10:20 AM

Panretinal Photocoagulation Versus Ranibizumab for Proliferative Diabetic Retinopathy: Should Baseline Characteristics Affect Choice of Treatment?

- Susan B. Bressler, MD

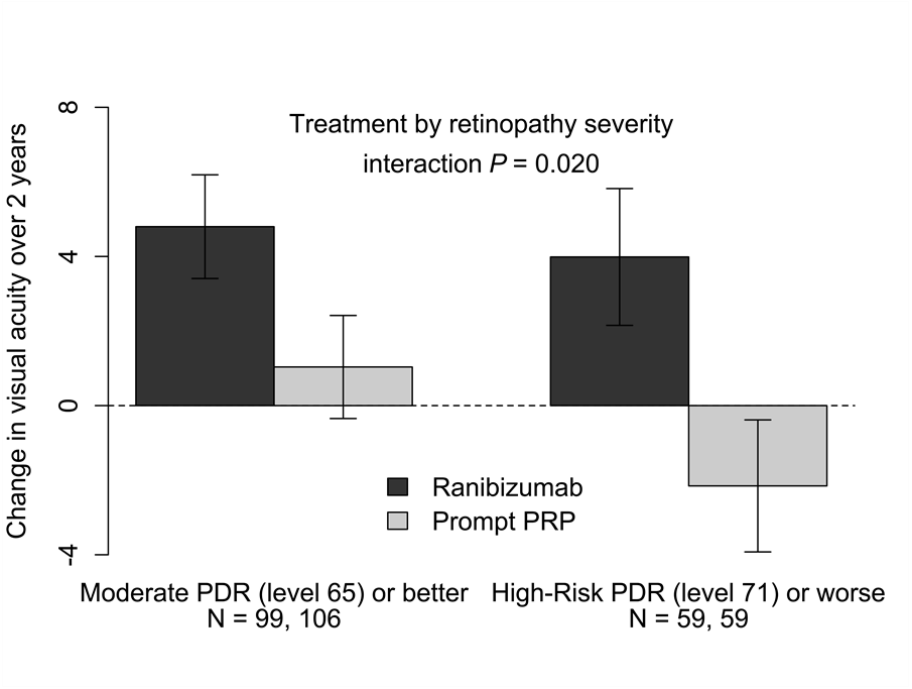
OBJECTIVE To identify subgroups in DRCR.net Protocol S for which panretinal photocoagulation is superior to ranibizumab for change in vision or development of diabetic macular edema over 2 years.

PURPOSE In Protocol S of the DRCR.net, change in vision at 2 years was non-inferior with ranibizumab versus panretinal photocoagulation (PRP); moreover, change in vision over 2 years and development of diabetic macular edema favored the ranibizumab group. The purpose of this analysis was to determine if there were any subgroups in which PRP was superior to ranibizumab for these two outcomes.

METHODS Post hoc analyses of randomized multicenter clinical trial data. All eyes had proliferative diabetic retinopathy (PDR). Eyes were randomized to panretinal photocoagulation or intravitreal ranibizumab (0.5 mg/0.05 mL). Main outcomes were change in visual acuity (VA) over 2 years (analysis cohort limited to eyes completing the 2-year visit [N=328]) and development of vision-impairing (20/32 or worse) central-involved diabetic macular edema (CI-DME) over 2 years (analysis cohort limited to eyes without vision-impairing CI-DME at baseline [N=302]). Twenty-five baseline characteristics were considered and all analyses were adjusted for baseline VA and central subfield thickness.

RESULTS Ranibizumab was superior to PRP for both outcomes in each subgroup. The relative benefit of ranibizumab over PRP for VA change appeared greater among participants with high mean arterial pressure (ranibizumab-PRP difference: ≥100 mmHg vs. <100 mmHg, 5.4 vs. 3.8 letters; *P*=.03), eyes without prior focal/grid laser (without vs. with, 5.1 vs. 1.0 letters; *P*=.03), eyes with neovascularization of the disc (NVD) and elsewhere (NVE) (NVD and NVE vs. NVD or NVE only, 6.7 vs. 3.6 letters; *P*=.04), and eyes with higher Early Treatment Diabetic Retinopathy Study (ETDRS) retinopathy severity level (high-risk PDR [level 71] or worse vs. moderate PDR [level 65] or better, 6.1 vs. 3.8 letters; *P*=.02). For development of vision-impairing CI-DME over 2 years, the benefit of ranibizumab vs. PRP appeared greater among non-white participants (hazard ratio non-white 0.10 vs. white 0.50; *P*=.02) and those with higher mean arterial pressure (ranibizumab/PRP HR: ≥100 mmHg vs. <100 mmHg, 0.16 vs. 0.39; *P*=.01).

CONCLUSION We did not identify any subgroups in which PRP was superior to ranibizumab with respect to change in VA over 2 years or development of vision-impairing CI-DME over 2 years. These results provide additional support that ranibizumab may be a reasonable alternative treatment to PRP for PDR at least for a period of 2 years. Follow-up through 5 years is ongoing.



HUMAN RESEARCH This study involves human research.

IRB Approval Status: Approved by institutional review board

10:28 AM

Analysis of Vitreous Biomarkers Associated With Diabetic Macular Edema in the Setting of Proliferative Diabetic Retinopathy- A Multicohort Study

- Kameran Lashkari, MD
- Namrata Nandakumar
- Francisco J. J Lopez, MD, PhD

OBJECTIVE To identify the profile of biomarkers associated with diabetic macular edema in the vitreous of subjects with proliferative diabetic retinopathy

PURPOSE Diabetic macular edema (DME) and proliferative diabetic retinopathy (PDR) are the most common causes of severe vision loss in diabetic subjects. The aim of this study is identify vitreous biomarkers associated with these conditions in 2 cohorts of subjects with PDR and control, and 1 cohort of subjects with PDR no DME, PDR with DME, non-diabetic cystoid macular edema (CME) and control.

