10/9/2021 10:05AM

Efficacy, Safety, and Durability of Faricimab in Diabetic Macular Edema (DME): One-Year Results From the Phase 3 YOSEMITE and RHINE Trials

- Caroline Baumal, MD
- Jeffrey R Willis, MD/PhD
- Zdenka Haskova, MD, PhD
- Anthony P Adamis, MD
- Jane Ives, MSc
- Francis Abreu, PhD
- Karen Basu, PhD
- Hugh S. Lin, MD

OBJECTIVE To evaluate the efficacy, safety, and durability of faricimab, a dual angiopoietin (Ang)-2 and VEGF-A inhibitor, in treatment-naïve and previously anti-VEGF–treated patients with DME.

PURPOSE Faricimab is a novel bispecific antibody designed to inhibit both Ang-2 and VEGF-A, reduce vascular leakage and inflammation, promote vascular stability, and improve outcomes beyond anti-VEGF monotherapy for DME. The phase 3 YOSEMITE (NCT03622580) and RHINE (NCT03622593) trials aim to assess the efficacy, safety, and durability of intravitreal faricimab versus aflibercept in patients with DME.

METHODS YOSEMITE and RHINE are randomized, double-masked, 100-week, active comparator–controlled trials of faricimab in patients with center-involving DME. Patients were randomized 1:1:1 to faricimab 6.0 mg Q8W after 6 Q4W doses, faricimab 6.0 mg per personalized treatment interval (PTI) after 4 Q4W doses, or aflibercept 2.0 mg Q8W after 5 Q4W doses (Figure 1). The PTI algorithm is a protocol-driven regimen based on treat-and-extend, with intervals adjusted (Q4W up to Q16W) based on CST and BCVA change at active dosing visits. The primary endpoint was mean change in BCVA from baseline at 1 year, averaged over weeks 48, 52, and 56. Other efficacy and safety endpoints were

assessed Q4W throughout.

RESULTS In total, 1891 patients were enrolled in YOSEMITE (N = 940) and RHINE (N = 951). Baseline characteristics were balanced across arms. The primary endpoint was met; mean 1-year BCVA gains with faricimab Q8W (10.7 and 11.8 letters in YOSEMITE and RHINE) or faricimab PTI (11.6 and 10.8 letters) were noninferior to aflibercept Q8W (10.9 and 10.3 letters). In treatment-naïve patients, 1-year BCVA gains were consistent with the ITT population and no faricimab arm showed superiority to aflibercept. Change in CST, absence of protocol-defined DME (CST < 325 µm), and absence of intraretinal fluid over 1 year consistently favored faricimab over aflibercept. Notably, 52.8% (YOSEMITE) and 51.0% (RHINE) of the faricimab PTI arm achieved Q16W dosing at week 52, and 73.8% and 71.1%, respectively, achieved ≥ Q12W dosing (Figure 2). Faricimab was well tolerated; intraocular inflammation event rates for faricimab were low (1.3% on average) and no cases of vasculitis or occlusive retinitis were reported.

CONCLUSION Faricimab administered Q8W or per PTI up to Q16W offered noninferior vision gains compared with aflibercept Q8W, while demonstrating improvements in anatomic endpoints and the potential for extended (up to Q16W) dosing at 1 year.

IRB APPROVAL Yes — *IRB Approval Letter may be requested*.

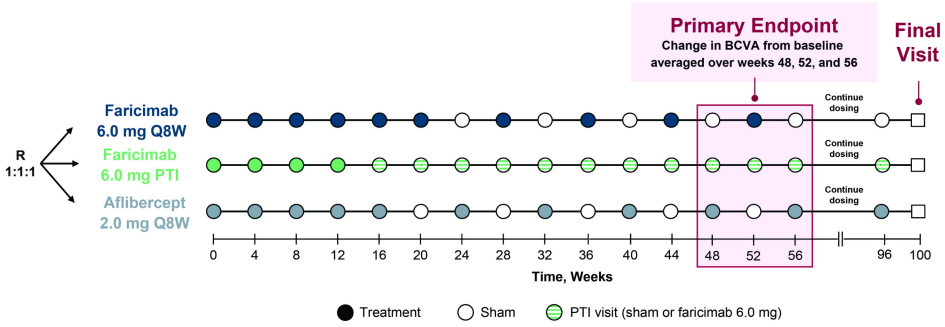


Figure 1. YOSEMITE and RHINE trial design. BCVA, best-corrected visual acuity; PTI, personalized treatment interval; Q8W, every 8 weeks; R, randomization.

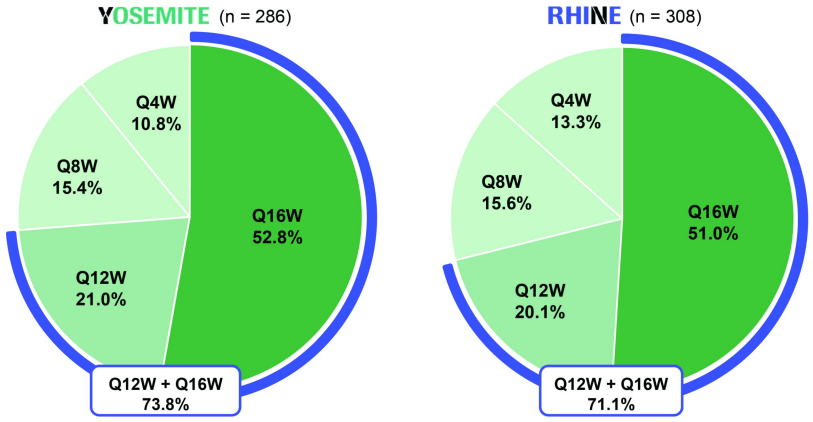


Figure 2. Proportion of patients in the faricimab PTI arm receiving Q4W, Q8W, Q12W, or Q16W dosing at week 52 of YOSEMITE (left) and RHINE (right). Analyses included patients with evaluable data at the week 52 study visit. PTI, personalized treatment interval; Q4W, every 4 weeks; Q8W, every 8 weeks; Q12W, every 12 weeks; Q16W, every 16 weeks.

