7/30/2023 12:00 am

Diabetic Retinopathy Symposium 2

Defining a "Strong" and "Weak" Response to Anti-VEGF Treatment CI-DME: Retrospective Analysis of 3 DRCR Retina Network Clinical Trials

Sharon Solomon, MD

Objective: To define “strong” versus “weak” anti-VEGF treatment response in eyes with center-involved diabetic macular edema.
Purpose: Identification of biomarkers associated with future response to anti-VEGF treatment is a major unmet need in the development of new therapies for center-involved diabetic macular edema (CI-DME). Lack of consensus on standardized phenotypes that allow comparison across studies, treatments, and methods of evaluation have hampered this issue. Our purpose is to develop standardized phenotypes for future research by characterizing visual and anatomic outcomes in eyes treated with anti-vascular endothelial growth factor (anti-VEGF) therapy for CI-DME among eyes enrolled in DRCR Retina Network randomized clinical trials
Methods: Participants enrolled in DRCR Retina Network Protocol I, Protocol T, and Protocol V were included in these analyses if they were randomly assigned to anti-VEGF therapy (aflibercept, bevacizumab, or ranibizumab) and had visual acuity of 83 letters or fewer (approximate Snellen equivalent 20/25 or worse) and OCT central subfield thickness (CST) greater than or equal to the threshold values for CI-DME. Phenotypes were developed based on change in visual acuity and optical coherence tomography from baseline at 24 weeks.
Results: Based on the distribution of change from baseline at 24 weeks, we defined strong VA response as ≥5, 10, or 15-letter gain when baseline VA was 20/25–20/32, 20/40–20/63, or 20/80–20/320, respectively. Similarly, we defined strong CST response as ≥50, 100, or 200-µm reduction in CST when baseline CST was <75 µm, 75–<175 µm, and ≥175 µm, respectively, above the CI-DME threshold. Eyes not meeting these criteria were categorized as having weak VA/CST response. At 24 weeks, outcomes for strong response were achieved by 50% (476 of 958 eyes) for VA and 53% (505) for CST; 32% (303) had both strong VA and CST responses. Among eyes with strong VA and CST response at 24 weeks, 69% (195 of 281) maintained strong VA and CST response and only 20 (7%) had weak VA and CST response. Outcomes rates were similar across Protocols and when alternative cutoffs were defined based on linear regression.
Conclusion: These phenotypes are suitable for efforts to identify predictive biomarkers for response to anti-VEGF therapy for DME and will be used in DRCR Retina Network clinical studies and artificial intelligence initiatives.

IRB APPROVAL Yes

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Diabetic Retinopathy Symposium 2

Geographic Trends in the Recruitment of Participants of Racial and Ethnic Minorities for Diabetic Retinopathy-Related Clinical Trials

- Vivienne Hau, MD, PhD
- Jennifer Pinal, BA

Objective: Where are the geographic trends in the recruitment of racial and ethnic minorities in diabetic-retinopathy-related US clinical trials in the last 10 years?
Purpose: This study identifies trends in the recruitment of racial and ethnic minorities by geographic location in retina clinical trials in the last 10 years to examine health inequities relating to representation. Our prior research of retina clinical trials revealed a lack of demographics reporting, underrepresentation of racial and ethnic minorities compared to U.S. Census data, and a majority of Black and Native Hawaiian/Pacific Islander (NH/PI) participants present in Diabetes-related trials (i.e. diabetic macular edema, non-proliferative diabetic retinopathy, proliferative diabetic retinopathy) compared to other disease states studied (i.e. Retinal Vein Occlusion and Age-Related Macular Degeneration). We hypothesize that limited trial sites are recruiting the majority of Black, NH/PI and Latinx/Hispanic patients and the majority of sites need to improve their diversity of recruitment.
Methods:
This cross-sectional study examined data from completed US-based ophthalmology trials registered on ClinicalTrials.gov from 1/26/12-1/26/22. Results available for completed interventional phase II, III, and IV clinical trials for U.S. participants of all ages, sexes, with the term “retinal diseases” were searched. To be included, trials had to be categorized as completed and have available results. Trials that were completed but without results reported were excluded. Also excluded were studies with unknown status and those that were not yet recruiting, still recruiting, enrolling by invitation, active but not recruiting, suspended, terminated, or withdrawn.
Results:
157 studies were identified with a total of 96 US- based trials with 13016 participants included in the study. 80 clinical trials, 7731 participants, were included for qualitative analysis. 31 Diabetes-related trials with 2677 participants were identified. Diabetes-related trials were stratified by race and ethnicity (Hispanic) per OMB standards, with the following race categories: Black, AIAN, NHPI. The lack of race data reduced the number of trials to 21. Of these, Black, AIAN, NHPI, and Hispanic participants were present in 20, 9, 5, and 13 of these trials, respectively. Studies with Black and Hispanic patients each had one trial site that comprised 2.89 and 2.5 standard deviations away from the mean, respectively.
Conclusion: Only a limited number of trial sites are recruiting participants of racial and ethnic minority groups. Sponsor-initiated studies need to proactively engage sites that can better reflect the demographics of the local population and individual sites must take into account local demographics as well. Further studies can examine the socioeconomic factors that may be barriers to accessing clinical trials based on these geographic findings.

