10/9/2021 8:05AM

Loss to Follow-up in Patients With Proliferative Diabetic Retinopathy Treated With Anti-VEGF Therapy and/or PRP in the United States

- Rahul N. Khurana, MD, FASRS
- Charles Li, BA
- Alayna Myrick, MS
- Flora Lum, MD

OBJECTIVE To determine the incidence of loss to follow up in patients with proliferative diabetic retinopathy treated with anti-VEGF therapy and/or PRP in the United States through the IRIS® Registry

PURPOSE When patients are lost to follow up, the ideal care is not delivered and patients likely suffer irreversible vision loss. The purpose of this study is to determine the incidence of loss to follow up in patients with proliferative diabetic retinopathy (PDR) treated with anti-VEGF injections and/or panretinal photocoagulation (PRP) in the United States and identify associated risk factors.

METHODS This is a retrospective cohort analysis involving 102,867 eyes of patients with PDR identified from the national IRIS Registry®. The patients were newly diagnosed between January 1, 2013- December 31, 2015 and treated with anti-VEGF therapy and/or PRP between January 1, 2013- December 31, 2018. Loss to Follow up (LTFU) was defined as interval greater than 12 months from last treatment. Multivariable logistic regression analysis involving baseline demographic and clinical conditions were utilized to determine odds ratios (OR) and 95% confidence intervals (CI).

RESULTS For PDR treated with anti-VEGF therapy alone, 10.7% (95% CI, 10.3-11.0) of patients were LTFU. For PDR treated with PRP alone, 9.5% (95% CI, 9.2-9.8) of patients were LTFU. For PDR treated with Anti-VEGF and PRP, 9.8% (95% CI, 9.4-10.1) of patients

were LTFU. For PDR treated with anti-VEGF therapy alone, odds of LTFU among African-American patients (OR, 1.2; 95% CI, 1.1-1.3; p=0.005) and Hispanic patients (OR, 1.2; 95% CI, 1.0-1.3; p=0.008) were greater than with white patients. Odds of LTFU were lower with Medicare Insurance (OR, 0.8; 95% CI, 0.7-0.9; p<0.0001) compared to Private Insurance. For PDR treated with PRP alone, odds of LTFU among African-American patients (OR, 1.4; 95% CI, 1.2-1.6; p<0.0001) and Hispanic patients (OR, 1.3; 95% CI, 1.1-1.5; p=0.0013) were greater than with white patients. Odds of LTFU were lower with Medicare Insurance (OR, 0.7; 95% CI, 0.6-0.8; p<0.0001) and higher with Medicaid (OR, 1.2; 95% CI, 1.0- 1.5; p=0.03) compared to Private Insurance.

CONCLUSION There is a high rate of LTFU after anti-VEGF injections and PRP among patients with PDR. Risk factors identified included increasing age, male sex, African-American ethnicity, Hispanic ethnicity, unilateral involvement and private insurance. Improving treatment adherence and follow up is critical to prevent vision loss in PDR.

IRB APPROVAL No — I received a determination that the study/activity qualified for **exempt status or that it did not require IRB approval** from an IRB or another authorized oversight body *(IRB Exemption Letter may be requested)*.

10/9/2021 8:11AM

Race Representation in Diabetic Macular Edema Randomized Control Trials Compared to the United States Census Data

- Abdul-Hadi Kaakour, MD, MS
- Hong-Uyen Hua, MD
- Aleksandra V. Rachitskaya, MD, FASRS

OBJECTIVE To compare the distribution of race in diabetic macular edema (DME) randomized control trials (RCTs) to that of United States (US) racial census data.

PURPOSE It is important that RCTs represent real world patient populations. Lack thereof might affect external validity of studies and limit real world applications to underrepresented minorities.

METHODS We performed a cross-sectional study of the racial demographics of 15 RCTs for DME and compared them to the US 2010 Census data. The number and percent of White, Black, Hispanic, Asian, American Indian/Alaska Native and Native Hawaiian/Pacific Islander participants were recorded. Each RCT demographic distribution was compared to the reported distribution of the 2010 US Census data using the chi-square test. The proportion of each race was also compared to its reported proportion from the 2010 Census data using one-sample z-test for proportion. A p-value of <0.05 was designated for the determination of statistical significance.