10/9/2021 10:11AM

Brolucizumab for the Treatment of Visual Impairment Due to Diabetic Macular Edema: 52-Week Results From the KESTREL and KITE Studies

- David M. Brown, MD
- Sebastian Wolf, MD PhD
- Justus Garweg, MD, PhD
- francesco bandello
- Andres Emanuelli, MD
- Jose Juan Escobar, MD
- Joao Figueira
- Vishali Gupta, MD
- NorFariza Ngah, MBBS, MS(OPH)
- Gerald Liew
- Raman Tuli, MDCM FRCSC
- Lixin Wang, MD., PhD
- Ying Wang
- Emmanuel Bouillaud
- Eric Souied, Dr

OBJECTIVE To evaluate the efficacy and safety of brolucizumab in diabetic macular edema.

PURPOSE Presentation of the 52-week results from KESTREL (NCT03481634) and KITE (NCT03481660), two prospective Phase III studies evaluating the efficacy and safety of brolucizumab (BRO) versus aflibercept (AFL) for the treatment of patients with visual impairment due to diabetic macular edema (DME).

METHODS KESTREL and KITE are two 2-year, ongoing, double-masked, randomized, active-controlled, multicenter studies. In KESTREL, patients were randomized 1:1:1 to BRO 3mg, BRO 6mg or AFL 2mg; in KITE, the randomization was 1:1 to BRO 6mg and AFL 2mg. The BRO groups received 5 loading doses every 6 weeks (q6w) followed by q12w dosing in Year 1, with an option to adjust to q8w at predefined disease activity assessment visits. The AFL group received 5 loading doses monthly followed by fixed q8w dosing. The primary endpoint was the change from baseline in BCVA at Week 52; secondary endpoints included

the proportion of BRO patients maintained at q12w dosing up to Week 52 and change from baseline in CSFT.

RESULTS In both KESTREL and KITE, the primary endpoint was met with BRO 6mg achieving non-inferiority to AFL 2mg in change of BCVA from baseline at Week 52. More than 50% of BRO 6mg patients were maintained on a q12w dosing interval through Week 52, following the loading phase in both studies. In KITE, BRO 6mg showed superior improvements versus AFL 2mg in change of CSFT from baseline over the period of Week 40 through Week 52; in KESTREL a significant improvement with BRO 6mg in change of CSFT from baseline over the period of Week 40 through Week 52 was observed. BRO 3mg did not demonstrate non-inferiority in BCVA versus AFL 2mg in KESTREL. Brolucizumab demonstrated an overall well-tolerated safety profile in both studies with no new safety signals.

CONCLUSION In the KESTREL and KITE studies, brolucizumab offered robust vision gains and improved anatomical outcomes with more than 50% of DME patients maintained on a q12w treatment interval after loading through Week 52, and demonstrated an overall well-tolerated safety profile.

IRB APPROVAL Yes — *IRB Approval Letter may be requested*.

10/9/2021 10:17AM

Intravitreal Gene Therapy for Diabetic Macular Edema With ADVM-022: First-Time Data Presentation of Prospective, Randomized Phase 2 INFINITY Trial

- Charles C Wykoff, MD, PhD, FASRS
- Andres Emanuelli, MD
- Mark R. Barakat, MD
- Arshad M. Khanani, MD, MA, FASRS
- David S. Boyer, MD
- Carol Hoang, PharmD, MBA
- Hersh Patel
- Carol Chung, PhD
- Adam Turpcu, PhD
- Aaron Osborne, MBBS, MRCOphth
- Julie Clark, MD, MS

OBJECTIVE A double-masked, multicenter, randomized, active control clinical trial to assess the safety, efficacy and durability of a novel intravitreal anti-VEGF gene therapy in diabetic macula edema (DME).

PURPOSE A single-injection intravitreal (IVT) AAV.7m8 gene therapy that durably expresses intraocular aflibercept via a biofactory approach could reduce the need for repeated anti-VEGF injections and improve outcomes for patients with DME. INFINITY is a phase 2 study assessing the durability, safety, tolerability and efficacy of a single IVT injection of ADVM-022 in patients with DME.