METHODS Undiluted vitreous samples (n=300) were collected from the following subjects: Cohort 1: PDR (n=35), control (n=28); Cohort 2: PDR (n=47), control (n=65); Cohort 3: PDR no DME (n=35); PDR with DME (n=30); CME (n=30), control (n=30). Samples were anlyzed by multiplex analysis (Bio-Rad) and ELISA. Data was transformed to allow for parametric analysis and analyzed by MANCOVA and correlation matrix analysis. The three variables considered were age, gender and disease state. The p-values were corrected using the Benjamini-Yeukeutili adjustment for false discovery. All tests were performed at an error level of 5%.

RESULTS There were no significant differences between age and gender in the control versus PDR groups. In Cohort 1, multiplex analysis identified 6 of 31 factors that were

statistically shifted in PDR. These included PLGF (p= 0.0000002), VEGF-A (p= 0.00004), sVEGFR-1 (p= 0.0104), sCD40L (p = 0.0026), IL-18 (p= 0.0048) and Pai-1 (p= 0.005). In Cohort 2, these levels of these 6 factors were re-measured by individual ELISA. 4 of 6 factors remained significantly elevated with similar p values, PLGF, VEGF-A, sVEGFR-1 and Pai-1. Multiplex analysis of Cohort 3 identified 8 factors that were associated with PDR and DME, and a distinct biomarker profile between PDR/DME and non-diabetic CME. Among these VEGF-A and PLGF were persistently elevated in all cohorts. Correlation matrix analysis showed that the profile can be explained by a few biomarkers.

CONCLUSION This study demonstrates that a variety of pro-inflammatory and pro-angiogenic biomarkers participate in PDR and DME. The biomarker profile of PDR and PDR with DME are not significantly different for each other. The biomarker profile of PDR with DME is distinct from CME, and explains the basis of this disease process.

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

10:33 AM

To Treat or Not to Treat: Are We Sacrificing Treatment Outcomes by Allowing Diabetic Retinopathy (DR) to Enter the Proliferative Stage?

- Michael J. Elman, MD
- Lauren Hill, BA, MS
- Kathleen Tarnowski, M.S.
- Zdenka Haskova, MD, PhD
- Ivaylo Stoilov, MD

OBJECTIVE To examine the impact of baseline diabetic retinopathy (DR) severity on the rates of clinically significant improvement in DR severity with anti-vascular endothelial growth factor A therapy.

PURPOSE Recent approval of an anti-vascular endothelial growth factor A (anti-VEGF) agent (ranibizumab [RBZ]) to treat all stages of DR with or without diabetic macular edema (DME) has opened debate on the optimal timing of such treatment. This analysis explored the effect of disease progression on the efficacy of VEGF inhibition in reversing the course of DR.

METHODS Data from RIDE (NCT00473382)/RISE (NCT00473330) phase 3 studies for patients receiving sham (n=254), 0.3 mg RBZ (n=245), or 0.5 mg RBZ (n=247) were pooled and the percentage of patients achieving a â‰¥2-step improvement in DR severity on the Early Treatment Diabetic Retinopathy Study (ETDRS) scale at month (M) 24 were compared across different baseline (BL) DR severity subgroups. Univariate

analysis of â‰¥2-step DR (â‰¥1-step for mild non-proliferative DR [NPDR]) improvement (Yes/No) and relationships with BL variables were also assessed for each subgroup.

RESULTS At BL, RIDE/RISE patients were evenly distributed among mild/moderate NPDR (28.8%), moderately severe/severe NPDR (33.2%), and proliferative DR (PDR; 31.1%). At M24, rates of â‰¥2-step improvement in DR severity on the ETDRS scale for patients receiving RBZ 0.3/0.5 mg were 10%/16% (mild/moderate NPDR), 78%/81% (moderately severe/severe NPDR) and 31%/36% (PDR; panretinal photocoagulation [PRP] naÃ¯ve patients). Improvement rates were significantly lower in the sham group. There were no significant BL predictors for lack of â‰¥1-step improvement at M24 in the mild NPDR group. In the moderately severe/severe NPDR group, increased fluorescein angiography (FA) leakage was a significant BL predictor for lack of â‰¥2-step improvement at M24. In the PDR without PRP group, subjects without a â‰¥2-step improvement were more likely to be of Hispanic/Latino ethnicity. Higher HbA1c and presence of macular non-perfusion (MNP) were significant predictors of a â‰¥2-step improvement at M24 in this group.

CONCLUSION RIDE/RISE patients with moderately severe/severe NPDR were most sensitive to anti-VEGF treatment at M24. Progression to PDR was associated with reduced DR severity improvement. Predictors for DR response to RBZ changed with disease progression. BL characteristics had no impact on the rates of DR improvement in mild DR, whereas FA leakage, ethnicity, HbA1c and MNP became significant in advanced DR.

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

10:38 AM

Earliest Diabetic Retinopathy Detection Using Optical Coherence Tomography Angiography (OCTA) Perfused Capillary Density

- Richard B. Rosen, MD, DSc(Hon)
- Toco Y Chui, PhD
- Rishard Weitz
- Brian D Krawitz
- Shelley X Mo
- Jorge S Andrade Romo, MD
- Amani A. Fawzi, MD
- Joseph Carroll, PhD
- Alexander Pinhas, BA
- Rachel Linderman, BA

OBJECTIVE To describe the earliest evidence of diabetic retinopathy detected using a customized OCTA capillary perfususion density algorithm

