potentially reducing the burden in the management of neovascular age related macular degeneration.

HUMAN RESEARCH This study involves human research.
IRB Approval Status: Approved by institutional review board

8:23 AM

A Comparison of the Anatomical Efficacy of Brolucizumab Versus Aflibercept in nAMD Patients: Matched 16-Week Results From the HAWK and HARRIER Studies

- Pravin U. Dugel, MD
- Rishi P. Singh, MD
- Andreas Weichselberger, PhD

OBJECTIVE Comparative assessment of anatomical outcomes up to Week 16 between brolucizumab and aflibercept

PURPOSE HAWK and HARRIER are two phase III, prospective studies investigating the efficacy and safety of brolucizumab in comparison to aflibercept in patients with neovascular age-related macular degeneration (nAMD). The current analysis assessed the anatomic outcomes from the first 16 weeks, particularly as related to the changes between week 12 and 16, the period immediately after the loading phase.

METHODS Patients were randomized 1:1:1 to brolucizumab 3mg (n=358), 6mg (n=360) or aflibercept 2mg (n=360) (HAWK), or 1:1 with either brolucizumab 6mg (n=370) or aflibercept 2mg (n=369) (HARRIER). Only one eye of each patient was designated as the study eye. After three loading doses, brolucizumab patients were treated every 12 weeks (q12w), with the possibility of adjusting to q8 during the first q12 interval and at each scheduled q12 treatment visit. Aflibercept patients were treated on a q8w regimen,

as per label. Spectral domain optical coherence tomography assessments were conducted and images were analyzed by independent central reading centers.

RESULTS The mean change in central subfield thickness (CST) from baseline to Week 16 for brolucizumab 6mg was -161.4 μM and for aflibercept 2mg was -133.6 μM ($p = 0.0016$) in the HAWK study. In HARRIER, the mean CST reduction from baseline to Week 16 for brolucizumab 6mg was -174.4 μM and for aflibercept 2mg was -134.2 μM ($p<0.0001$). At Week 16, fewer patients on brolucizumab 6mg had retinal fluid (IRF and/or SRF) relative to aflibercept and the corresponding fluid reduction rates for brolucizumab 6mg were 35% (HAWK) and 33% (HARRIER) lower as compared to aflibercept ($p < 0.0001$). Fewer brolucizumab 6mg patients had sub-RPE fluid compared to aflibercept patients at Week 16, i.e. 30% ($p=0.0021$) and 33% ($p=0.0041$) less fluid with brolucizumab in HAWK and HARRIER, respectively, relative to aflibercept. Changes in CST, IRF and/or SRF, and sub RPE fluid status between week 12 and 16, when patients are extended after the loading phase, will also be presented.

CONCLUSION From the matched head-to-head period of HAWK and HARRIER, brolucizumab demonstrated statistically better anatomical outcomes compared to aflibercept with respect to retinal thickness, IRF and/or SRF fluid status and sub-RPE fluid status.

HUMAN RESEARCH This study involves human research.
IRB Approval Status: Approved by institutional review board

8:31 AM

Phase 3 Randomized, Double-Masked Studies of Brolucizumab Versus Aflibercept in nAMD: Expanded Primary and Secondary Outcomes From HAWK/HARRIER

- Arshad M. Khanani, MD
- Adrian H.C. Koh, MBBS, FRCS(C)
- Yuichiro Ogura, MD
- Andreas Weichselberger, PhD
- Frank Holz, MD, FEBO
- Pravin U. Dugel, MD

OBJECTIVE Phase III trials designed to compare the efficacy and safety of brolucizumab versus aflibercept in patients with neovascular age-related macular degeneration.

PURPOSE Brolucizumab is a single-chain antibody fragment with potent anti-VEGF attributes. Its molecular structure enables concentrated molar dosing and may facilitate effective tissue penetration, which together may support a long-lasting effect. These studies compared the efficacy and safety of brolucizumab versus aflibercept in patients with nAMD.

METHODS Patients were randomized 1:1:1 to brolucizumab 3mg (n=358), 6mg (n=360) or aflibercept 2mg (n=360) (HAWK), or 1:1 with either brolucizumab 6mg (n=370) or aflibercept 2mg (n=369) (HARRIER). One eye of each patient was designated as the study eye. After three loading doses, brolucizumab patients were treated every 12 weeks

(q12w), with the option of 8-week dosing (q8w) during the first q12 interval and at each scheduled q12 treatment visit; aflibercept was dosed in a fixed q8w regimen. The primary endpoint was non-inferiority of brolucizumab to aflibercept in best corrected visual acuity (BCVA) change at Week 48. Secondary endpoints included assessment of anatomic, visual and safety outcomes.