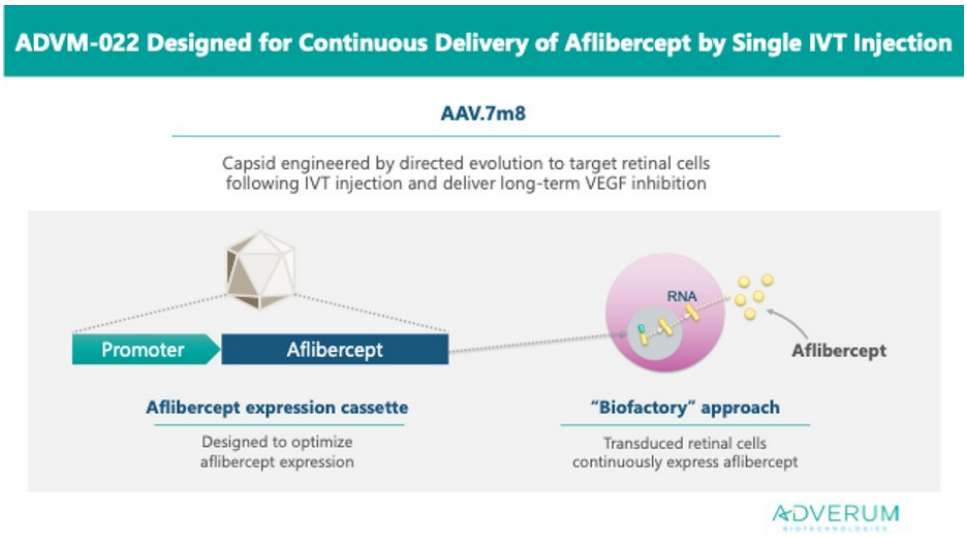
METHODS Patients with newly diagnosed DME (within 6 months of screening) that have received up to 2 prior injections of anti-VEGF therapy in the study eye were enrolled (n=36 randomized across 10 US sites). Patients receive a single IVT injection of ADVM-022 2x1011 vg/eye or 6x1011 vg/eye or standard of care bolus IVT aflibercept and were evaluated monthly for 48 weeks. Primary endpoint is time to worsening of DME disease activity in the study eye. Incidence and severity of adverse events, change in visual acuity, change in central retinal thickness, need for and number of supplemental aflibercept

injections were evaluated.

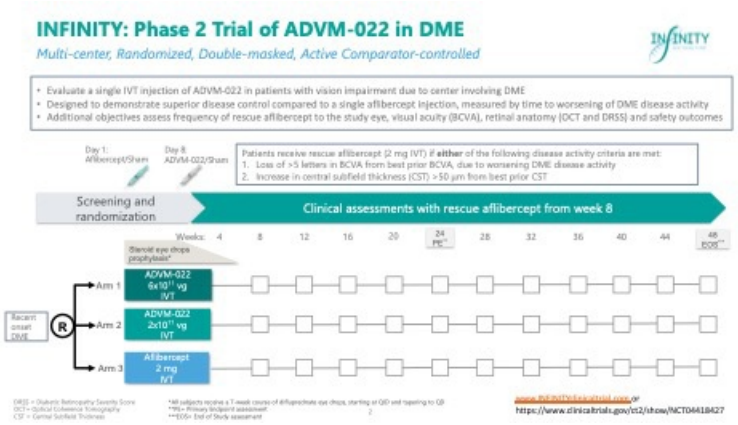
RESULTS First-time presentation of the results from the 24-week interim efficacy and safety analysis of INFINITY will be presented.

CONCLUSION ADVM-022 is designed to provide stable and sustained therapeutic levels of aflibercept following a single IVT injection and is a novel investigational approach to addressing the unmet clinical needs among patients with retinal conditions requiring repeated anti-VEGF therapy. Primary endpoint data from the first randomized clinical study of gene therapy in DME will be presented.

IRB APPROVAL Yes — *IRB Approval Letter may be requested*.



ADVM-022 is an investigational gene therapy that utilizes a novel AAV.7m8 vector designed by directed evolution to deliver a transgene encoding aflibercept directly to retinal cells. Following a single intravitreal injection in NHPs, ADVM-022 establishes an intraocular biofactory producing aflibercept levels within the therapeutic window for standard of care aflibercept.



INFINITY is phase 2, multi-center, randomized, double-masked, active comparator-controlled study of ADVM-022 in patients with recently diagnosed diabetic macular edema. INFINITY is the first gene therapy clinical study in this diabetic patient population.

10/9/2021 10:23AM

Suprachoroidal Delivery of RGX-314 for Diabetic Retinopathy Without CI-DME: Early Results From the Phase II ALTITUDE Study

- Dennis M. Marcus, MD

OBJECTIVE To evaluate the safety, tolerability, and efficacy of RGX-314 by suprachoroidal delivery in patients with Diabetic Retinopathy (DR) without Center-Involved Diabetic Macular Edema (CI-DME).

PURPOSE In eyes with severe non-proliferative DR (NPDR), anti-VEGF therapy by sustained intravitreal injections has been demonstrated to decrease DR severity and reduce vision threatening complications. This regimen has not been preferred, as it is associated with a high treatment burden and risk of repeated injections. Sustained anti-VEGF delivery by gene therapy may provide a more desirable approach.

METHODS RGX-314 is designed as a single gene therapy utilizing the NAV AAV8 vector to deliver a soluble anti-VEGF fab transgene to provide continuous anti-VEGF therapy. ALTITUDE, a Phase II trial, will evaluate the efficacy, safety, and tolerability of suprachoroidal delivery of RGX-314 at two doses using the SCS Microinjector, an in-office route of administration. Forty patients with severe NPDR and non-high-risk PDR will be randomized to receive RGX-314 versus observational control at a 3:1 ratio. The primary endpoint is the proportion of patients that improve ≥ 2-steps on the DR Severity Scale (DRSS) at 48 weeks. Other endpoints include safety and development of DR-related ocular complications.