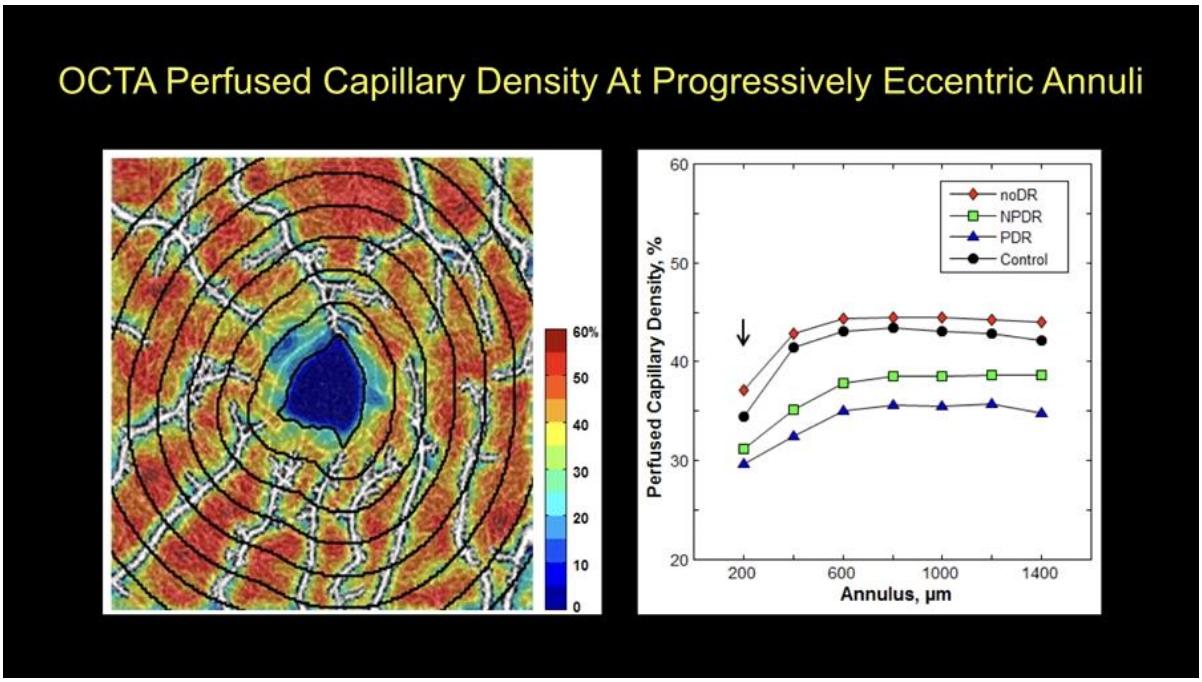
PURPOSE Earliest detection of diabetic retinopathy is critical for identifying the progression of disease in order to preserve visual function. We studied perfused capillary density (PCD) in diabetic patients and healthy controls using optical coherence tomography angiography (OCTA)in order to detect evidence of earliest change prior to conventional clinical lesions.

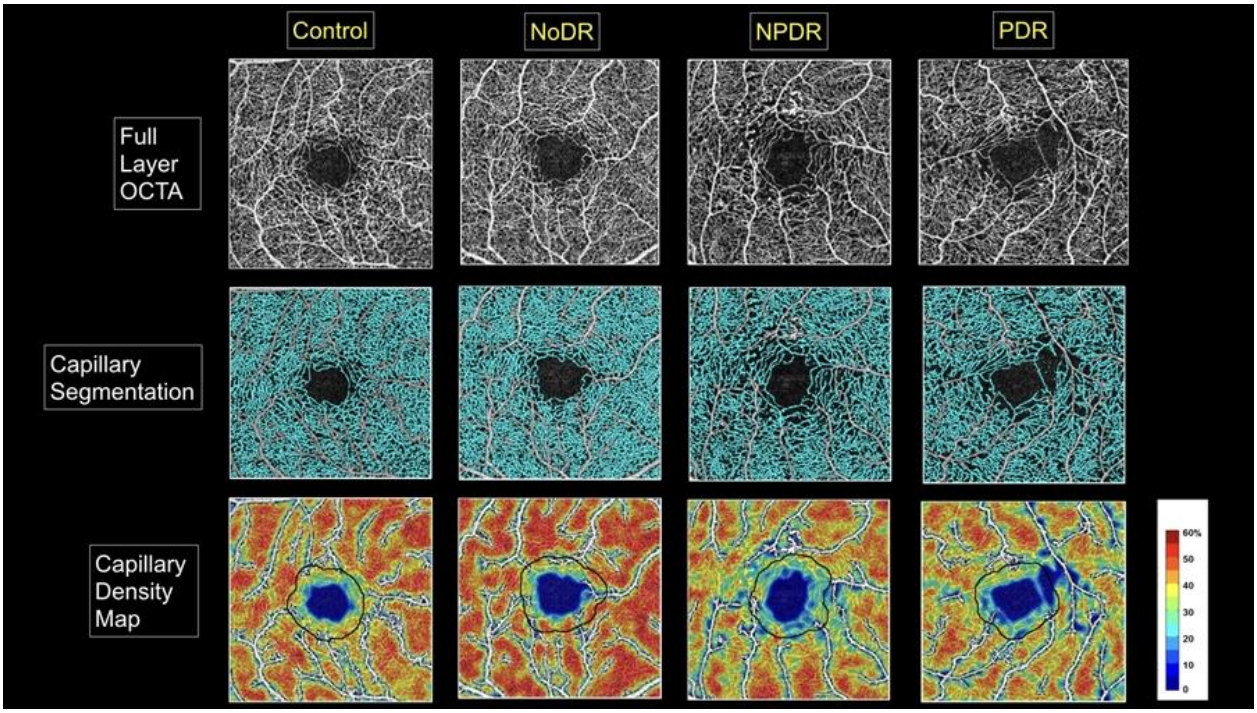
METHODS 30 controls, 30 diabetics without clinical retinopathy (NoDR), 22 with nonproliferative retinopathy (NPDR), and 26 with proliferative retinopathy (PDR) were imaged using SD-OCT. A 3x3 mm full-thickness parafoveal OCTA scan was obtained in each participant. FAZ area, perimeter, and acircularity index were determined. Seven

equidistant 200-µm-wide annular segments were drawn at increasing eccentricities from the FAZ margin. Annular PCD (%) was defined as perfused capillary area divided by the corresponding annulus area after subtraction of large blood vessel areas. Analysis of variance (ANOVA) and post hoc Tukey-Kramer testing measured PCD differences between study groups at each annulus.

RESULTS Patients with diabetes but no clinical evidence of retinopathy(NoDR) group demonstrated consistently higher PCD compared to the control group in all seven perifoveal annuli, reaching statistical significance (37.2±3.10% vs 34.4±3.85%, p<.05) at the first annulus (FAZ margin to 200-µm out). The NPDR and PDR groups demonstrated progressively decreasing PCD. Differences in all FAZ metrics between the NoDR and control groups were not statistically significant.