RESULTS Mean change in BCVA from baseline to Week 48 for brolucizumab was non-inferior versus aflibercept in both studies ($p<0.0001$, both studies). In HAWK, mean change in BCVA (±SE) for brolucizumab 3mg, 6mg and aflibercept 2mg was 6.1 (0.69), 6.6 (0.71) and 6.8 (0.71) ETDRS letters, respectively. In HARRIER, mean change in BCVA (±SE) for brolucizumab 6mg and aflibercept was 6.9 (0.61) and 7.6 (0.61) letters, respectively. At Week 48, the percentage of patients who gained ≥15 letters in the brolucizumab 6mg and aflibercept arms were 33% and 26% in HAWK, and 29% and 30% in HARRIER, respectively. The percentage of patients who lost ≥15 letters were 6% each in brolucizumab 6mg and aflibercept in HAWK and 4 % and 5 % in HARRIER respectively. Superior reductions in central subfield thickness were achieved with brolucizumab 6mg vs aflibercept, and significantly, fewer patients had IRF and/or SRF in the brolucizumab 6mg group versus aflibercept. Overall, safety was comparable between treatment arms.

CONCLUSION Brolucizumab met the primary endpoint of non-inferiority in BCVA change versus aflibercept, with the majority of brolucizumab patients maintained on a q12w dosing interval after loading until Week 48.

HUMAN RESEARCH This study involves human research.
IRB Approval Status: Approved by institutional review board

8:46 AM

Canadian Treat-and-Extend Analysis Trial With Ranibizumab in Patients With Neovascular AMD: CANTREAT Study 1-Year Results

- Peter J. Kertes, MD, FRCS(C)
- Tom Sheidow, MD, FRCS(C)
- R. Geoff Williams, MD, FRCS(C)
- Mark D.J. Greve, MD, FRCS(C)
- I. John Galic, MD, FRCS(C)
- Emmanouil Rampakakis, PhD
- Joanne Gavalakis, MSc
- Andrea Scarino, PhD

OBJECTIVE To compare the effectiveness of ranibizumab using a treat-and-extend (T&E) regimen to once-monthly (OM) dosing in treatment-naïve neovascular age-related macular degeneration (AMD) patients.

PURPOSE AMD is the leading cause of severe, irreversible vision loss in developed countries and is more common with increasing age. To date, there have been few large prospective randomized clinical studies which have assessed the efficacy of a T&E regimen compared with monthly dosing for the treatment of neovascular AMD.

METHODS This is a 24-month prospective, randomized (1:1), open-label, multicenter, post-authorization study conducted in Canada. Interim analysis describing baseline characteristics, visual acuity, and injection frequency over 24 months. Patients enrolled as of September 5th, 2017 were included. Summary statistics including the mean and standard deviation for continuous variables and counts and percentages for categorical

variables were produced for baseline and outcome parameters. Between group differences were assessed with the one-sided independent Samples t-test for change in best corrected visual acuity (BCVA). The full 24-month data will be available and analyzed after July 6 2018.

RESULTS 580 patients (T&E=287; OM=293) were included at the time of writing; of these, 526 patients (T&E=268; OM=258) and 343 patients (T&E=175; OM=168) had 12 and 24-month follow-up, respectively. Mean (SD) age was 78.8 (7.8) years, 60.3% were females, and 94.3% were Caucasian. No significant between-group differences were observed in baseline characteristics. Mean (SD) baseline BCVA was 58.7 (14.2) and 59.4 (13.5) for T&E and OM, respectively, and was comparable for both groups. At Month 12, after an average of 9.4 (T&E) and 11.8 (OM) injections, mean (SD) BCVA improvement was 8.4 (11.9) and 6.0 (11.9) (p=0.012) letters, respectively. At Month 24, after an average of 18.0 (T&E) and 23.6 (OM) injections, mean (SD) BCVA was comparable between groups with 6.4 (14.7) and 7.0 (12.1) letters (p=0.336), respectively. In the T&E group, patients extended to ≥8 weeks of treatment at 12 and 24 months was 69.3% and 70.9% and those extended to 12 weeks was 29.9% and 40.0%, respectively.

CONCLUSION The results of the current analysis showed that a T&E dosing regimen appears to induce significantly higher BCVA improvement at 12 months compared to a monthly dosing regimen, though comparable improvement was observed at 24 months but with fewer injections.

HUMAN RESEARCH This study involves human research.
IRB Approval Status: Approved by institutional review board

8:54 AM

Outcomes of Antivascular Endothelial Growth Factor (VEGF) Therapy for Neovascular Age-Related Macular Degeneration in Routine Clinical Practice

- Andrew A. Moshfeghi, MD, MBA
- John D Pitcher, MD
- Genevieve Lucas
- Nick Boucher
- Namrata Saroj, OD

OBJECTIVE To assess outcomes of patients with neovascular age-related macular degeneration following treatment with intravitreal anti-VEGF agents in routine clinical practice.

PURPOSE To evaluate outcomes in neovascular age-related macular degeneration (AMD) following treatment with intravitreal anti-VEGF agents in routine clinical practice.

METHODS This retrospective analysis evaluated data obtained through electronic medical records from patients at multiple clinical sites (Vestrum Health Retina Research Dataset; Naperville, IL) who were newly diagnosed with neovascular AMD and were initiated on treatment with intravitreal anti-VEGF agents. Patients with less than one year of treatment were excluded. Visual acuity (VA) through 1 year was evaluated in two dosing subgroups that were predetermined: A) ≤6 injections B) ≥7 injections. VA measurements were converted into an approximate ETDRS letter score.