RESULTS The first patient has been dosed and Cohort 1 continues to enroll. As of December 31, 2020, suprachoroidal delivery of RGX-314 is reported to be generally well-tolerated. Updated safety and efficacy information will be presented, and a thermal imaging video will be presented to demonstrate drug delivery by this route of administration.

CONCLUSION RGX-314 has the potential to provide sustained clinical outcomes in the treatment of diabetic retinopathy with a one-time treatment administered in-office.

IRB APPROVAL Yes — *IRB Approval Letter may be requested*.

10/9/2021 10:37AM

Impact of Delayed Treatment in Diabetic Retinal Disease: Experience From VISTA/VIVID and PANORAMA

- Sunil Srivastava, MD
- Sumit Sharma, MD

OBJECTIVE To assess the impact of delayed treatment in diabetic macular edema (DME) in VISTA/VIVID and early treatment in moderately severe to severe non-proliferative diabetic retinopathy (NPDR) in PANORAMA.

PURPOSE To determine whether delaying treatment with intravitreal aflibercept injection (IAI) in eyes with DME or moderately severe and severe NPDR without DME provides outcomes comparable to those obtained with earlier IAI treatment.

METHODS In VISTA/VIVID, eyes with DME received IAI 2 mg every 4 weeks (2q4; n=290) or 8 weeks after 5 monthly doses (2q8; n=286), or laser (with IAI rescue [2q8] for vision loss initiated from week 24; n=109) to week 100. For this analysis, data timepoints were synchronized to the number of weeks post rescue initiation (RI) to more easily compare laser/rescue and IAI groups. In PANORAMA, eyes with NPDR received IAI 2q16 (n=135) or 2q8/PRN (n=134) after loading phase, or sham (n=133). Eyes could be rescued for complications including PDR/anterior segment neovascularization (ASNV; 1 IAI 2 mg and/or panretinal photocoagulation or vitrectomy), or for center-involved DME (CI-DME; IAI PRN or laser).

RESULTS In VISTA/VIVID, mean best-corrected visual acuity (BCVA, letters) with 2q4 and 2q8, respectively, was 59.8 and 59.1 at baseline and 71.5 and 70.2 at week 100. Mean BCVA with laser/rescue was 59.5 at baseline, 49.0 at RI, and 57.9 at week 100. Mean central subfield thickness (CST) (μm) with 2q4 and 2q8, respectively, was 493.1 and 497.6 at baseline and 289.4 and 290.1 at week 100. Mean CST with laser/rescue was 537.5 at baseline, 538.5 at RI, and 272.9 at week 100. In PANORAMA, a higher proportion of patients in the sham group who received rescue still had a DRSS ≥61 and CST ≥300 at week 100, compared with IAI groups. This was seen for sham patients rescued due to either PDR/ASNV or CI-DME, respectively.

CONCLUSION Eyes with DME in VISTA/VIVID that received IAI rescue had BCVA gains but did not achieve final BCVA seen in eyes receiving IAI at study start. In PANORAMA, sham-treated eyes with NPDR were more likely than IAI-treated eyes to have PDR/ASNV or retinal thickening at week 100, despite rescue therapy. Earlier treatment with IAI in eyes with DME or NPDR improved outcomes over 100 weeks.

IRB APPROVAL Yes — *IRB Approval Letter may be requested*.

10/9/2021 10:43AM

A Randomized Trial of Intravitreous Anti-VEGF for Prevention of Vision Threatening Complications of Diabetic Retinopathy (Protocol W)

- Raj K. Maturi, MD

OBJECTIVE To determine the efficacy of intravitreous aflibercept treatment in preventing vision-threatening complications among eyes with moderate to severe non-proliferative diabetic retinopathy (NPDR).

PURPOSE Eyes with moderate to severe NPDR are at high risk for disease progression and development of vision-threatening complications. The DRCR Retina Network Protocol W assessed whether aflibercept treatment prevented the development of proliferative diabetic retinopathy (PDR) and center-involved diabetic macular edema (CI-DME) with vision loss and if there were associated visual benefits at 2 years.

METHODS A multi-center randomized clinical trial assigned eyes with moderate to severe NPDR (ETDRS severity levels 43-53) and without CI-DME to aflibercept (2.0-mg) or sham injections. Eyes received injections at baseline, 1, 2, and 4 months and every 4 months through 2 years. After that, through 4 years, treatment was deferred if the eye had no worse than mild NPDR on clinical exam. Aflibercept was provided in both groups if high-risk PDR or vision impaired CI-DME developed. Marginal Cox regression models analyzed the time to development of PDR or vision impaired CI-DME (primary outcome), and linear mixed models analyzed the 2-year change in visual acuity.