IRB APPROVAL No - exempt

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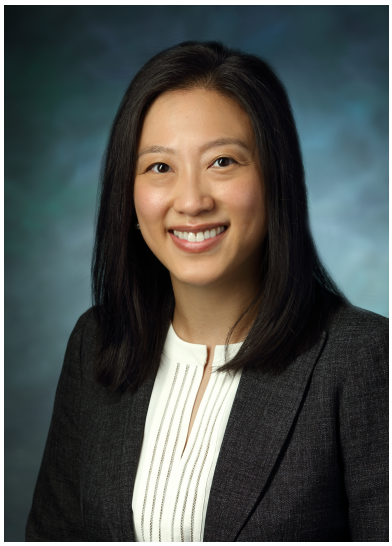
Diabetic Retinopathy Symposium 2

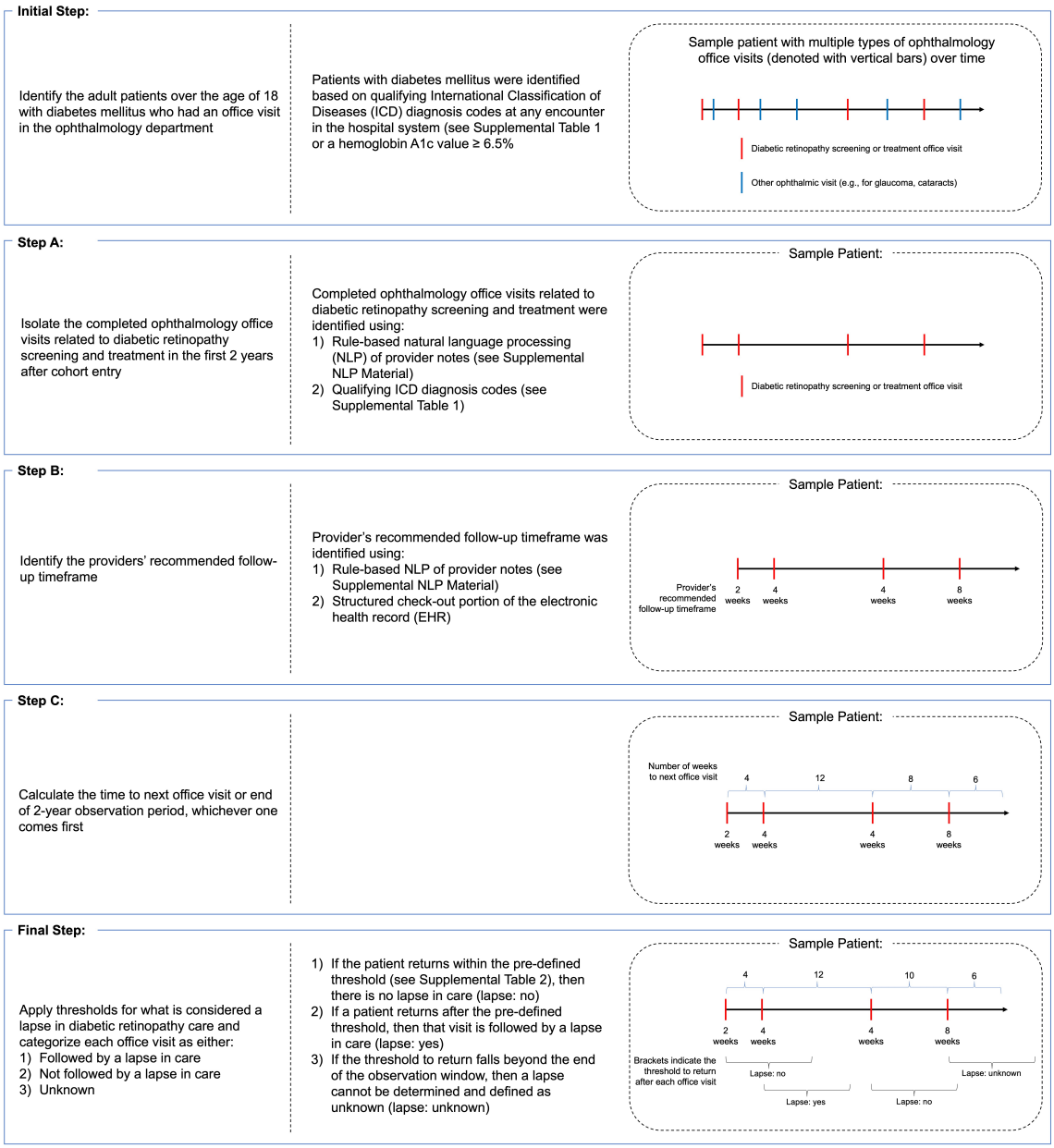
Health Disparities in Lapses in Diabetic Retinopathy Care