RESULTS Of the 8127 patients with AMD, 1840 (23.0%) patients received ≤6 injections, and 6287 (77%) patients received ≥7 injections through 1 year. Corresponding baseline mean VA was 61 and 66 letters, respectively. In the subgroup of patients who received ≤6 injections, 23% of the patients presented with VA of ≥20/40; 39% with VA of <20/40-20/100, 13% with VA of <20/100-20/200, and 24% with VA of <20/200 at baseline. Corresponding proportions of patients in the subgroup receiving ≥7 injections were 21%, 49%, 15%, and 15%, respectively. The mean number of injections in patients receiving ≤6 injections was 4.5 with a mean VA gain of 2.1 letters. In patients receiving ≥7 injections, the mean number of injections was 9.1 with a mean VA gain of 6.4 letters.

CONCLUSION Data from routine clinical practice suggests that average visual gains are higher in patients who received at least 7 injections during the first year of treatment for neovascular AMD compared to those who received fewer injections.

HUMAN RESEARCH This study involves human research.
IRB Approval Status: Approved by institutional review board

8:59 AM

Percentage of Patients Maintained on Quarterly Anti-VEGF Dosing for the Treatment of Neovascular Age-Related Macular Degeneration Across Key Clinical Trials

- David A. Eichenbaum, MD
- Bann-mo Day, PhD
- Lisa L. Tuomi, PharmD

OBJECTIVE Can patients with neovascular age-related macular degeneration maintain or improve their vision with reduced frequency of treatment with anti-VEGF therapy?

PURPOSE Patients receiving anti-VEGF therapy for nAMD typically receive an injection on a monthly, bi-monthly, or *pro re nata* basis. Many patients achieve clinically relevant vision gains or stability with less-than-monthly dosing. This study investigates this subset of patients across 7 clinical trials to determine the visual gains of these patients treated with quarterly anti-VEGF dosing.

METHODS This cross-trial investigation assessed vision gains [Early Treatment Diabetic Retinopathy Study (ETDRS) and Best Corrected Visual Acuity (BCVA)] of nAMD patients who received ≥12-week anti-VEGF dosing after 3 consecutive monthly loading doses. Patients were from CABERNET (NCT01016873; n=163), EXCITE [NCT00275821; Ranibizumab (RBZ) 0.3 mg (n=120) and RBZ 0.5 mg (n=118)], year 2

of VIEW 1/VIEW 2 [NCT00509795/NCT00637377; 0.5 mg RBZ q4w (n=218); Aflibercept (AFL) 2 mg q4w (n=284); AFL 2 mg q8w (n=245)], PIER [NCT00090623; 0.3 mg RBZ (n=60) and 0.5 mg RBZ (n=61)], HAWK (NCT02307682), and HARRIER (NCT02434328). Additional analyses will identify predictors of response to quarterly (q12w) dosing.

RESULTS In CABERNET, at month (M) 12, 71% of patients receiving q12w 0.5 mg RBZ required no interventional therapy, gaining a mean 8.2 ETDRS letters from baseline (BL). At M12 of EXCITE, patients in the RBZ 0.3 mg and 0.5 mg q12w groups (intent-to-treat) gained a mean 4.0 and 2.8 ETDRS letters from BL, respectively, and 41.6% of q12w RBZ patients maintained these gains. During weeks 52–96 of the VIEW trials (VIEW 1/VIEW 2 pooled), 43%, 54% and 48% of patients in the RBZq4, AFLq4 and AFLq8 groups, respectively, achieved a ≥12 week dosing interval. At week 96, these patients gained a mean 9.2 (AFL2q8), 8.8 (AFL2q4), and 8.5 (RBZq4) ETDRS letters from BL. In PIER, patients receiving q12w 0.3 mg or 0.5 mg RBZ through M12, maintained vision, with mean changes from BL of –1.6 and –0.2 ETDRS letters, respectively, and 54% of patients maintained their initial VA gains at M12. In HAWK and HARRIER, 57% and 52% of patients receiving brolucizumab 6 mg maintained vision over 48 weeks with q12w dosing.

CONCLUSION These studies suggest that ~50% of patients with nAMD respond well to a 12-week dosing interval when treated with anti-VEGF monotherapy of RBZ, AFL, or brolucizumab, maintaining or improving their vision. Additional analyses will investigate predictors of response of these patients to identify others who respond well to a 12-week dosing interval, minimizing patient and physician burden.

HUMAN RESEARCH This study involves human research.
IRB Approval Status: Approved by institutional review board

9:04 AM

A Real-World Analysis in 49,485 Eyes of Visual Acuity Outcomes and Anti-VEGF Therapy Intensity in Neovascular AMD Patients

- David F. Williams, MD, MBA
- John S. Pollack, MD

OBJECTIVE To assess anti-VEGF therapy intensity and visual acuity outcomes, in “real world” neovascular AMD patients, using a demographically diverse sample of U.S. retina specialists’ EMR.

PURPOSE Neovascular AMD (nAMD) patients most commonly receive “treat and extend” regimens of anti-vascular endothelial growth factor (VEGF) therapy, instead of fixed interval dosing, in an attempt to limit treatment burden. This analysis assessed anti-VEGF therapy intensity, as well as the relationship between treatment intensity and visual acuity (VA) outcomes, in “real world” nAMD patients.