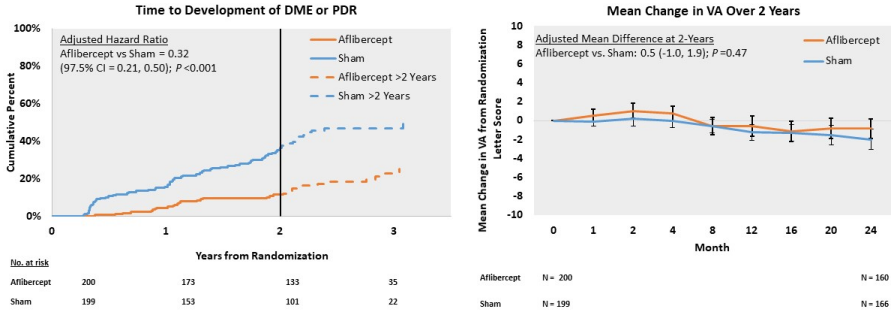
RESULTS Protocol W randomly assigned 399 eyes to aflibercept (n = 200) or sham (n = 199) injections from 328 participants (mean age 56 years; 42.4% female). The 2-year cumulative probability of developing PDR or vision impaired CI-DME was 16.3% with aflibercept vs. 43.5% with sham; adjusted hazard ratio = 0.32 (97.5% confidence interval

[CI]: 0.21 to 0.50, P <.001). The 2-year cumulative probability of developing PDR was 13.5% with aflibercept vs. 33.2% with sham and of developing vision impaired CI-DME was 4.1% with aflibercept vs. 14.8% with sham. The mean change in visual acuity from randomization to 2 years was -0.9 (standard deviation (SD) = 5.8) letters with aflibercept and -2.0 (SD = 6.1) letters with sham; adjusted mean difference = 0.5 letters (97.5% CI: -1.0 to 1.9, P = .47).

CONCLUSION Periodic aflibercept treatment in eyes with moderate to severe NPDR lowered the probability of developing PDR or vision impaired CI-DME through at least 2 years. However, preventive treatment with aflibercept compared with observation plus anti-VEGF only if high-risk PDR or vision impaired CI-DME developed did not confer visual acuity benefit at 2 years. Four year results will be assessed.

IRB APPROVAL Yes — *IRB Approval Letter may be requested*.

Figure 1. DRCR Retina Network Protocol W



Left panel: Time from randomization to development of proliferative diabetic retinopathy or center-involved diabetic macular edema (CI-DME). Vertical line is the end of the 2-year visit window. Hazard ratio includes all available data through 4 years. Figure was truncated when data from less than 20 eyes in each treatment group were available.Right panel: Mean Change in Visual Acuity Over 2 Years

10/9/2021 10:49AM

What Is the Clinical Significance of Improving Diabetic Retinopathy for Vision Outcomes? A Meta-Analysis of 5 Ranibizumab Trials

- Sophie Jane Bakri, MD
- Steven Blotner
- Lauren Hill, BA, MS
- Ivaylo Stoilov, MD

OBJECTIVE To investigate the impact of ranibizumab-induced changes in diabetic retinopathy (DR) severity on vision outcomes.

PURPOSE To investigate the clinical significance of improvements in DR on vision outcomes.

METHODS In this meta-analysis, study eyes treated with ranibizumab were evaluated using data from RIDE/RISE (NCT00473382/NCT00473330), Protocol I (NCT00444600), Protocol T (NCT01627249), and Protocol S (NCT01489189). These analyses were stratified by change from baseline in Diabetic Retinopathy Severity Scale (DRSS) score at month (M) 24. Outcomes included change from baseline to M24 in best-corrected visual acuity (BCVA; Early Treatment Diabetic Retinopathy Study [ETDRS] scale), central subfield thickness (CST) over time, as well as frequency of ≥ 15 ETDRS letter gain/loss at M24. Associations between change in DRSS score and change in vision or CST outcomes from baseline at M24 were examined.

RESULTS This meta-analysis included 1118 patients. A significant trend for greater BCVA gains was found as DRSS improved (baseline to M24: any DR worsening, 6.5 letters [95% CI, 2.3, 10.7]; no change, 8.6 letters [7.1, 10.0]; 1-step improvement, 10.2 letters [8.7, 11.8]; 2-step improvement, 12.4 letters [10.6, 14.1]; ≥ 3-step improvement, 11.1 letters [8.9, 13.2]; Figure 1). The highest rate of ≥ 15-letter gain from baseline at M24 was in eyes with a 2-step DRSS improvement from baseline at M24 (43.6% [89/204]); the lowest rate was seen in eyes with any DR worsening from baseline at M24 (24.2% [16/66]). There was a

significant trend for greater CST reduction from baseline at M24, with increasing change in DRSS from baseline at M24 (Figure 2).

CONCLUSION In this meta-analysis of patients receiving monthly ranibizumab for DR, greater DR severity improvements were associated with better vision outcomes and reduction in CST.

IRB APPROVAL Yes — *IRB Approval Letter may be requested*.

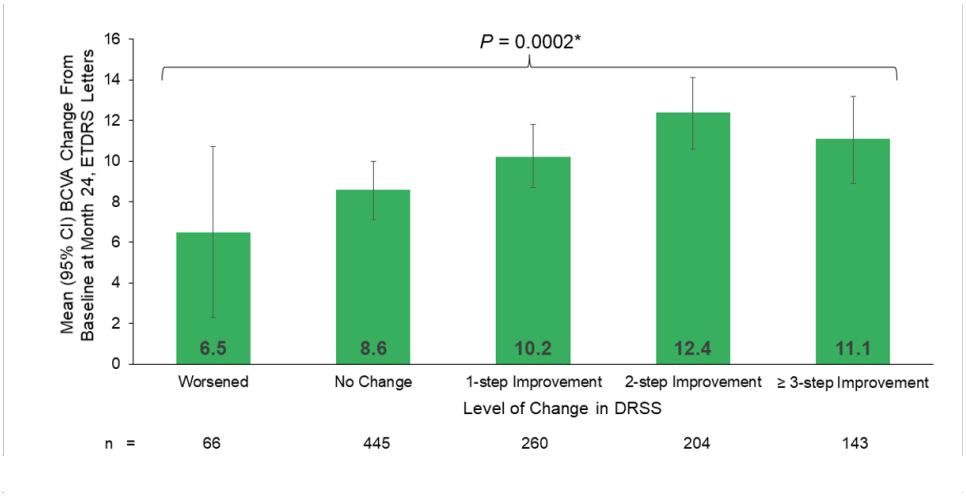


Figure 1. Greater vision gains from baseline at Month 24 were observed with DRSS improvements at Month 24. *P value based on Jonckheere-Terpstra test for trend.