CONCLUSION Compared to healthy controls, increased PCD values in the NoDR group signal the onset of autoregulatory activation from increased metabolic demand. The decrease in PCD that follows in NPDR and PDR results largely from an incremental loss of capillary segments. These findings, demonstrate the potential of OCTA as a clinical tool for earlier objective detection of preclinical diabetic retinopathy.





HUMAN RESEARCH This study involves human research.

IRB Approval Status: Approved by institutional review board

10:43 AM

Intravitreal Aflibercept for Moderately Severe to Severe Non-Proliferative Diabetic Retinopathy (NPDR): The Phase 3 PANORAMA Study

- Charles C. Wykoff, MD, PhD

OBJECTIVE To evaluate the efficacy & safety of anti-VEGF therapy for treatment of patients with moderately severe to severe non-proliferative diabetic retinopathy (NPDR) without diabetic macular edema (DME).

PURPOSE Microvascular damage to the retina, diabetic retinopathy (DR), is a common manifestation of diabetes mellitus, and its course can be altered with anti-vascular endothelial growth factor therapy. Our goal was to evaluate the efficacy & safety of intravitreal aflibercept injection (IAI) for treatment of moderately severe to severe non-proliferative DR (NPDR) in eyes without diabetic macular edema.

METHODS PANORAMA is a double-masked, randomized, phase 3 trial. Patients (pts) ≥18 years of age with diabetes mellitus could be eligible if they had (a) moderately severe to severe NPDR (Diabetic Retinopathy Severity Scale [DRSS] levels 47 to 53) without diabetic macular edema, and (b) baseline best corrected visual acuity (BCVA) ≥69 letters (approximately ≥20/40). Pts were randomized equally to 1 of 3 arms: IAI 2 mg q8 weeks

after 5 monthly doses (2q8), IAI 2 mg q16 weeks after 3 monthly doses and one 8-week interval (2q16), or sham injections through week 48. The primary endpoint is the proportion of pts demonstrating ≥2-step improvement in DRSS score at week 24 in the combined IAI groups.

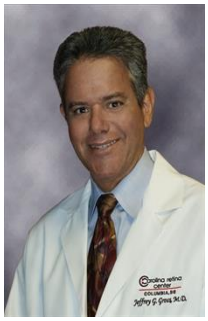
RESULTS PANORAMA enrolled 402 pts from 5 countries. Baseline demographics as well as patient and eye characteristics were balanced between the groups. Overall, mean age was 56 years, HbA1c was 8.5, mean diabetes duration was 14 years, 44% were women, 77% were white, and 92% had type 2 diabetes. Mean baseline BCVA and central retinal thicknesses were 82.3 v 82.7 letters and 249.4 v 246.4 um in the sham and combined IAI groups respectively. DRSS levels were 47 and 53 in 74.4% v 75.5% and 25.6% v 24.5% in the sham and combined IAI groups respectively. IAI treated pts received a mean of 4.4 treatments through week 24. Overall, 58.0% (156/269) of IAI treated pts experienced a ≥2-step improvement in DRSS score at week 24 compared with 6.0% (8/133) of sham treated patients (P<0.0001). No new safety signals were observed. There was one case of mild intraocular inflammation (IOI) in a patient treated with IAI (0.085% rate per IAI), consistent with the rate of IOI reported in previous clinical trials.

CONCLUSION A mean of 4.4 intravitreal aflibercept injections through 24 weeks given without new safety signals achieved a clinically meaningful improvement of at least 2 DRSS steps among eyes with moderately severe to severe NPDR without DME in 58% of eyes compared to 6% of sham treated eyes.

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

10:51 AM

Randomized Trial of Panretinal Photocoagulation Versus Ranibizumab for Proliferative Diabetic Retinopathy: 5-Year Outcomes



- Jeffrey G. Gross, MD

OBJECTIVE Is visual acuity at 5 years in eyes with proliferative diabetic retinopathy receiving intravitreous ranibizumab with deferred panretinal laser non-inferior to eyes receiving prompt laser treatment.

PURPOSE The primary purpose of this randomized clinical trial is to determine if the non-inferior visual acuity and positive secondary outcomes previously reported at 2 years are maintained at 5 years in eyes with proliferative diabetic retinopathy receiving intravitreous ranibizumab with deferred panretinal photocoagulation (PRP), if needed, compared to those eyes that receive standard prompt PRP.

METHODS At 56 sites in the Diabetic Retinopathy Clinical Research Network (DRCR.net), 394 eyes of 305 adults with proliferative diabetic retinopathy and no prior PRP were assigned randomly to prompt PRP or a standardized treatment protocol of 0.5-mg intravitreous ranibizumab with deferred PRP if needed. Eligible eyes had visual acuity

equivalent to Snellen of 20/320 or better. Eyes with or without diabetic macular edema could be eligible, but could not have had intravitreous anti-VEGF within 2 months or intravitreous or peribulbar steroids within 4 months of enrollment. Follow-up visits were every 4 weeks to 16 weeks depending on treatment group and treatment course for a total of 5 years.

RESULTS The 2 year outcomes of this study demonstrated that intravitreous ranibizumab was non-inferior to prompt PRP for change in visual acuity at 2 years and resulted in superior visual outcomes over the course of 2 years (area under the curve analysis -AUC) and less complications. Final outcomes will include visual acuity at 5 years, AUC visual outcomes over 5 years, proportion of eyes in the deferred PRP group requiring PRP treatment, need for supplemental PRP after completion of initial PRP, need for vitrectomy, frequency of vitreous hemorrhage, frequency of CME development, and treatment frequency in the ranibizumab group to assess durability of anti-VEGF monotherapy for PDR. The results of this clinical trial will be presented; however because of the potential public health impact of these results, the DRCR.net requests that the results be presented only after the 5-year primary manuscript is published, which is expected to occur prior to the 2018 ASRS annual meeting.

CONCLUSION Conclusions will follow from the results presented.