METHODS Analysis was performed on a large database of aggregated, longitudinal EMR from a demographically diverse sample of U.S. retina specialists (Vestrum Health). The HIPAA-compliant Vestrum Health Retina Research Dataset was used retrospectively. Treatment naïve nAMD patients who underwent anti-VEGF injections between January 1, 2012 and October 31, 2016 were eligible if follow up data was available through

October 31, 2017. VA outcomes were assessed at 1 year and stratified based on number of injections received over 1 year.

RESULTS 49,485 eyes were included in this analysis. The mean age at initial presentation was 81 years. At 1 year, the mean number of letters gained was 1 letter after a mean of 7.3 injections. There was a linear relationship between mean letters gained and mean number of injections, up to 10 injections over 1 year, after which the relationship plateaued. The mean change in VA was -1.7, -0.4, +2.5, and +3.0 in those 2313, 5250, 6212, and 2134 patients who received a mean of 3, 6, 9, and 12 injections respectively. This analysis corroborates prior observations that nAMD patients may be under-treated and that visual outcomes following anti-VEGF therapy for nAMD in the "real world" do not achieve those seen in randomized controlled trials.

CONCLUSION Treatment intensity in the "real world" correlates with VA outcomes over the first year of treatment, and that, on average, regimens that meaningfully decrease treatment intensity in the first year may result in under-treatment in some patients. This observation highlights the need for more intensive therapy and treatment compliance in nAMD.

HUMAN RESEARCH This study involves human research.
IRB Approval Status: Exempt from approval

9:16 AM

CFH and ARMS2 Genetic Risk Determines Progression to Neovascular Age-Related Macular Degeneration After Antioxidant and Zinc Supplementation

- Demetrios Vavvas, MD, PhD
- Kent W. Small, MD
- Carl C. Awh, MD
- Brent Zanke, MD,PhD
- robert Tibshirani, PhD
- Rafal Kustra, PhD

OBJECTIVE To evaluate the influence of genetics and AREDS formulation treatment on progression to neovascular AMD or geographic atrophy, using an expanded AREDS data set (1626 patients) and a validation data set

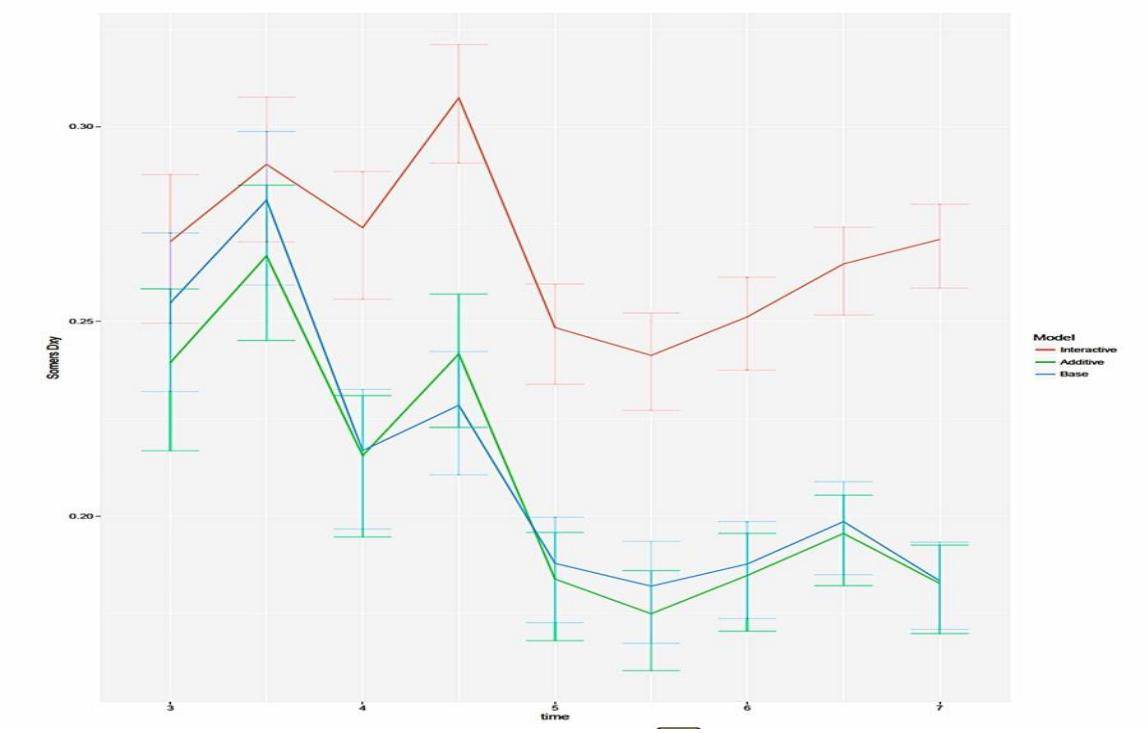
PURPOSE Pharmacogenetics is an important field in medicine that helps us maximize efficacy and minimize risks of treatments. We wanted to evaluate the influence of genetics on the effect of the AREDS formulation (AREDSF) on progression to neovascular AMD (NV) or central geographic atrophy (GA) and determine the individualized benefit/risk of patients with AMD on AREDS formulation.

