Tuesday, July 24

8:00 AM

Treat-and-Extend Versus Bimonthly Dosing With Aflibercept for the Treatment of Diabetic Macular Edema, 1-Year Outcomes (EVADE Study)

- Dilsher S. Dhoot, MD

OBJECTIVE Is treat and extend (TE) dosing with intravitreal aflibercept injections (IAIs) a viable treatment option for diabetic macular edema patients compared with a fixed interval (FI) dosing?

PURPOSE To determine the benefits of a treat and extend (TE) regimen versus a fixed interval (FI) dosing regimen in subjects with diabetic macular edema (DME) receiving intravitreal aflibercept injections (IAIs).

METHODS Prospective trial of 50 eyes with DME randomized on a 1:1 ratio into a FI arm (N=25) or a TE arm (N=25). Eyes in the FI arm received 5 consecutive monthly injections of IAI followed by IAI every 8 weeks thereafter. Eyes in the TE arm received IAI as frequently as every 4 weeks and could be extended to a maximum of 16 weeks in the first year based on pre-determined visual acuity and OCT parameters. Main outcome measures included change in best-corrected visual acuity (BCVA), mean central retinal

thickness (CRT), percentage of eyes gaining/losing 3 lines of vision, and the mean number of injections received.

RESULTS At 1 year, the mean BCVA improved from 57 to 64 (7±9) and 61 to 74 (13±7) letters in the FI and TE groups, respectively (P=0.002, p<0.001); the BCVA in the TE arm was significantly more improved when compared to the FI arm (p=0.007). The percentage of patients gaining 3 lines of vision was 21.7% and 31.6% in the FI and TE groups, respectively (P=0.47). Mean CRT improved from 484 to 315 ï□m (169±147 ï□-m) in the FI arm and from 516 to 302 ï□m (214±81 ï□m) in the TE arm (both p<0.001). The TE arm showed significantly more visits (10.1 vs 8.8, p=0.02) and injections (9.9 vs 8.8, p=0.03) than the FI arm. In the TE arm, 5 subjects (28%) were maintained at 4 week intervals, 2 (11%) were reduced to 6 weeks, 3 (17%) remained at 8 weeks, 6 (33%) were increased to 10-weeks, none (0%) were increased to 12-weeks, 1 subject (6%) was increased to 14 weeks, and 1 subject (6%) was increased to 16-weeks. The incidence of APTC events was 2% and there were no cases of endophthalmitis.

CONCLUSION At 1 year, VA gains significantly favored the TE arm which also had increased number of injections and visits. Although both the FI and TE arms had similar anatomic outcomes at 1 year, the increased frequency of treatment when fluid recurred in the TE arm was associated with better visual outcomes than in the FI q 8 week arm of this small study. TE is a viable treatment option in some patients.

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

8:08 AM

2-Year Outcomes From Randomized Trials of Anti-VEGF Treatments for Diabetic Retinopathy (DR) and Diabetic Macular Edema (DME)

- Geeta A. Lalwani, MD
- Bann-mo Day, PhD
- Carlos Quezada-Ruiz, MD
- Lisa L. Tuomi, PharmD

OBJECTIVE To investigate and compare the safety and efficacy of approved/commonly used anti-VEGF therapies for DR in patients with DR and DME across 10 clinical trials.

PURPOSE Anti-VEGF therapies are currently used in the management of DR. To further inform the management of patients with DR and DME, we conducted an exploratory analysis to compare the effects of anti-VEGF agents in patients with DR and DME across large clinical trials of the FDA-approved agents ranibizumab (RBZ) and aflibercept (AFL), as well as bevacizumab (BVZ), which is often used off-label.