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

11:07 AM

Applying the DRCR.net Anti-VEGF Treatment Algorithm for Proliferative Diabetic Retinopathy: Neovascular Outcomes Over 2 Years

- Christina Joy Flaxel, MD

OBJECTIVE To present the DRCR.net Protocol S proliferative diabetic retinopathy (PDR) anti-VEGF treatment rationale and outcomes with ranibizumab over 2 years

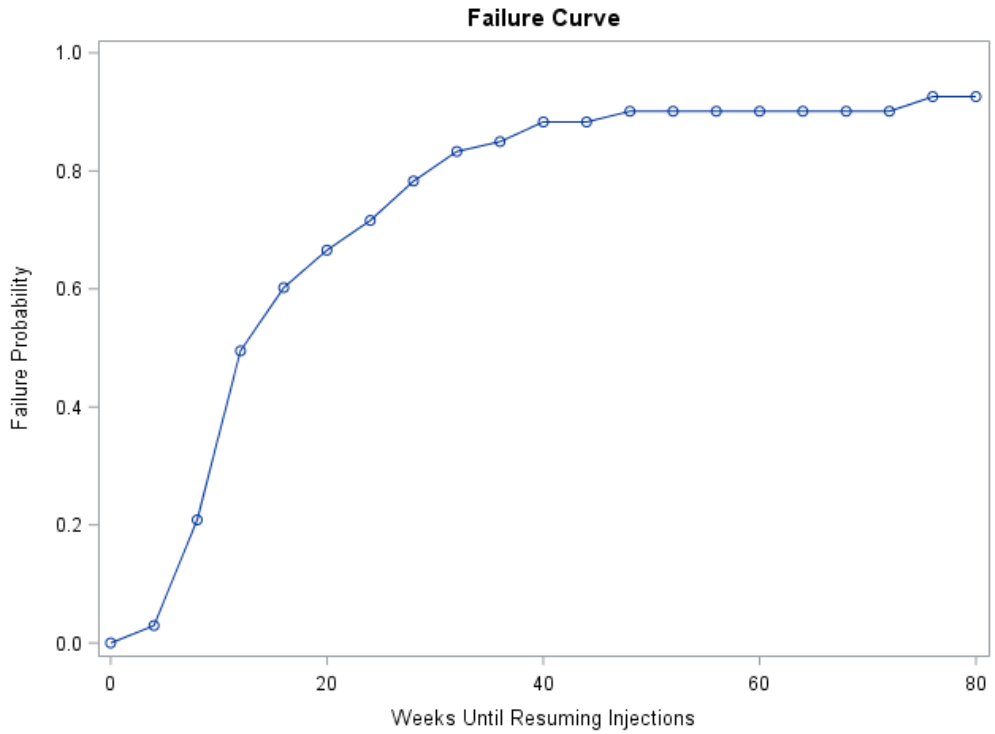
PURPOSE Evaluate neovascular status and injections required over 2 years based on the DRCR.net anti-VEGF treatment algorithm for proliferative diabetic retinopathy (PDR).

METHODS Among 55 clinical sites, 394 study eyes from 305 participants with PDR were randomly assigned to 0.5-mg ranibizumab or PRP (DRCR.net Protocol S). Eyes in the ranibizumab group (N= 191) received injections every month over the first 6 months unless neovascularization (NV) completely resolved at 4 or 5 months. Injections could be deferred after the initial 6 months if NV was stable over 2 consecutive visits but if NV worsened, ranibizumab treatment resumed and PRP could be initiated if failure or futility criteria were met. Ranibizumab was also given if central-involved diabetic macular edema (CIDME) was present at baseline and at investigator discretion during follow-up.

RESULTS Based on investigator assessment, NV completely resolved at 1 month for 19% of eyes assigned to ranibizumab (35/188) and an additional 60% (113/188) were improved. At 6 months NV resolution occurred in 52% of eyes (80/153) with 3% (4) improved, 37% (56) reaching stability, 8% (13) worsening since the last visit, and 1% (2) receiving PRP. The median (interquartile range) number of injections between 6

months and 2 years among the 80 eyes with resolved versus non-resolved NV (N=73) was 4 (1, 7) versus 7 (4, 11) (P<0.001). For eyes deferring at least one injection for stability (N=69), 51% resumed injections by 16 weeks post-deferral and 14% (N=10) did not require any additional injections (Figure).

CONCLUSION The DRCR.net anti-VEGF treatment algorithm for PDR resulted in the vast majority of eyes having resolved, stable or improved NV at each visit through 2 years, however, treatment for PDR should be guided by consideration of individual patient needs. Caution is advised for less frequent dosing or longer follow-up intervals as it remains unknown if this might result in a greater NV recurrence.



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

11:15 AM

Outcomes in Proliferative Diabetic Retinopathy Patients Lost to Follow-up After Panretinal Photocoagulation Versus Antivascular Endothelial Growth Factor

- Daniel Su, MD
- Anthony Obeid, Medical Doctorate
- Joshua Uhr, MD
- Jason Hsu, MD
- Samir N Patel, MD

OBJECTIVE To determine outcomes of proliferative diabetic retinopathy patients who are lost to follow-up immediately after receiving either panretinal photocoagulation vs anti-vascular endothelial growth factor

PURPOSE While the DRCR.net Protocol S demonstrated comparable treatment outcomes in proliferative diabetic retinopathy (PDR) with either anti-vascular endothelial growth factor (VEGF) or panretinal photocoagulation (PRP), such results are contingent on timely follow-up. This study aims to determine the outcomes of PDR in patients who are temporarily lost to follow-up after treatment with PRP vs anti-VEGF.