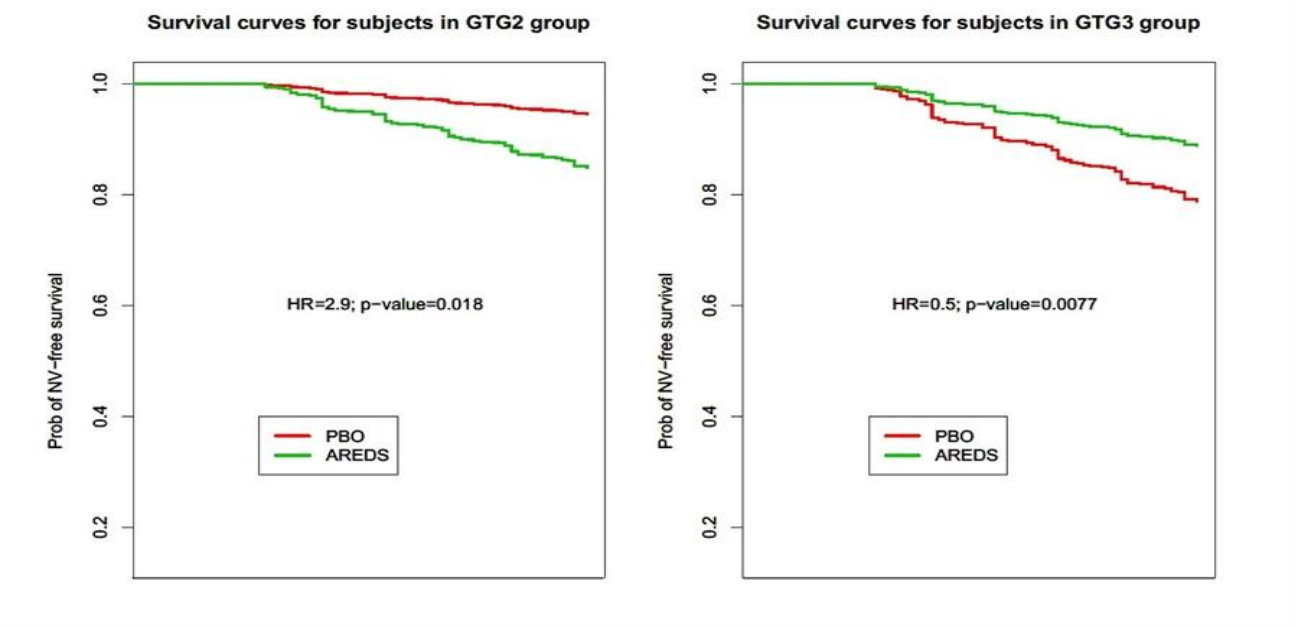
METHODS Data and DNA from 802 Age-Related Eye Disease Study (AREDS) subjects with category 3 or 4 AMD at baseline treated with placebo or the AREDS formulation were evaluated for differences in the risk of progression to NV or central GA as a function of CFH and ARMS2 genotype group. We used published genetic grouping: a 2 SNP haplotype risk calling algorithm to assess CFH and either the single SNP rs10490924 or 372_815del443ins54 to mark ARMS2 risk. Progression risk was determined using the Cox Proportional Hazard model. Genetics/treatment interaction

on NV risk was assessed and validated using a multi-iterative Bootstrap validation analysis.

RESULTS The AREDS formulation influenced progression only to NV, and not to GA. We identified strong interaction of genetics with AREDS formulation treatment on the development of NV. Individuals with high CFH and no ARMS2 risk alleles had increased progression to NV if treated with the AREDSF (HR 2.92, p = 0.018), but those with low CFH risk and high ARMS2 risk had decreased progression risk (HR 0.05, p = 0.008) [Figure 1]. Analysis of CFH and ARMS2 genotype groups from a subset of 299 patients which excluded all subjects included in prior analyses validates these findings. Bootstrapping analysis, a computer-based statistical technique employing tens of thousands of paired comparisons, further confirms the presence of a genetics/treatment interaction [Figure 2] and suggests that the individual treatment response to AREDS formulation is determined by genetics.

CONCLUSION Our analysis suggests that, as in the original AREDS analysis, the AREDSF appears to modify the risk of progression to NV, but not to GA. However, there appears to be a strong pharmacogenetic interaction with CFH and ARMS2 risk alleles for individuals with category 3 or 4 AMD. Personalized use of the AREDS formulation based on genotype could maximize overall benefit.





HUMAN RESEARCH This study involves human research.

IRB Approval Status: Exempt from approval

9:21 AM

Do Anti-VEGF Injections Affect the Development of Neovascular AMD in Fellow Eyes? A Meta-analysis of Clinical Trials

- Robert L. Avery, MD
- Gabriel M Gordon, PhD

OBJECTIVE To determine if intravitreal injections of anti-VEGF can work systemically to affect development of disease in the other eye.

PURPOSE Anti-VEGF drugs pass into the bloodstream after intravitreal injection (IVI), and reduce circulating VEGF, but other systemic effects of these agents are controversial. The systemic exposure of ranibizumab after IVI is at least 10 fold less than bevacizumab or aflibercept, and the possibility of a lesser effect on development of AMD in fellow eyes was evaluated by meta-analysis of clinical trials.