METHODS Study designs, baseline values, inclusion/exclusion criteria, primary end points, long-term vision and DR outcomes, and injection frequencies were compared retrospectively for Diabetic Retinopathy Clinical Research Network Protocol I, T, and S studies, RIDE (NCT00473382)/RISE (NCT00473330), RESOLVE, RESTORE, VIVID/VISTA, and BOLT across approved/commonly used doses and treatment regimens. The percentages of patients achieving a ≥ 2-step improvement in DR on the

Early Treatment Diabetic Retinopathy Study (ETDRS) DR Severity Scale (DRSS), changes in best-corrected visual acuity (BCVA), and safety outcomes, including Antiplatelet Trialists' Collaboration event rates, were assessed.

RESULTS At baseline, 21%–38% of eyes in Protocol I, Protocol T, and RIDE/RISE had mild to high-risk proliferative DR (PDR) (DRSS 60–75) vs 2%–5% of eyes in VIVID/VISTA and BOLT. In Protocol S, which included patients with and without DME, 87% of eyes had PDR at baseline. At 2 years, RBZ 0.3–0.5 mg and AFL 2.0 mg produced similar improvements in DRSS (21%–47% of patients with ≥ 2-step improvement). Baseline BCVA varied between 55 and 65 ETDRS letters (RIDE/RISE, VIVID/VISTA, Protocol I, RESTORE, Protocol T), and mean BCVA change at 2 years ranged from +7 to +13 ETDRS letters. Cardiovascular safety exclusion criteria varied across trials. At 2 years, Antiplatelet Trialists' Collaboration event rates were low but varied across trials and treatments (4.2%–13% for sham/laser, 8% for BVZ, 5%–7.2% for AFL 2.0 mg, 2.4%–12% for RBZ 0.3–0.5 mg).

CONCLUSION At 2 years, DR outcomes were comparable for RBZ and AFL in patients with DR and DME. Antiplatelet Trialists' Collaboration arterial thromboembolic event rates were generally low across trials. However, due to the limitations of cross-trial comparisons, these findings should be interpreted with caution.

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

8:16 AM

Effect of Adding Dexamethasone to Continued Ranibizumab Treatment in Patients With Persistent Diabetic Macular Edema

- Raj K. Maturi, MD

OBJECTIVE To compare continued intravitreous ranibizumab vs ranibizumab plus intravitreous dexamethasone implant in eyes with persistent diabetic macular edema.

PURPOSE Edema and vision loss persist in some eyes despite anti-vascular endothelial growth factor (anti-VEGF) therapy for diabetic macular edema (DME). Thus additional treatments are needed for eyes with suboptimal response to anti-VEGF therapy. It was hypothesized that better outcomes may be achieved by adding intravitreous corticosteroids to the treatment regimen than continued anti-VEGF therapy alone.

METHODS 236 eyes (from 203 adults) that had persistent DME with visual acuity 20/32-20/320 following at least 3 prior anti-VEGF injections were enrolled in a Phase 2 multicenter randomized clinical trial. After receiving 3 monthly 0.3-mg ranibizumab injections in a run-in phase, 129 eyes (from 116 adults) that met the randomization criteria were randomly assigned to receive 700-µg dexamethasone ("combination group", n=65) or sham treatment ("ranibizumab group", n=64) in addition to continued

0.3-mg ranibizumab as often as every 4 weeks in both arms based on a structured re-treatment protocol. The primary outcome was change in best-corrected E-ETDRS visual acuity from randomization to 24-week visit.

RESULTS Both treatment groups on average improved 3 letters in visual acuity during the run-in phase. At 24 weeks, mean visual acuity letter score was 66 (Snellen equivalent, 20/50) in both groups. Mean improvement in visual acuity from randomization was similar in both groups, and was approximately 3 additional letters. Mean reduction in central subfield thickness from randomization measured on optical coherence tomography was -110±86 μm in the combination group and -62±97 μm in the ranibizumab group (adjusted difference = -52 μm; 95% CI, -82 to -22; P<0.001). Subgroup analysis for baseline lens status, visual acuity and OCT thickness changes during the run-in phase will be reviewed. In the combination group, 19 eyes (29%) experienced increased intraocular pressure (IOP) or initiated IOP-lowering treatment compared with 0 in the ranibizumab group (P<0.001).