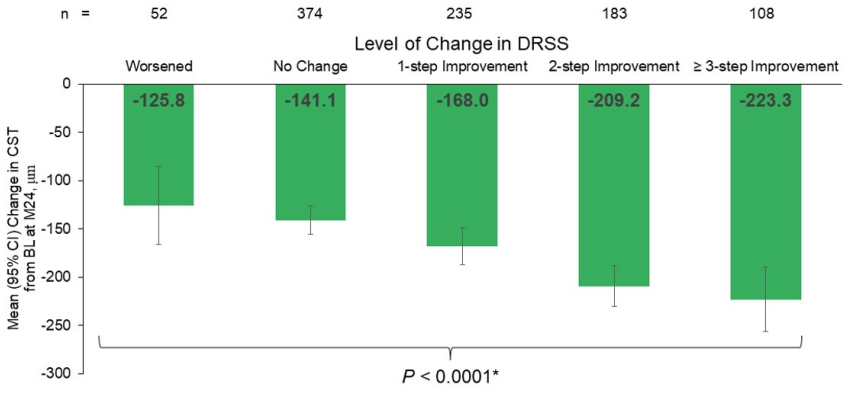


Figure 2. DR improvements were associated with a trend toward greater reductions in CST from baseline at Month 24. *P value based on Jonckheere-Terpstra test for trend.

10/9/2021 10:55AM

Qualitative and Quantitative Evaluation of Diabetic Choroidopathy Using Ultra-Widefield Indocyanine Green Angiography (UWF ICGA)

- Young Hee Yoon, MD, PhD
- Sang Uk Choi, MD
- Junyeop Lee, MD, PhD

OBJECTIVE To describe structural features caused by diabetes mellitus (DM) to the choroid using ultra-widefield (UWF) indocyanine green angiography (ICGA), and to compare with UWF fluorescein angiography (FA).

PURPOSE The underlying changes of choroid in diabetic patient remain uncertain. The advent of UWF ICGA enabled a more comprehensive inspection of choroidal circulation. This study was performed to describe characteristics of diabetic choroidopathy (DC) for better understanding of choroidal circulation in patients with DM.

METHODS A cross-sectional, observational study was performed. Patients with DM who underwent diabetic retinopathy (DR) screening were included. All patients underwent UWF FA and ICGA using an Optos California (Optos PLC, Dunfermline, UK) system. At first, qualitative evaluation of DC in UWF ICGA image was done. The outline of the choroidal hyperpermeable area was demarcated using ImageJ software. ICGA images were binarized and skeletonized by using imageJ software. Total vascular area and choroidal vascular density (CVD) from the ICGA image were calculated. Choroidal vascular fractal dimension (CFD) was obtained using skeletonized ICGA image.

RESULTS One hundred six eyes of 61 DM patients were included (31 females, 50.8%). Thirty-three patients (54.1%) had hypertension medication. Mean age was 49.11 ± 16.31 years (range, 21-76 years) and mean HbA1c (%) was 7.72 ± 1.28. No DR was seen in 18 eyes (16.9%), mild non-proliferative DR in 32 (30.2%), moderate non-proliferative DR in 10 (9.4%), severe non-proliferative DR in 16 (15.1%), and proliferative DR in 30 (28.3%).

Hypofluorescent spots in early ICGA was most common qualitative abnormality of DC. Salt and pepper pattern was significantly more frequent in advanced DR than early DR. Both qualitative DC findings were predominantly observed in macular area. Choroidal hyperpermeable area was positively correlated with DR severity ($P < 0.05$). Less number of microaneurysm (MA)s were observed in ICGA than in FA. CVD and CFD were negatively correlated with the severity of DR.

CONCLUSION Diabetic patients present inflamed choroidal vessels predominantly at the macula demonstrated as hypofluorescent spots. The major features of DC in advanced DR are the choroidal hyperpermeability and stromal inflammation. As the DR progresses, the density and complexity of choroidal blood vessels decreases. These findings imply the possible interrelation between DC and DR.

IRB APPROVAL Yes — *IRB Approval Letter may be requested*.

10/9/2021 11:11AM

Diabetic Retinopathy Telemedicine Outcomes With Artificial Intelligence-Based Image Analysis, Reflex Dilation, and Image Overread Protocol

- Andrew J. Barkmeier, MD
- Ankur Anil Mehra, MD

OBJECTIVE To report real world telemedicine outcomes for diabetic retinopathy screening with artificial intelligence-based image analysis, reflex dilation, and image overread protocol in a primary care setting.

PURPOSE Emerging telemedicine technologies offer an opportunity to improve diabetic retinopathy screening adherence safely and conveniently in the primary care setting. We report real world results following the introduction of IDx AI-based image interpretation with reflex dilation and image overread into an existing primary care-based diabetic retinopathy photoscreening telemedicine program.