METHODS Meta-analysis of prospective, randomized studies of anti-VEGF treatment of neovascular AMD in which the development of fellow eye neovascular AMD was evaluated. As pharmacokinetic studies have demonstrated ranibizumab to have much less systemic exposure following IVI than bevacizumab or aflibercept, it was considered the lower systemic exposure agent when compared to these agents, and the higher systemic exposure agent when compared to sham arms.

RESULTS Literature search revealed 3 studies of 5 trials (ANCHOR, MARINA, CATT, VIEW 1, VIEW 2) in which development of fellow eye nAMD was assessed. When comparing the arms with more systemic exposure to anti-VEGF agents to arms with less or no systemic exposure, a decreased risk of fellow eye nAMD was found with greater systemic anti-VEGF exposure, odds ratio 0.80 (0.66-0.97), p=0.02 (table 1).

CONCLUSION This study provides evidence of the biologic plausibility that following IVI, anti-VEGF agents escape the eye at concentrations sufficient to potentially have effects on distant organs, such as fellow eyes.

9:26 AM

The Cilioretinal Artery is Protective Against Choroidal Neovascularization in Age-Related Macular Degeneration

- Glenn C. Yiu, MD, PhD
- Kiersten R Snyder, MS
- Amirfarbod Yazdanyar, MD. , PhD.

OBJECTIVE To determine if the presence and location of a cilioretinal artery may affect the risk of developing advanced age-related macular degeneration (AMD) in the age-related eye disease study (AREDS).

PURPOSE A hemodynamic contribution to AMD pathogenesis has been proposed, but the role of retinal circulation has not been explored. We hypothesize that a cilioretinal artery may alter the oxygen tension in the central macula, and investigate a possible protective effect of a cilioretinal artery against progression to late AMD, including choroidal neovascularization (CNV) and/or geograhpic atrophy (GA).

METHODS Retrospective analysis of prospective, randomized, clinical trial data from 3647 AREDS participants. Fundus photographs of AREDS participants were reviewed by two masked graders for the presence or absence of a cilioretinal artery, and if any branch extend within 500mm of the center of the macula. Multivariate regressions were used to determine the association of the cilioretinal artery and vessel location, adjusted for age, sex, and smoking status, with the prevalence of choroidal neovascularization (CNV) or

central geographic atrophy (CGA), as well as AMD severity score, for eyes at randomization and progression at 5 years.

RESULTS Among AREDS participants, 26.9% of subjects had a cilioretinal artery in one eye, and 8.4% had the vessel bilaterally. Subjects with no cilioretinal arteries had a higher proportion of AMD category 4 (P = 0.02). At randomization, eyes with a cilioretinal artery had a lower prevalence of CNV (5.0% vs. 7.6%, OR 0.66, P = 0.001), but no difference in central GA (1.1% vs 0.8%, OR 1.33, P = 0.310). In eyes without late AMD, those with a cilioretinal artery also had a lower AMD severity score (3.00 Â± 2.35 vs. 3.19 Â± 2.40, P = 0.019). At 5 years, eyes at risk with a cilioretinal artery had lower rates of progression to CNV (4.1% vs 5.5%, OR 0.75, P = 0.050), but no difference in developing central GA (2.2% vs. 2.7%, OR 0.83, P = 0.354) or change in AMD severity score (+0.65 Â± 1.55 vs. +0.73 Â± 1.70, P = 0.112). In subjects with a unilateral cilioretinal artery, eyes with the vessel showed a lower prevalence of CNV than the fellow eyes (4.7% vs. 7.2%, P=0.012).

CONCLUSION The presence of a cilioretinal artery may be protective against the development of CNV, but not central GA. This finding suggests a hemodynamic contribution to neovascular AMD pathogenesis.

HUMAN RESEARCH This study involves human research.
IRB Approval Status: Exempt from approval

9:31 AM

Comparing Outcomes of Standard and Reduced-Fluence Photodynamic Therapy in the Treatment of Polypoidal Choroidal Vasculopathy

- Colin S Tan, MBBS, MMed (Ophth), FRCSEd (Ophth)
- WEI KIONG NGO, MBBS, MMED (Ophth)
- Tock Han Lim, MBBS, MMed (Ophth), FRCSEd

OBJECTIVE To compare the visual outcomes between Polypoidal Choroidal Vasculopathy treated with full-fluence and reduced-fluence photodynamic therapy.

PURPOSE The EVEREST II study reported favourable polyp closure in polypoidal choroidal vasculopathy (PCV) using standard-fluence Verteporfin photodynamic therapy (PDT). However, some suggest that reduced-fluence PDT may reduce complications. We aimed to compare the efficacy and safety between reduced-fluence and standard-fluence PDT in the treatment of PCV.

METHODS Review of all treatment-naive PCV cases treated with PDT from January 2011 to December 2013 at a tertiary ophthalmology center. Patients treated with reduced (light dose, 50 J/cm^2; dose rate, 600 mW/cm^2; wavelength, 689 nm; time, 42 seconds) and standard-duration (light dose, 50 J/cm^2; dose rate, 600 mW/cm^2; wavelength, 689 nm; time, 83 seconds) PDT were recruited for this study.