CONCLUSION Among eyes with persistent DME following multiple anti-VEGF injections, the addition of dexamethasone to continued ranibizumab injections does not improve visual acuity at 24 weeks more than ranibizumab therapy alone, although a greater reduction in retinal thickness was observed in the combination group. Increases in intraocular pressure were more common in eyes receiving dexamethasone treatment.

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

8:24 AM

Prospective Evaluation of Pain and Inflammation Following Injection of Aflibercept or Ranibizumab in Patients With Diabetic Macular Edema: SOLAR Study

- Nikolas JS London, MD
- Arshad M. Khanani, MD
- Greggory Gahn, BS
- Gregory Cohen, MD
- Lauren Hill, BA, MS

OBJECTIVE This randomized, prospective clinical trial evaluated eye pain and intraocular inflammation following intravitreal injection of aflibercept or ranibizumab in patients with diabetic macular edema.

PURPOSE To compare intraocular inflammation and eye pain within the first 7 days following an intravitreal (IVT) injection of either aflibercept (AFL) or ranibizumab (RBZ) in patients with diabetic macular edema (DME).

METHODS Patients with DME (treatment naïve or no IVT within 90 days), with best correct visual acuity (BCVA) of 20/400 or better and no history of uveitis, were randomized to receive either AFL 2.0 mg or RBZ 0.3 mg. A non-injecting ophthalmologist (GC), masked to treatment allocation, evaluated patients at baseline, at visit 1 (24-48 h post injection) and at visit 2 (5-7 days post injection). Anterior chamber inflammation (ACI) was graded using the Standardization of Uveitis Nomenclature working group classifications. Vitreous inflammation (VI) was defined as the presence

of vitreous cells on a graded scale from 0 to 4. Pain was assessed using a standard script and quantified on a scale of 0 to 10.

RESULTS 100 patients were enrolled. 50 received RBZ and 50 received AFL. Patients in each group had similar baseline characteristics, with 61% being male, a mean age of 64.1 years, and a mean BCVA of 70.8 letters. 6 RBZ patients (12%) and 10 AFL patients (20%) had ACI at visit 1 (p=0.41). At visit 2,1 patient (2%) in the RBZ group and 3 patients (6%) in the AFL group had ACI (p=0.62). VI was minimal at both visits, with 2 RBZ patients (4%) and 3 AFL patients (6%) at visit 1 and 0 RBZ patients and 2 AFL patients (4%) at visit 2 experiencing VI. Absence of pain was similar between groups at visit 1, with 22 subjects (44%) in each group experiencing no pain. At visit 1, 9 patients (18%) in the AFL group had severe pain compared to 7 patients (14%) in the RBZ (p=0.83). At visit 2, 40 patients (80%) in the RBZ group experienced no pain compared with 45 patients (90%) in the AFL group, while 3 patients (6%) in the AFL group and 2 patients (4%) in the RBZ group had severe pain (p=0.14).

CONCLUSION ACI occurred more often in patients receiving AFL compared to RBZ, though this difference was not statistically significant. Absence of pain at visit 1 was comparable between RBZ and AFL. These findings suggest that AFL treated eyes may be more likely to have post injection inflammation. Further studies with larger sample sizes will be necessary to verify this observation.

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

8:36 AM

Randomized, Prospective, Double-Masked, Controlled Phase 2b Trial to Evaluate the Safety and Efficacy of ALG-1001 (LUMINATE®) in Diabetic Macular Edema

- Peter K. Kaiser, MD
- David S. Boyer, MD
- Baruch D. Kuppermann, MD, PhD
- Jeffrey S. Heier, MD
- Peter A. Campochiaro, MD
- Julia Kornfield, PhD
- Hugo Quiroz-Mercado, MD
- Vicken Karageozian
- Hampar L Karageozian, Parm.D, MSC, MBA
- John Park, PhD
- Lisa Karageozian, MBA
- Melvin Sarayba, MD

OBJECTIVE To report the Phase 2b, 5-month results of DEL MAR clinical trial using ALG-1001 1.0 mg and 0.5 mg as sequential and in combination therapy in patients with centrally-involved diabetic macular edema.