METHODS A retrospective cohort study was performed on PDR patients between September 2013 and September 2016 who had either intravitreal injection (IVI) with anti-VEGF or PRP on the initial visit before being LTFU for > 6 months. Charts were for reviewed for demographics, visual acuity (VA), intraocular pressure, hemoglobin A1c, and clinical findings at the initial visit (prior to LTFU), return visit (immediate visit after

being LTFU) and the final follow-up visit. Specifically, the presence of vitreous hemorrhage, tractional retinal detachment, neovascularization of the iris, and neovascular glaucoma was recorded. Statistical significance was defined as $p<0.05$

RESULTS 59 eyes met inclusion criteria, of which 32 had received only IVI of anti-VEGF and 27 had only received PRP prior to LTFU (Table 1). In the IVI group, mean logarithm of the minimum angle of resolution (logMAR) VA significantly worsened from the initial visit (0.62, Snellen 20/83) to the return visit (1.18, Snellen 20/300, $p<0.001$) and final visit (1.03, Snellen 20/210, $p=0.02$). In the PRP group, no significant difference in logMAR VA was found when comparing the initial visit (0.40, Snellen 20/50) to the return visit (0.64, Snellen 20/87, $p=0.05$) and final visit (0.57, Snellen 20/75, $p=0.16$). At the initial visit, one eye in each group had a traction retinal detachment (TRD). At the final visit, 7 eyes (21.9%) in the IVI group vs. 2 eyes (7.4%) in the PRP group had a TRD. At the initial visit, no eyes in the IVI group and one eye in the PRP group had neovascular glaucoma (NVG). At the final visit, 4 eyes (12.5%) in the IVI group vs. 1 eye (3.7%) in the PRP group had NVG.

CONCLUSION Patients with PDR who received only anti-VEGF prior to being lost to follow-up had worse final outcomes on return compared to those who had received PRP. In real-world clinical practice, the risk of lost to follow-up should be considered when deciding between treatment with anti-VEGF vs PRP.

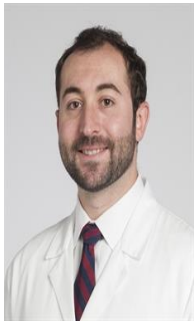
Table 1. Study characteristics of patients LTFU after either IVI with anti-VEGF or PRP and returned for follow-up after 6 months.

Characteristic	Intravitreal Injection	Panretinal photocoagulation	Total	P-value
Number of eyes	**32**	**27**	**59**	
Number of patients	**21**	**23**	**44**	
Age (years), Mean (±SD)	57.3 (±9.8)	53.7 (±14.8)	55.4 (±12.7)	0.36
Race, (n%)				0.37
Caucasian	13 (61.9%)	10 (43.5%)	24 (54.5%)	
African American	5 (23.8%)	10 (43.5%)	14 (31.8%)	
Asian	1 (4.8%)	0 (0.0%)	1 (2.3%)	
Unknown	2 (9.5%)	3 (13.0%)	5 (11.4%)	
Gender (n%)				0.13
Male	13 (61.9%)	9 (39.1%)	22 (50%)	
Female	8 (38.1%)	14 (60.9%)	22 (50%)	
HbA1c, Mean (±SD)*				
Initial Visit	8.8 (±2.3)	7.6 (±1.1)	8.4 (±2.0)	0.16
Return Visit	9.0 (±2.8)	7.9 (±1.4)	8.4 (±2.2)	0.22
Duration from date LTFU to return visit, Mean (±SD)	382 (±182)	549 (±158)	469 (±188)	0.002
Duration from date LTFU to final visit, Mean (±SD)	712 (±198)	769 (±267)	742 (±236)	0.42

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

11:23 AM

Quantitative Ultra-widefield Angiography: Correlation of Microaneurysm Burden With Anatomic and Angiographic Features in Diabetic Retinopathy



- Joseph D Boss, MD
- Alice Jiang, MS
- Sunil Srivastava, MD
- Ming Hu, Ph.D.
- Jamie Reese, RN
- Justis P. Ehlers, MD

OBJECTIVE To evaluate the association of microaneurysm burden on panretinal ischemic index, angiographic findings, and macular edema in diabetic retinopathy utilizing quantitative ultra-widefield angiography.

PURPOSE The purpose of this study is to quantify microaneurysm (MA) burden on ultra-widefield angiography (UWFA) in diabetic retinopathy (DR) and to correlate this to other disease features, including DR severity, panretinal ischemic index, presence of vascular leakage, and diabetic macular edema (DME).

METHODS An IRB-approved retrospective image analysis study completed for subjects with underlying DR. All eyes underwent UWFA and SD-OCT. Eyes were excluded for previous laser, intravitreal injections within the last 6 months, and poor image quality. UWFA images were segmented utilizing a novel angiographic analysis system with manual verification/correction for MA count and ischemia areas. Ischemic index

was calculated as the area of capillary nonperfusion divided by the total retinal area. Zonal assessment was also performed based on distribution of angiographic pathology. SD-OCTs were reviewed for the presence of DME. The DR severity was assessed based on fundus photo review.

RESULTS A total of 273 eyes of 160 patients were included. The mean age was 62 years with 96 males (60%) and 64 females (40%). Twenty-nine eyes (11%) were classified as mild nonproliferative diabetic retinopathy (NPDR), 64 (23%) had moderate NPDR, 110 (40%) had severe NPDR, and 70 (26%) had proliferative diabetic retinopathy (PDR). Mean MA count was strongly associated with DR severity [mild NPDR (mean MA count: 31.5), moderate NPDR (116.5), severe NPDR (162.2), and PDR (210.4), $p<0.0001$]. In addition, MA count was directly correlated with ischemic index ($p=0.03$). Total MA count was not associated with the presence of DME. However, zonal assessment demonstrated significant correlation of macular MA count with DME. Total MA count was associated with vascular staining ($p=0.004$), neovascularity elsewhere (NVE) ($p=0.01$), however was not associated with neovascularity of the disc (NVD) ($p=0.16$).

CONCLUSION Quantitative UWFA enabled panretinal assessment of MA burden utilizing an automated analysis platform. Total MA count was associated DR severity and ischemic index. Macular MA burden was associated with DME. This platform provides a unique opportunity for disease burden assessment and to evaluate retinal vascular dynamics that occur with treatment response.

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

11:34 AM

Effect on Treatment Burden Post- Versus Pre-Iluvien Based on Prior DME Treatments

- Caesar K. Luo, MD
- Melissa D. Neuwelt, MD

OBJECTIVE In the USER real world dataset of patients treated with 0.2 µg/day fluocinolone acetonide (FAc) implant for DME, patients were categorized by number of DME treatments prior to FAc.