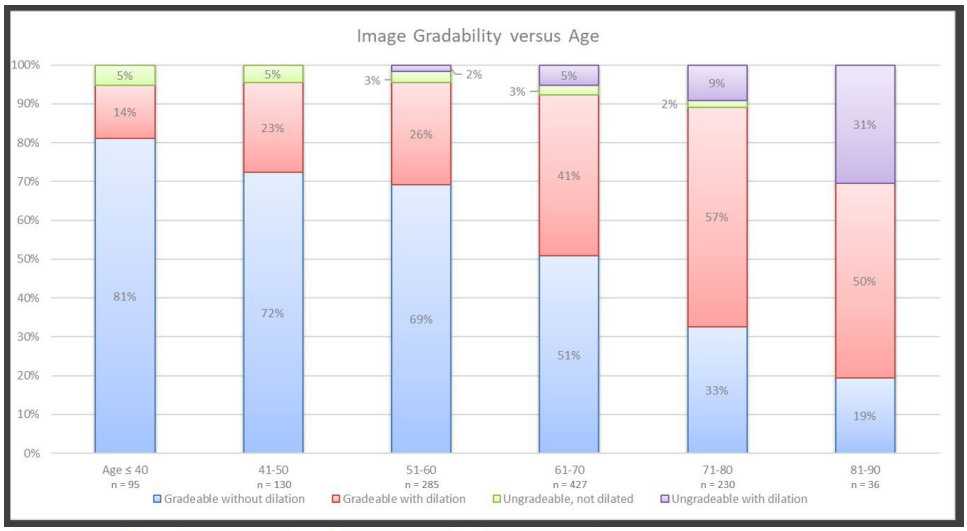
METHODS Medical records were retrospectively reviewed for 1,204 consecutive patients who received diabetic retinopathy screening in a primary care setting over an 18-month period. Nonmydriatic color fundus photographs were acquired and analyzed by the IDx AI-based system for presence of more than mild nonproliferative diabetic retinopathy (NPDR). If images were ungradable after one or more attempts, 1% tropicamide drops were given and the process was repeated. IDx results that were positive for more than mild NPDR were manually reviewed within days, and images graded as negative were batch-reviewed monthly. If more than mild NPDR was present, the patient was referred for dilated eye examination.

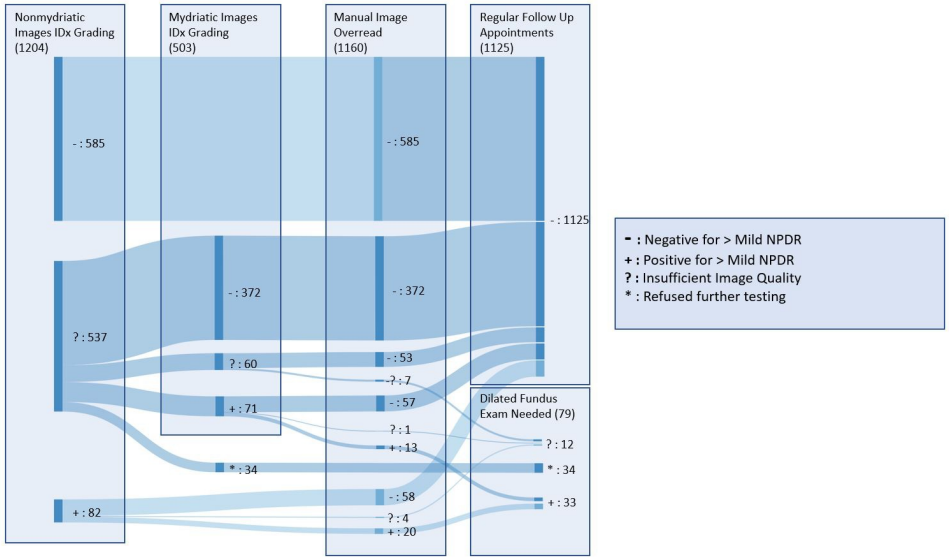
RESULTS 55.5% of 1,204 patients had IDx-gradable nonmydriatic images, which increased to 92.2% following reflex dilation. Successful IDx nonmydriatic image interpretation was age-dependent, with gradability for 81.1% of patients aged 18-40, 72.3% aged 41-50, 69.1% aged 51-60, 50.8% aged 61-70, 32.6% aged 71-80, and 9.4% aged 81-90. Mean age of patients with gradable nonmydriatic images was 56.9 years, versus 65.3 years ungradable ($p<0.001$). Post-dilation gradability was also age-dependent, with successful

IDx interpretation of 100% of patients aged 18-50, 93.7% aged 51-60, 88.9% aged 61-70, 86.1% aged 71-80, and 62.1% aged 81-90. Mean age of patients with gradable images following reflex dilation was 65.1 years, versus 71.6 years ungradable ($p<0.001$). IDx interpretation sensitivity for greater than mild NPDR was 100%, with manual overread agreement in all 585 patients graded negative. 21.6% (33/153) of patients graded positive by IDx required prompt eye exams following manual overread.

CONCLUSION Combining artificial intelligence-based image analysis with a formal reflex dilation protocol and manual overread of positive results may allow for safe and efficient diabetic retinopathy screening while minimizing follow-up clinic visits. Most patients over age 60 require dilation for successful image interpretation.