PURPOSE Currently, there is only one predominant treatment paradigm for diabetic macular edema (DME): anti-VEGF agent as first line, followed by corticosteroids as second line. We performed a double-masked, placebo-controlled, randomized multi-center phase 2b trial to evaluate the safety & efficacy of ALG-1001, a novel first-in-class integrin inhibitor, as compared to bevacizumab in DME.

METHODS We previously reported a successful study on ALG-1001 used as monotherapy. In this study, we evaluate its use in sequential or combination therapy with anti-VEGF. 80 subjects were randomized to 5 treatment groups: 1.25 mg bevacizumab control arm

of 5 monthly injections (Group 1); single treatment of 1.25 mg bevacizumab at week 0 followed by three ALG-1001 injections (1.0 mg or 0.5 mg) at weeks 1, 4 and 8 (Groups 2 & 3); ALG-1001 (1.0 mg or 0.5 mg) given in direct combination with bevacizumab 1.25 mg at weeks 1, 4 and 8 (Groups 4 & 5). Efficacy outcomes were change from baseline in BCVA and OCT CMT at week 20.

RESULTS The per protocol population included 65 subjects. 1.0 mg ALG-1001 in sequential therapy demonstrated the best efficacy among the ALG-1001 groups. Mean change in BCVA was 6.7 letters for 1.25 mg bevacizumab and 7.1 for 1.0 mg ALG-1001 in sequential therapy. BCVA improved earlier than CMT, suggesting a new mechanism of action unlike anti-VEGF. Sub-group analysis shows that subjects with prior anti-VEGF treatment had poorer response to bevacizumab (8.3 max letters gain) compared to ALG-1001 (13.8 max letters gain). There were no drug related SAEs in ALG-1001 groups.

CONCLUSION Primary endpoint of non-inferiority in BCVA was met with sequential dosing of a single bevacizumab treatment plus 3 doses of 1.0 mg ALG-1001 vs 6 doses of 1.25 mg bevacizumab (≤3 letters difference) at week 20. ALG-1001 showed 12-week durability in all study subjects in sequential therapy arms.

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

8:44 AM

Combination Therapy With Intravitreal Nesvacumab+Aflibercept in Diabetic Macular Edema: The Phase 2 RUBY Trial

- Jeffrey S. Heier, MD

OBJECTIVE To evaluate if a combination of an Ang-2 blocker and an anti-VEGF agent offers additional anatomic or visual acuity benefits over anti-VEGF monotherapy in diabetic macular edema.

PURPOSE To evaluate if a combination of an intravitreal Ang-2 blocker (nesvacumab) and a potent anti-VEGF (aflibercept) offered additional anatomic or visual acuity benefits over monotherapy with intravitreal aflibercept injection (IAI) in patients (pts) with diabetic macular edema (DME).

METHODS RUBY was a double-masked, active-controlled, multicenter, phase 2 study randomizing 302 pts with DME in a 1:2:3 ratio to receive low dose combination (LD combo; nesvacumab+aflibercept 3 mg:2 mg), high dose combination (HD combo; nesvacumab+aflibercept 6 mg:2 mg) or IAI 2 mg monthly through week (wk) 12 following which pts receiving LD combo were treated q8 wks; pts receiving HD combo were re-randomized to treatment q8 or q12 wks; pts receiving IAI were re-randomized to IAI q8 or q12 wks or HD combo q8 wks. The primary outcome was change from baseline in best-corrected visual acuity (BCVA) at wks 12 and 36 as measured by the Early Treatment Diabetic Retinopathy Study (ETDRS) letter score.