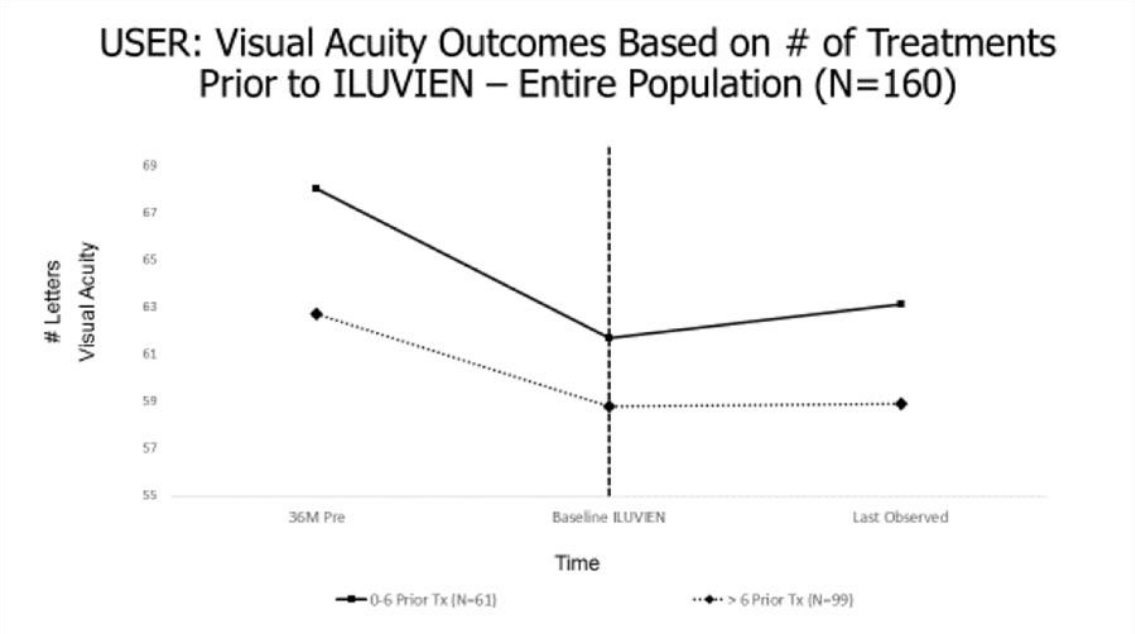
PURPOSE The USER study captured treatment for DME in patients from 4 US clinical sites on 160 eyes treated with the FAc implant. Up to 36 months of data prior to FAc (mean follow up =902.9 days) and all follow up data post FAc (mean follow up =407.8 days) were collected. Patient subgroups were stratified based on the number of treatments prior to FAc, and treatment burden pre vs. post FAc was compared.

METHODS Patients were grouped by number of prior treatment for DME based on the categories Group A: 0-6 treatments (n=61), Group B: >6 (n=99). For each category, treatment burden was compared as pre FAc vs. post FAc treatment. Treatment burden is presented as the mean number of treatments.

RESULTS Mean number of treatments prior vs. post FAc implantation for lesser treated (0-6) vs. greater treated (>6) eyes were 2.7 vs. 0.8 ($p<0.001$) and 14.1 vs. 1.6 ($p<0.001$) respectively. In the greater treated category pre FAc implant, the percentage of patients requiring no further treatments following FAc implant was 58.6%. In the lesser treated

category pre FAc implant, the percentage of patients requiring no further treatments following FAc implant was 68.9%. In both pre-FAc implant treated subgroups VA was maintained during the post-FAc period, with a trend towards improved VA in the lesser treated category.

CONCLUSION Prior analyses have demonstrated that the FAc implant significantly reduces treatment burden irrespective of visual acuity at the time of implantation. These data show that treatment burden is also significantly reduced with the FAc implant irrespective of amount of prior therapy for DME, further demonstrating the benefit of a foundation of continuous microdosing associated with FAc for DME.



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

11:39 AM

Best Corrected Visual Acuity (BCVA) and Central Macular Thickness (MAT) Outcomes After Fluocinolone Acetonide Intravitreal Implant Injection

- Dana M. Deupree, MD
- Manuel Paez-Escamilla, MD, FICO
- Eric Deupree, BS
- Michael Tolentino, MD

OBJECTIVE To evaluate BCVA and MAT after Fluocinolone acetonide intravitreal (FAc) implant in diabetic patients who had previously received other modes of treatment

PURPOSE Diabetic retinopathy (DR) is an important cause of visual impairment and blindness. The most common cause of vision loss is diabetic macular edema (DME). FAc is an intravitreal device that its released over a 3 years. There have been previous European reports about the effectiveness of FAc in refractory eyes. Thus, the purpose of this study is to evaluate the efficacy of FAc in the United States

METHODS A retrospective observational case series from a single retina practice in Florida, involving 62 patients and 80 eyes, treated with FAc intravitreal implant from February 2015 to December 2017. The variables measured were best corrected visual acuity (BCVA), central macular thickness by OCT (CMT), intraocular pressure (IOP), follow-up before injection, follow-up after injection and cataract surgery. The patient population in this case series had been previously treated with intravitreal and

periocular steroids, anti-vascular endothelial growth factor inhibitors (anti-VEGF), focal laser, micropulse laser, pan-retinal photocoagulation (PRP), and pars plana vitrectomy (PPV)