RESULTS Thirty-seven eyes of 37 patients with an average age of 69.9 years old (range 50 – 89 years, S.D. ± 8.9) were included. Of these, 29 (78.4%) were treated with standard-fluence PDT while 8 (21.6%) had reduced-fluence PDT. Patients treated using reduced-fluence PDT had better visual acuity (VA) outcomes when compared to standard-fluence PDT at 6 months (mean LogMAR 0.22 vs. 0.56) and 12 months (mean LogMAR 0.23 vs. 0.48). There was no difference between standard-fluence and reduced-fluence groups in terms of the number of rescue anti-vascular endothelial growth factor (VEGF) injections required subsequently (5.6 vs. 4.8). Time to quiescence in the standard-fluence group was shorter when compared to the reduced-fluence group (2.8 vs. 3.6 months). There was no statistical difference in recurrence of disease activity between the two groups (58.6% recurrence in standard-fluence group vs. 37.5% in reduced-fluence group). There were no significant adverse events reported in either group.

CONCLUSION Reduced-fluence PDT showed better VA outcomes while having comparable need for rescue anti-VEGF injections, recurrence rates and time to disease quiescent when analysed against standard-fluence PDT in the treatment of PCV.

HUMAN RESEARCH This study involves human research.
IRB Approval Status: Approved by institutional review board

9:46 AM

OCT Angiography (OCTA) Monitors the Influence of Different VEGF-I Drugs on a Specific CNVM

- Paul E. Tornambe, MD
- Nikolas JS London, MD
- Anne M. Hanneken, MD
- Lon S. Poliner, MD

OBJECTIVE To show how OCTA defines the effect of currently used VEGF-I on AMD CNVM's whch may determine the best VEGF-I for a specific CNVM, optimum treatment intervals, and when to stop treatment.

PURPOSE To report how weekly OCT Angiography can monitor the influence of three different monthly injections of VEGF Inhibitor Drugs on a recurrent choroidal neovascular membrane (CNVM) secondary to exudative age related macular degeneration.

METHODS Prospective case report which illustrates a potential new way to customize and manage eyes with exudative AMD. An 80 year old male treated for a decade for exudative macular degeneration was evaluated. The latest recurrence was treated monthly with a different VEGF Inhibitor (VEGFI) and evaluated weekly for 4 weeks with OCT angiography (OCTA). The order of monthly injections were Aflibercept, Ranibizumab, Bevicizumab, and Aflibercept.

RESULTS OCTA showed the effect, on the same CNVM, of Aflibercept, Ranibizumab, and Bevicizumab and then repeated Aflibercept. OCTA showed this specific CNVM is made up of VEGFI responsive and VEGFI non responsive components. OCTA showed re-perfusion of the responsive component preceded the development of sub retinal fluid and is an earlier marker for re-treatment than the development of fluid .
OCTA also showed the development of a new CNVM complex elsewhere on the previously inactive component of the CNVM. OCTA revealed and compared the time to re-perfusion among the different VEGF-I drugs and showed the active membrane re-perfused but did not grow. In this specific case, there was no difference in the response between Aflibercept and Ranibizumab. Bevicizumab showed the least effect on perfusion and re-accumulation of fluid, but visual acuity was not negatively affected by any of the drugs used.

CONCLUSION Weekly OCTA provides side by side analysis of how a specific VEGF-I affects a specific CNVM and serially compares how each drug affects or doesn't affect the CNVM complex. It provides a customized, safe, fast, non invasive method of how to manage CNVM's in AMD. It shows if some or part of the membrane is influenced by the VEGF-I providing information if treatment should be continued or stopped.

HUMAN RESEARCH This study involves human research.
IRB Approval Status: Exempt from approval

9:51 AM

Inflammation After Aflibercept Injection in Association With a Specific Brand of Syringe That Releases Silicone Oil Droplets: A Case-Control Study

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OBJECTIVE What might contribute to inflammation after Aflibercept intravitreal injection?

PURPOSE To determine factors causing inflammation after intravitreal aflibercept injections.

METHODS This retrospective case-control study included aflibercept-treated eyes with inflammation post-injection and aflibercept-treated control eyes. Medicals records were analyzed to identify possible factors contributing to the inflammation (age, gender, visual acuity, diagnosis, times to presentation/resolution, signs/symptoms, syringe brand, silicone oil droplets in the vitreous cavity, and others). Since the attending physicians usually agitated the syringes before injections, tests were performed to characterize the effects of two brands of syringes and the properties of particle aggregation of aflibercept and bevacizumab under steady-state and agitated conditions.

RESULTS Inflammation developed in six eyes from May to August 2016 (within 3 days post- injection in five of them). Three patients reported pain and had anterior chamber cells; five patients had vitreous cells. Oil droplets were seen in the vitreous in all cases. The inflammation resolved in all patients within 3 weeks; 83% had complete visual recovery. Saldanha Rodrigues (SR) syringes were used in all cases. Among controls, SR and Becton-Dickinson syringes were used in 10 and 17 eyes, respectively. Regression analysis (odds ratio, 21.66; 95% confidence interval, 1.10-425.06; P=0.043) showed an association between SR syringes and inflammation. Biophysical analyses primarily showed aggregation possibly from free oil droplets or protein-oil droplet interaction and aggregation.