RESULTS LD combo and HD Combo did not provide further visual gains over IAI (least-square (LS) mean gain of 6.6 and 8.7 vs 8.7 letters at wk 12). Anatomically, HD combo reduced CRT significantly more than IAI at wk 12 (LS mean CRT change of -191.6 vs -163.8 μm; *P*=0.0183). Proportion of pts who achieved CRT ≤300 μm at wk 12 was significantly higher with HD combo than with IAI (57.6% vs 35.3%; *P*=0.0006). Proportions of pts who achieved complete resolution of fluid at wk 12 was significantly higher with HD combo than with IAI (66.3% vs 53.7%; *P*=0.0489). Proportions of pts with ≥2-step improvement in DRSS score at wk 12 were 21.3% and 15.2% with HD combo and IAI, respectively (*p*=0.2268). Corresponding proportions among pts with DRSS score ≥47 at baseline were 30.2% and 22.0% (*P*=0.2526), and among those with DRSS score ≥53 at baseline were 48.4% and 34.0% at wk 12, respectively. Similar visual and anatomic results were observed at wk 36. There were no new safety signals.

CONCLUSION The results from the phase 2 RUBY study showed anatomic benefits primarily with combo HD Ang-2 blockade with aflibercept but similar visual results with both LD combo and HD combo compared to monotherapy with IAI in treatment of pts with DME.

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

8:52 AM

Anti-VEGF/Anti-Angiopoietin-2 Bispecific Antibody RG7716 in Diabetic Macular Edema: 36-Week Results From the Phase 2 BOULEVARD Clinical Trial

- Rishi P. Singh, MD
- Jayashree Sahni, MBBS, FRCOphth, PhD
- Shamil Sadikhov
- Meike Pauly-Evers, PhD
- Piotr Szczesny, MD PhD
- Robert Weikert

OBJECTIVE To investigate the safety and efficacy of the novel anti-vascular endothelial growth factor/anti-angiopoietin-2 bispecific antibody RG7716 for the treatment of diabetic macular edema.

PURPOSE RG7716 is a novel bispecific, monoclonal antibody that simultaneously binds and inactivates vascular endothelial growth factor A (VEGF-A) and angiopoietin-2 (Ang-2). The phase 2 BOULEVARD study compared the efficacy and safety of RG7716 with ranibizumab (RBZ) in treatment-naïve and previously treated patients (pts) with diabetic macular edema (DME).

METHODS BOULEVARD (NCT02699450) is an ongoing prospective, randomized, comparator-controlled, double-masked, phase 2 study. The trial enrolled anti-VEGF-treatment naïve pts and pts previously treated with anti-VEGF, aged ≥ 18 years, with

center-involving DME, best-corrected visual acuity (BCVA) between 73 and 24 ETDRS letters, and central subfield thickness of ≥ 325 μm. Pts were randomized 1:1:1 to receive intravitreal RG7716 6.0 mg, RG7716 1.5 mg, or RBZ 0.3 mg. All pts were dosed monthly (28 days ± 7 days) for 20 weeks. Pts were then observed monthly for up to 16 weeks, for a total study length of 36 wks. The primary endpoint was mean change in BCVA from baseline to week 24 in treatment-naïve pts.

RESULTS The study is ongoing at the time of abstract submission and by the time of presentation at the ASRS annual meeting, complete week 36 data will be available forall pts. Demographics, baseline characteristics, safety, visual and anatomic outcomes, and time to re-treatment data will be presented for all pts.

CONCLUSION Safety and efficacy outcomes through week 36, including visual and anatomic measures, from the phase 2 BOULEVARD study comparing RBZ anti-VEGF monotherapy to dual VEGF/Ang-2 inhibition with the bispecific RG7716 antibody will be presented during the congress.

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

9:06 AM

Reduction in the Frequency of Diabetic Macular Edema (DME) Therapies Post-0.2 µg/Day Fluocinolone Acetonide (FAc) Implant Treatment Results

- Sam E. Mansour, MD, MSc,FACS, FRCS(C)

OBJECTIVE To assess the effect of the continuous release FAc on frequency of DME treatments based on real world data from the PALADIN Phase IV study and the US Retrospective Chart Review (USER).

PURPOSE Two independent studies were conducted to evaluate the effect of FAc implantation on the frequency of DME treatments based on pre- and post-treatment data with up to 36 months (mo) of pre-FAc treatment data available. Both studies were designed to assess the safety and effectiveness of the sustained release 0.2 µg/day FAc implant when administered based on the US indication.