RESULTS Mean age was 67 years(33-97),23(42.59%) were female and 31(57.40%) were male,DME duration ranged between 2 and 9 years.Follow up before FAc was 41 months(2-96),follow up after injection was 10 months(1-26).67 eyes (83.75%) were previously treated with dexamethasone intravitreal implant,21 (26.25%) with sub-Tenon's TAC,58(72.5%) with anti-VEGF therapy,15(18.7%) with micro-pulse laser,15(18.7%) with FL coagulation,26 (32.5%) with PRP,and 15(18.7%) with PPV.4 eyes(5%) were treated with ranibizumab,51(63.8%) with bevacizumab, and 2 eyes(2.5%%) with aflibercept.76 eyes passed a steroid challenge.Baseline mean BCVA was 75.27 letters(10-100),mean CMT was 326.321µm(276-377),and mean IOP was 16 mmHg(of 8-24) .Final BCVA was 83.57 letters(35-100),CMT was 271.846µm (244-298),7 eyes(8.8%) required cataract surgery.BCVA before FAc injection versus BCVA after FAc injection,had a mean of 8 letters of gain(*P=0.011)*.Mean CMT decreased by 54.884µm(*P=0.003)*.IOP increased by a mean of 0.78 mmHg

CONCLUSION FAc implant represents a safe and effective alternative in the management of chronic refractory diabetic macular edema, it is effective in improving best corrected visual acuity, and in decreasing central macular thickness. Results from this real-life setting shows that FAc is a safe treatment modality with sustained results that can be safely offered to patients

11:44 AM

Preoperative Intravitreal Bevacizumab for TRD Secondary to PDR: A Prospective Randomized Clinical Trial of the PACORES Group

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OBJECTIVE The purpose of this study was to determine the effectiveness and safety of an intravitreal injection of 1.25 mg of bevacizumab as a pre-operative adjunct to PPV in eyes with TRD secondary to PDR.

PURPOSE To assess the effectiveness and safety of an intravitreal injection of 1.25 mg of bevacizumab (IVB) as a pre-operative adjunct to small-gauge pars plana vitrectomy (PPV) compared to PPV alone in eyes with tractional retinal detachment (TRD) secondary to proliferative diabetic retinopathy (PDR).

METHODS Prospective, double-masked, randomized, active-controlled clinical trial. Study arm: Pre-operative bevacizumab (3-5 days) before PPV. Control arm: PPV without pre-

operative bevacizumab (sham injection). All eyes underwent a baseline exam included best corrected visual acuity (BCVA), color photos, optical coherence tomography (OCT) and fluorescein angiography (FA). Improving surgical field visualization, reducing operative time, and intra-operative complications were the main outcome measures. Patients were followed for 12 months.

RESULTS 211 (211 eyes) patients were enrolled and randomized with a 3:1 ratio to PPV plus IVB ([IVB group] 158 eyes) or PPV plus sham ([control] 53 eyes). Iatrogenic retinal breaks were intraoperatively noted in 63 eyes (39.8%) in the IVB group, and 38 eyes (56.6%) in the control group (p=0.003). In the IVB group 50 (31.6%) eyes had grade 2 intraoperative bleeding, while 38 (53%) eyes had that level of intraoperative bleeding in the control group (p=0.001). All these patients required endo-diathermy. Mean operative time was 55 minutes in the IVB group and 68 minutes in the control group (p=0.072). Early postoperative vitreous hemorrhage was observed in 51 (32.2 %) eyes in the IVB group, and 38 (71.6%) eyes in the control group (p=0.001). In the IVB group BCVA improved from logMAR 2 ± 0.5 to logMAR 0.7 ± 0.48, in the control group, BCVA improved from logMAR 1.9 ± 0.5 to logMAR 0.9 ± 0.31 (p=0.068). There was no significant difference between groups in terms of retinal reattachment.

CONCLUSION Pre-operative intravitreal bevacizumab therapy as an adjuvant to pars plana vitrectomy may be helpful and beneficial for patients with TRD secondary to severe PDR. Pre-operative IVB seems to reduce intraoperative bleeding, improve surgical visual field visualization, and reduce intraoperative and postoperative complications.

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

11:49 AM

Does the Presence of Diabetic Retinopathy Influence the Visual Outcome After Cataract Surgery?

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OBJECTIVE Is the visual outcome of cataract surgery in diabetic eyes inferior to non-diabetics?

PURPOSE Given the recent advances in diabetic management with tighter blood glucose control, better treatment of retinopathy, and recent advances in pharmacotherapy of diabetic macular edema with anti-vascular endothelial growth factor agents, this large scale study evaluates the visual outcome and the current incidence of postoperative CME in a real-world clinical setting.

METHODS Retrospective review of eyes that underwent cataractextraction in 8 United Kingdom (UK) National Health Service Hospitals that uses the same electronic medical records software (Medisoft Ophthalmology; Leeds, UK) was performed. Eyes with associated co-pathologies including glaucoma, uveitis and age related macular degeneration were excluded and so were eyes that underwent other intraocular surgery prior to or combined with cataract surgery. Eyes were classified into 2 groups based on diabetic status; diabetic group and non-diabetic (reference) group. Change in vision and incidence of cystoid macular edema (CME) after cataract extraction were analyzed as the primary outcomes.

RESULTS Of 202,564 eyes that underwent phacoemulsification surgery between 2005 - 2015, 27,561 and 90,686 in the diabetic and the reference group were included in the analysis. Mean ± SD change in visual acuity at 4-12 weeks visit was 0.4 ± 0.5 logMAR in

the diabetic group and 0.42 ±0.48 in the reference group. The proportion of eyes achieving 0.3 logMAR (20/40) vision were 60.9% and 63.8% in the diabetic and reference group, respectively, (P<0.001), and the percentage of eyes gaining ≥ 0.3 log MAR units was 82.7% in the diabetic group and 89.0% in the reference group (P<0.001). The rate of postoperative CME varied between the 2 groups (3% vs 0.8%, respectively; P<0.001). Multiple logistic regression showed that the presence of diabetic macular edema, and the diabetic retinopathy grade were independent factors for developing CME after surgery with the the odds being 2.2, 5.6, 5.4, 7.9, and 5.67, in eyes with very mild NPDR, mild NPDR, moderate NPDR, severe NPDR and PDR, respectively

CONCLUSION We found a significant improvement in VA of 0.4 logMAR units after cataract surgery in eyes with diabetes and diabetic retinopathy. However, compared to non-diabetic eyes, there were significantly higher rates of CME after surgery and a lower postoperative vision. Risk of developing CME was mostly proportionate to the grade of retinopathy.

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