IRB APPROVAL Yes — *IRB Approval Letter may be requested*.





10/9/2021 11:23AM

Comparing Rates of Vitrectomy in Proliferative Diabetic Retinopathy Patients Treated With Anti-VEGF or Panretinal Photocoagulation Monotherapy

- Nadim M Rayess, MD
- Amee D Azad, MD, MS
- Bryce Hwang
- Evan Chen
- John W Hinkle, MD
- Ravi Parikh, MD MPH
- Prithvi Mruthyunjaya, MD, MHS

OBJECTIVE Does the rate of vitrectomy in proliferative diabetic retinopathy differ between patients treated with pan-retinal photocoagulation or anti-vascular endothelial growth factor (VEGF) monotherapy?

PURPOSE The Protocol S trial compared ranibizumab with Pan Retinal Photocoagulation (PRP) found that treatment with ranibizumab lead to less vitrectomy procedures. It is unknown if these findings are reproducible in a large national cohort study. Using a large national cohort study, we report rates of vitrectomy after PRP or anti-VEGF injections in the treatment of proliferative diabetic retinopathy

METHODS A retrospective cohort of patients from a nationally representative claims-based cohort, Clinformatics™ Data Mart Database. Patients with proliferative diabetic retinopathy (PDR) who had at least 2 years of continuous enrollment between January 1, 2012 to December 31, 2017 was analyzed. Patients were then stratified into one of two groups: Anti-VEGF group represented patients who were only receiving anti-VEGF therapy, whereas the PRP group consisted of patients who were treated with PRP monotherapy for their PDR. The main outcome measure was comparing rates of pars plana vitrectomy (PPV) between the 2 groups. Secondary outcome was to compare median time to vitrectomy between the 2 groups.

RESULTS A total of 2,368 PDR patients met inclusion criteria. The rate of vitrectomy was similar between PRP (4.9%, 87/1787) treated eyes and anti-VEGF (3.4%, 20/581) treated eyes (p=0.15). Median time to PPV was 113.5 days for eyes treated with anti-VEGF therapy

and 188 days for PRP (p=0.08) treated eyes. With adjustment for gender and age, the odds of vitrectomy were not different between eyes treated with PRP only compared to those treated with anti-VEGF only (OR 1.14, 95%CI 0.69-1.96, p=0.629).

CONCLUSION In a real-world cohort, although median time to vitrectomy trended towards a longer duration in anti-VEGF monotherapy compared to PRP monotherapy, both treatment modalities had the same likelihood of ultimately requiring a vitrectomy. The implications for clinical practice and patient counseling should be further explored.

IRB APPROVAL Yes — *IRB Approval Letter may be requested*.

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Baseline Factors Influencing Diabetic Macular Edema (DME) Resolution After Intravitreal Aflibercept Injection (IAI) or Laser Treatment in VISTA/VIVID

- Rishi P. Singh, MD
- Carolina Carvalho Soares Valentim, MD
- Katherine E Talcott, MD

OBJECTIVE To assess the relationship between baseline factors and DME resolution in patients (pts) randomized to IAI or laser control in VISTA/VIVID.

PURPOSE Identification of specific baseline factors that influenced DME resolution in pts treated with either IAI or laser control may help to inform physician and pt expectations.

METHODS Of 862 pts in the VISTA/VIVID full analysis set, this analysis included 558 pts treated with IAI 2 mg (given either q4 weeks [wks] or q8 wks after 5 monthly doses) and 274 pts treated with laser control; 30 pts with baseline central subfield thickness (CST) <290 µm were excluded. Effect of baseline factors (age, gender, race, ethnicity, diabetes type and duration, HbA1c, hypertension, hyperlipidemia, smoking status, CST, best-corrected visual acuity [BCVA], and DRSS) on time to first DME resolution (CST <290 µm) was assessed in univariate and multivariate models and was further evaluated by Kaplan–Meier method based on tertiles of baseline factors.

RESULTS IAI pts had a 2.5-fold higher DME resolution rate, with median (95% confidence interval [CI]) time of 33.0 (28.1, 40.0) wks vs not achieved with laser. In the IAI group, lower DME resolution rate was associated with thicker CST (HR [95% CI]/100 µm CST increase: 0.79 [0.72, 0.86]) and better BCVA (HR [95% CI]/5 letters increase: 0.87 [0.83, 0.92]). Tertiles of increasing CST (T1: ≤419, T2: 419–541, T3: >541 µm) were associated with significantly longer median time to DME resolution (20.1, 39.1, and 49.1 wks for T1–T3, respectively; P≤0.0001 for T2 and T3 vs T1) and lower cumulative event incidence (HR: 0.6, 0.6 for T2 and T3 vs T1, respectively; P<0.001 for T2 and T3 vs T1). Tertiles of increasing BCVA (T1: ≤57, T2: 57–66, T3: >66) were also associated with relatively longer

median time to DME resolution (28.4, 31.7, and 44.1 wks for T1–T3, respectively; P<0.05 for T3 vs T1) and lower cumulative event incidence (HR: 0.9, 0.8 for T2 and T3 vs T1, respectively; P<0.05 for T3 vs T1).

CONCLUSION Thicker CST and better BCVA in the IAI group were baseline factors associated with longer time to and lower rate of DME resolution in VISTA and VIVID. These findings may inform physicians and pts regarding expectations of DME therapy.

IRB APPROVAL Yes — *IRB Approval Letter may be requested*.