METHODS Patients in both PALADIN and USER were diagnosed with DME and received treatment with the 0.2 µg/day FAc implant based on the US indication. Patients were followed post FAc for ≥12 months for each study. Treatment (T_x) frequency was calculated as the reciprocal of the mean number of treatments per month. Patient subgroups were analyzed to determine the effect of baseline visual acuity (VA) on

treatment frequency pre- and post-0.2 μg/day FAc implant administration. In addition to post-FAc treatment findings, each of these studies included up to 36 months of pre-FAc outcomes related to functional/anatomic changes, DME treatments, and safety data for analysis.

RESULTS Pre-FAc, eyes received ~1 T_x every (q) 2–4 mo irrespective of baseline VA. Post-FAc, 53% and 63% of eyes did not require further DME treatments in PALADIN and USER respectively. Significant differences in DME treatment frequency were observed pre- and post-FAc in the PALADIN trial (1 T_x q 3.7 mo vs 1 T_x q 7.9 mo, P<0.001) and USER study (1 T_x q 2.9 mo vs 1 T_x q 14.3 mo, P<0.001). VA remained stable post-FAc in eyes with better baseline VA (≥20/40) with reduction in DME treatment frequency for both studies (PALADIN: 1 T_x q 3.4 mo vs 1 T_x q 10.2 mo, P<0.001; USER: 1 T_x q 2.9 months vs 1 T_x q 22.0 mo, P<0.001). Eyes with worse VA (<20/40) pre-FAc achieved improvements in VA with significantly fewer injections post-FAc (PALADIN: 1 T_x q 4.0 mo vs 1 T_x q 6.9 mo P<0.001; USER: 1 T_x q 2.9 mo vs 1 T_x q 10.6 mo, P<0.001).

CONCLUSION Adjunctive DME treatment frequency was significantly reduced post-FAc compared to pre-FAc implant. Data from PALADIN and USER support reduced DME treatment burden irrespective of VA at time of FAc treatment. Optimization of additional DME therapies can be tailored with the FAc implant according to baseline VA.

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

9:14 AM

Advanced Image Analysis and Machine-Learning Assessment of the Impact of Aflibercept on Anatomic Feature and Flow Dynamics in the PERMEATE Study

- Justis P. Ehlers, MD
- Natalia Albuquerque Lucena de Figueiredo, MD
- Prateek Prasanna, PhD
- Ming Hu, Ph.D.
- Sunil Srivastava, MD
- Sumit Sharma, MD
- Rishi P. Singh, MD
- Aleksandra V. Rachitskaya, MD
- Atsuro Uchida, MD
- Jamie Reese, RN
- Soumya Ghose
- Anant Madabhushi, PhD

OBJECTIVE To utilize higher order image assessment and machine-learning to evaluate anatomic and retinal vascular dynamics in retinal vascular disease following therapy with intravitreal aflibercept.

PURPOSE Higher order assessment of the impact of anti-VEGF therapy on retinal vascular dynamics, outer retinal integrity, and quantitative fluid parameters may provide unique insights into potential imaging biomarkers. The purpose of this study is to assess the impact of intravitreal aflibercept injection (IAI) on these imaging features in diabetic macular edema (DME) or retinal vein occlusion (RVO).

METHODS PERMEATE is a prospective study for treatment-naïve eyes with foveal-involving edema secondary to DME or RVO utilizing monthly IAI 2 mg for the initial 6

months. A novel ellipsoid zone (EZ) and retinal fluid mapping tool was utilized for SD-OCT assessment. Quantitative metrics included macular EZ-RPE volume and *en face* percentage of EZ attenuation. In addition, volumetric assessment of retinal fluid was performed. OCT angiography (OCTA) perfusion density analysis was utilized on the 3-mm superficial and deep retinal plexus scans. All imaging was analyzed for baseline and 6 month visits. Machine learning data assessment was utilized to explore complex feature associations.