- Cindy Cai, MD
- DIep Tran
- Tina Tang
- Wilson Liou
- Keith Harrigian
- Emily Scott
- Paul Nagy
- Hadi Kharrazi
- Deidra Crews
- Scott Zeger

Objective: Are there health disparities by race and ethnicity in risk of lapses in diabetic retinopathy care?
Purpose: The purpose was to develop a novel methodology to identify lapses in diabetic retinopathy care in the electronic health record (EHR) and evaluate health disparities by race and ethnicity.
Methods: This was a retrospective cohort study of adult patients with diabetes mellitus evaluated at a single academic institution from 1/1/2013 to 4/2/2022. The methodology to identify lapses in care first identified diabetic retinopathy screening or treatment visits, and then compared the providers' recommended follow-up timeframe with the patient's actual time to next encounter. The methodology used a combination of structured data (e.g., International Classification of Diseases codes) and natural language processing of provider progress notes. The main outcome measure was a lapse in diabetic retinopathy care—when the patient did not return for care within the provider's recommended timeframe. The association of race and ethnicity with odds of lapses in care was evaluated using a mixed effects logistic regression model controlling for age, sex, insurance, severity of diabetic retinopathy, presence of other retinal disorders, and glaucoma.
Results: The methodology to identify diabetic retinopathy-related visits had a 95.0% (95% confidence interval (CI) 93.0 to 96.6) sensitivity and 98.8% (98.1 to 99.3) specificity as compared to a gold standard grader. The methodology resulted in a 97.3% (96.2 to 98.4) sensitivity and 98.1% (97.3 to 98.9) specificity for detecting a follow-up recommendation, with an average error of -0.05 (-0.31 to 0.21) weeks in extracting the precise timeframe. A total of 39,561 patients with 91,104 office visits were included in the analysis. The average age was 61.4 years. More than three in four (77.6%) patients had a lapse in care. In multivariable analysis, non-Hispanic Black patients had 1.24 (1.19 to 1.30) odds and Hispanic patients had 1.26 (1.13 to 1.40) odds of ever having a lapse in care compared to non-Hispanic White patients, ($p<0.001$, respectively).
Conclusion: We have developed a reliable methodology for identifying lapses in diabetic retinopathy care that is tailored to a provider's recommended follow-up. Using this approach, we find that three in four patients experience a lapse in diabetic retinopathy care and that these rates are higher among non-Hispanic Black and Hispanic patients. Deploying this methodology in the EHR is one potential means by which to identify and mitigate lapses in critical ophthalmic care in patients with diabetes.