CONCLUSION Post-injection inflammation might be associated with silicone oil droplets from SR syringes. Silicone oil droplets, especially after syringe agitation, might be instrumental in the inflammatory reaction.

HUMAN RESEARCH This study involves human research.
IRB Approval Status: Approved by institutional review board

9:59 AM

Prophylactic Ranibizumab for Exudative AMD in Vulnerable Eyes With Nonexudative AMD Trial (PREVENT): A Prospective Controlled Clinical Trial

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OBJECTIVE To prevent exudative AMD (Ex-AMD) using intravitreal ranibizumab (IVR) in eyes with non-exudative AMD (NE-AMD) in patients with history of Ex-AMD in their fellow eye.

PURPOSE To report baseline demographics and interim results of PREVENT for the purpose of preventing Ex-AMD using IVR in eyes with NE-AMD in patients with history of Ex-AMD in their fellow eye.

METHODS PREVENT is a multicenter, prospectively randomized, single-masked, controlled, interventional investigator sponsored phase I/II study of eyes with NE-AMD treated with IVR for prophylaxis of Ex-AMD. 100 eyes with NE-AMD in the study eye & history of Ex-AMD in the fellow eye are randomized (1:1) to sham injection (SHAM) or

0.5 mg IVR. Baseline ETDRS BCVA, IOP, exam, FP, AF, FA, SD-OCT tomography (Cirrus, Carl Zeiss Meditec) & genetic testing are obtained. Reading centers confirm same day diagnosis & OCT parameters. Patients return every 3 months for evaluation & treatment (IVR or Sham). The primary outcome measure is conversion to Ex-AMD confirmed by reading center.

RESULTS Eighty-four (84) eyes of 84 patients are reported in this interim analysis; 47 (56.0%) IVR, 37 (44.0%) SHAM. All patients are Caucasian, 47 female, mean age 78 and mean baseline BCVA 20/28 (78 ETDRS letters) and 20/31 (76 letters) at last visit (p=0.19). Baseline characteristics (age, gender, vision) were balanced between the two groups. Twenty-seven (27) patients completed the 2 year study, while 50 are actively enrolled. Seven (7) patients (3 IVR, 4 SHAM) withdrew early from the study; 2 opted out by choice (SHAM), 1 relocated (IVR) and 4 due to medical issues (2 SHAM). Thus far, 6 eyes have converted to Ex-AMD; 3 of 37 (8.1%) SHAM group (at 6, 1, 18 months) and 3 of 47 (6.4%) in IVR group (at 9, 9, 3 months); No statistically significant difference on Fisher's exact test. No ocular complications or adverse events were reported.

CONCLUSION Interim analysis of PREVENT suggests that prophylactic anti-VEGF therapy (IVR) is tolerated well, but may not prevent Ex-AMD. This topic warrants continued investigation as enrollment of this study is pending completion and a moderate level of attrition has occurred. Continued follow-up of this cohort should provide further insight into the role of prophylactic IVR.

HUMAN RESEARCH This study involves human research.
IRB Approval Status: Approved by institutional review board

10:04 AM

Endophthalmitis Rates After Bilateral Same Day Intravitreal Anti-VEGF Injections

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OBJECTIVE To evaluate practice patterns for bilateral same day intravitreal anti-VEGF injections and determine the rate of post-injection endophthalmitis.

PURPOSE Neovascular age-related macular degeneration and diabetic macular edema often require bilateral intravitreal anti-VEGF treatment. Practice patterns vary in performing bilateral same day intravitreal injections given concern for bilateral endophthalmitis. However, separate visits for bilateral treatment can significantly increase the visit burden for treatment of these chronic conditions.

METHODS The medical and billing records of a large academic private practice in Philadelphia, PA were electronically queried for all office visits during which bilateral intravitreal anti-VEGF injections were performed between April 1, 2012 and August 21, 2017. Demographic information, as well as indication for injection, were recorded for each patient and office visit. An additional query was done to identify all cases of endophthalmitis based on both ICD-9 or ICD-10 diagnosis codes, as well as procedure billing codes. Charts of patients with endophthalmitis were individually reviewed, and information was collected on presentation vision and clinical exam, culture data, and visual outcomes.

RESULTS During the study period, 104,372 bilateral same day intravitreal anti-VEGF injections were performed over 52,171 office visits for 6,009 patients. The mean (+/- standard deviation) age of patients in this cohort was 73.8 (14.4) years and 60.5% of patients were female. Of the 104,372 injections, 69,396 injections (66.5%) were performed for neovascular age related macular degeneration, while 28,096 injections (26.9%) were performed for diabetic macular edema. The most common anti-VEGF agent used was ranibizumab (55,051 injections), followed by aflibercept (32,542 injections) and bevacizumab (14,339 injections). Twenty-eight cases of endophthalmitis (0.027%) occurred during the study period. There were no cases of bilateral endophthalmitis, and no patients had more than one occurrence of endophthalmitis.

CONCLUSION In this large cohort of patients, there were no cases of bilateral endophthalmitis. Additionally, the overall rate of endophthalmitis was low and comparable to prior studies of unilateral injections.

HUMAN RESEARCH This study involves human research.
IRB Approval Status: Approved by institutional review board