RESULTS Twenty-three eyes were included in this 6-month interim analysis. A mean gain of 17.3 letters ($p<0.001$) was achieved. A dramatic 55% reduction in retinal central subfield thickness was noted ($p<0.001$). EZ analysis demonstrated a significant increase in EZ-RPE volume (+10%, $p=0.02$) and EZ-RPE mean CST (+65%, $p<0.001$). Macular percentage of partial and total EZ attenuation improved significantly at 6-months (-82% and -85%, respectively, $p<0.02$). IAI therapy resulted in a 94% reduction of intraretinal fluid volume at 6 months ($p<0.001$). Retinal perfusion density analysis demonstrated a 9% improvement in the superficial retinal plexus ($p=0.01$). In the RVO subgroup, changes in the foveal superficial plexus directly correlated with visual acuity change ($p=0.03$). EZ integrity parameters demonstrated significant correlation with 6-month visual acuity ($p<0.0001$). Machine-learning analysis identified baseline retinal thickness as the strongest predictor of visual acuity improvement.

CONCLUSION Improvement in outer retinal integrity parameters, quantitative fluid burden, and OCTA-based retinal perfusion at 6 months was demonstrated following IAI therapy. Ongoing research includes quantitative angiographic assessment and integrative analysis of imaging parameters to better understand the role of these potential imaging biomarkers in assessing disease prognosis and therapeutic response.

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

9:19 AM

A Model to Predict the 3-Year Risk of Needing Treatment for Diabetic Macular Edema

- Bobeck S Modjtahedi, MD
- Yunxun Wang, M.Sc.
- Tiffany Q. Luong, MPH
- Donald S Fong, MD, MPH

OBJECTIVE To create a model to predict which patients will require treatment for diabetic macular edema in the next three years.

PURPOSE Diabetic macular edema (DME) is a significant cause of visual morbidity. The ability to predict who will require anti-vascular endothelial growth factor (anti-VEGF) treatment for DME could allow for earlier and more aggressive control of systemic risk factors as well as closer ophthalmic monitoring and possibly earlier treatment in high risk patients.

METHODS Diabetic patients ≥ 18 years old without baseline severe retinopathy or a prior history of DME and with at least three years of follow-up were included in this retrospective analysis. IRB approval was attained. 124,155 patients met inclusion criteria. Age, sex, race, BMI, HgA1c, years of diabetes (YD), GFR, lipid levels, smoking status, baseline degree of retinopathy on fundus photos, as well as history of hypertension, dialysis, sleep apnea, CHF, CVA, insulin use, ACE or ARB use, and glitazone use were included in a model utilizing multiple Cox regressions to identify which combinations of factors were associated with the need for anti-VEGF for DME within three years.

RESULTS Of 124,155 patients, 673 received anti-VEGF for DME within three years. The three-year risk of DME requiring treatment could be estimated from the combination of age, BMI, HgA1c, YD, GFR, degree of baseline retinopathy, history of CHF, insulin use, and glitazone use with the following equation: $2.72^{(0.026\times age + 4.61\times 1/\sqrt{(YD * BMI/100)} + \log_e (YD*BMI/100) + 0.26\times HgA1c - 0.0088\times GFR + 0.59\times insulin\ use + 0.59\times glitazone\ use + 0.41\times history\ of\ CHF + adjustment\ factor\ for\ degree\ of\ baseline\ retinopathy)}$ where history of insulin use, glitazone use, and CHF is represented by 0 or 1. Based on this model patients could be stratified into a high-risk group which was 587% more likely to require DME treatment over three years (HR 5.87, 95% CI 4.89-7.04), if they had these characteristics: age ≥68 years old AND BMI ≥28.5 AND HgA1c ≥8.4 AND ≥10.6 years of diabetes AND GFR ≤67 AND baseline mild or moderate retinopathy AND a history of CHF AND a history of insulin use AND a history of glitazone use.