IRB APPROVAL Yes



Methodology for identifying lapses in diabetic retinopathy care

	Ever have a lapse in care N (%)	Adjusted Odds Ratio* (95% Confidence Interval)	P-value
Age (years)			
≤20	87 (83.7)	(reference)	
>20 to ≤45	3960 (84.3)	0.68 (0.42, 1.08)	0.103
>45 to ≤65	14,971 (79.3)	0.50 (0.31, 0.8)	0.004
>65	11,689 (73.6)	0.38 (0.24, 0.61)	<0.001
Sex			
Female	16,169 (78.4)	(reference)	
Male	14,538 (76.8)	0.97 (0.93, 1.01)	0.103
Race and Ethnicity			
Non-Hispanic White	13,492 (72.7)	(reference)	
Non-Hispanic Black	11,905 (82.1)	1.24 (1.19, 1.30)	<0.001
Hispanic	1577 (82.5)	1.26 (1.13, 1.40)	<0.001
Other	3733 (81.5)	1.38 (1.29, 1.47)	<0.001
Insurance			
Private	11,478 (77.4)	(reference)	
Medicare	11,888 (75.7)	1.05 (0.99, 1.10)	0.096
Medicaid	3693 (87.6)	1.26 (1.18, 1.35)	<0.001
Other	2208 (69.8)	0.81 (0.75, 0.87)	<0.001
None	893 (85.5)	1.46 (1.27, 1.68)	<0.001
Diabetic Retinopathy (DR)			
No DR	23,895 (76.3)	(reference)	
Non-proliferative diabetic retinopathy (NPDR)	4879 (81.9)	0.47 (0.45, 0.49)	<0.001
Proliferative diabetic retinopathy (PDR)	1933 (85)	0.31 (0.29, 0.33)	<0.001
Other retinal disorders			
Absent	29,342 (77.5)	(reference)	
Present	1365 (81.2)	0.76 (0.70, 0.82)	<0.001
Glaucoma			
Absent	25,691 (76.6)	(reference)	
Present	5016 (83.5)	1.18 (1.12, 1.24)	<0.001

* Marginal odds ratios are presented

Adjusted odds ratio for having a lapse in diabetic retinopathy care

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Diabetic Retinopathy Symposium 2

Elevatum Study Design and Rationale: A Phase 4 Trial of Faricimab (VABYSMO) in Underrepresented Patients With Diabetic Macular Edema

- Joseph Coney, MD, FASRS
- Adrienne Scott, MD, FASRS
- Manuel Amador, MD
- Jennifer Chang, PharmD, MBA
- Ivaylo Stoilov, MD
- Matt Meldorf, MD
- Luis Gonzalez, MD, MPH
- Matthew Cunningham, MD, FASRS

Objective: The aim of Elevatum is to evaluate the treatment response and safety of faricimab in traditionally underrepresented, treatment-naïve patients with diabetic macular edema.
Purpose: Patients from minority populations are historically underrepresented in clinical trials. The phase 4 Elevatum trial was designed to evaluate the treatment response and safety of VABYSMO (faricimab-svoa, which is approved by the US Food and Drug Administration for the treatment of diabetic macular edema [DME] and neovascular age-related macular degeneration) in underrepresented patients with DME and identify factors that limit their participation in clinical trials.

Methods: Elevatum (NCT05224102) is a phase 4, multicenter, open-label, single-arm, 1-year trial of faricimab that includes patients who self-identify as Black or African American (~45% of the total enrollment); Hispanic or Latin American (~45% of the total enrollment); or Native American, Alaska Native, Native Hawaiian, or Pacific Islander (~10% of the total enrollment). Approximately 120 patients in the United States (aged ≥ 18 years) with treatment-naïve DME will be enrolled from 40 sites. Key ocular inclusion criteria are central subfield thickness ≥ 325 µm and best-corrected visual acuity (BCVA) of 20–73 Early Treatment Diabetic Retinopathy Study letters (~20/40–20/400 Snellen equivalent). All patients will receive intravitreal faricimab 6.0 mg every 4 weeks (Q4W) up to week 20 (6 injections), then faricimab 6.0 mg Q8W up to week 52.

Results: The primary outcome is change in BCVA from baseline at week 56. Other variables to be collected through week 56 include diabetic retinopathy severity, multimodal imaging (spectral-domain optical coherence tomography [OCT] and OCT angiography), aqueous humor samples, and systemic and diabetic disease assessments, including HbA1c (glycated hemoglobin), lipid panel, urinalysis, genotyping (whole-genome and whole-exome sequencing and apoliprotein-1), and hip and waist measurements. Patient-reported measures of diabetes disease burden (Diabetes Symptom Checklist-Revised, Diabetic Distress Scale, International Physical Activity Questionnaire, and Mediterranean Diet Adherence Screener) and social determinants of health (primary language, housing status, education, employment, insurance, and zip codes) will also be assessed.

Conclusion: The Elevatum trial was designed to improve understanding of the use of faricimab in underrepresented patients with DME and the associated social, health, and operational barriers that limit trial recruitment and retention in these populations.

IRB APPROVAL Yes