CONCLUSION The three-year risk of DME requiring treatment can be calculated with the above equation. Predication models can be integrated into electronic medical records to identify patients at high risk for DME. These patients may benefit from earlier and more aggressive management of their systemic risk factors as well as their ocular disease.

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

9:24 AM

Outcomes of Intravitreal Antivascular Endothelial Growth Factor (VEGF) Therapy for Diabetic Macular Edema in Routine Clinical Practice

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

OBJECTIVE To assess outcomes of patients with diabetic macular edema following treatment with intravitreal anti-VEGF agents in routine clinical practice.

PURPOSE To evaluate outcomes in diabetic macular edema (DME) 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 DME 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 3028 patients with DME, 1303 (43%) patients received ≤6 injections and 1725 (57%) patients received ≥7 injections through 1 year. Corresponding baseline mean VA was 71 and 70 letters, respectively. In the subgroup of patients who received ≤6 injections, 29% of the patients presented with VA of ≥20/40; 50% with VA of <20/40-20/100 11% with VA of <20/100-20/200, and 10% with VA of <20/200 at baseline. Corresponding proportions of patients in the subgroup receiving ≥7 injections were 25%, 51%, 12%, and 12%, respectively.The mean number of injections in patients receiving ≤6 injections was 4.0 with a mean VA gain of 3.7 letters. In patients receiving ≥7 injections, the mean number of injections was 9.1 with a mean VA gain of 8.1 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 DME compared to those who received fewer injections.

9:29 AM

2 Real-World Analyses of Treatment Burden Associated With Intravitreal Injections for DME Prior to 0.2 µg/Day Fluocinolone Acetonide (FAc)

- Nancy M. Holekamp, MD

OBJECTIVE To look at the pre-ILUVIEN treatment burden associated with the management of DME in two real world studies, USER and PALADIN.

PURPOSE These analyses of DME treatment burden focus on the time prior to 0.2 µg/day fluocinolone acetonide (FAc) implantation. Other studies of real world anti-VEGF treatment demonstrate less frequent dosing compared to randomized clinical trials.

METHODS The PALADIN study collected real-world data on treatment frequency and outcomes up to 36 months pre-FAc implantation in 153 DME patients for a total of 201 eyes. The USER study collected real world data on treatment frequency and outcomes for up to 36 months pre-FAc implant in 130 DME patients for a total of 160 eyes. Treatment burden was evaluated by baseline visual acuity subgroups (20/40 or better, <20/40-20/100, <20/100-20/200, <20/200) to compare differences in treatment frequency by severity of visual acuity deficit.

RESULTS In PALADIN (N=201 eyes), treatment frequency averaged 1 treatment every 3.35 months in the period prior to 0.2 µg/day FAc for all patients (mean follow up 23.4 months). In USER (N=160 eyes), treatment frequency averaged 1 treatment every 2.9 months prior to 0.2 µg/day FAc for all patients (mean follow up 30.1 months). When visual acuity was assessed at the time of FAc treatment, no significant differences in pre-FAc treatment frequency were observed. PALADIN 20/40 or better: = 1 Tx every 3.03

months (N = 74) <20/40 to 20/100: = 1 TX every 3.50 (N = 88) <20/100 to 20/200: Pre = 1 Tx every 4.33 (N = 18) Worse than 20/200: Pre = 1 Tx every 3.12 (N = 12) USER 20/40 or better: = 1 Tx every 2.9 months (N = 67) <20/40 to 20/100: = 1 TX every 3.2 (N = 61) <20/100 to 20/200: Pre = 1 Tx every 2.3 (N = 20) Worse than 20/200: Pre = 1 Tx every 2.9 (N = 12) Patients received on average 1 treatment every 3 months prior to 0.2 μg/day FAc.

CONCLUSION In this study we show the extended treatment burden in selected DME patients over time and continued low treatment frequency, mirroring real world data from Kiss (2016) where patients received 1 intravitreal anti-VEGF injection every 3 months over 1 year. Intensive treatment schedules for DME patients are challenging to maintain long-term and may be optimized by long-term drug delivery

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