RESULTS Compared to the US Census data, in the 15 RCTs for DME treatment, the White patient cohort was underrepresented in 2 RCT and overrepresented in 10 RCT. The difference was not statistically significant in 3. The Black patient cohort was underrepresented in 6, overrepresented in 3 RCT, and not statistically different in 6. The Hispanic patient cohort was underrepresented in 9, overrepresented in 3 RCT, and not statistically different in 3. The Asian patient cohort was underrepresented in 8, overrepresented in 3 RCT, and not statistically different in 4. The American Indian/Alaska Native and Hawaiian/Pacific Islander patient cohort was underrepresented in 4 RCT and not statistically different in 11. The chi-square values comparing RCT demographic distribution to US 2010 Census data were significantly different (p-value <0.05) in 15 out of 15 RCTs.

CONCLUSION This study finds that that racial demographic data of subjects in the majority of RCTs for treatment of DME does not reflect that of the US population, according to the 2010 Census. Subjects identified as White tend to be overrepresented in RCTs. More efforts should be made to recruit underrepresented minorities to improve trial external validity and to better serve these populations.

IRB APPROVAL Not applicable — I responded “No” to previous question regarding human

subjects.

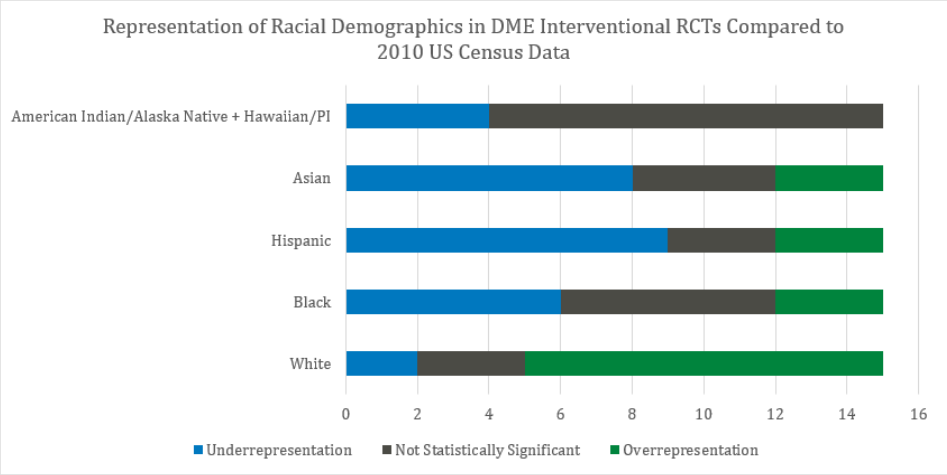


Figure 1: Stacked bar chart showing the number of RCTs (x-axis) and under/overrepresentation of each race compared to US 2010 Census data. The number of trials with significant underrepresentation of each race is in blue; the number with significant overrepresentation of each race is in green. The number of RCTs that did not have significantly differing representation of each respective race is marked in gray.

10/9/2021 8:17AM

Impact of Race on Vision Outcomes in Ranibizumab-Treated Patients With Diabetic Macular Edema: A Meta-Analysis of 5 Clinical Trials

- M. Ali Khan, MD
- Lauren Hill, BA, MS
- Ivaylo Stoilov, MD
- Julia A. Haller, MD

OBJECTIVE To assess the impact of race on vision outcomes in patients with diabetic macular edema (DME) treated with ranibizumab.

PURPOSE Visual responses to anti–vascular endothelial growth factor therapy for DME may differ between races. This meta-analysis investigated whether vision outcomes differ between Black and White patients treated with ranibizumab (0.3 mg or 0.5 mg) for DME.

METHODS All treatment arms were pooled (RIDE/RISE [NCT00473382/NCT00473330] and DRCR.net Protocols I [NCT00444600], S [NCT01489189], and T [NCT01627249]). Included patients had best-corrected visual acuity (BCVA) data at baseline (BL), month (M) 12, and M24. Outcomes included mean BCVA over time and mean change in BCVA from BL at M24 adjusted for BL BCVA. To control for differences in BL characteristics, RIDE/RISE data were also evaluated in propensity-matched cohorts of Black and White patients, based on the following variables: age, sex, BL glycated hemoglobin, BL central subfield thickness, BL BCVA, number of ranibizumab injections by M24, and total number of clinic visits.

RESULTS Across trials, 181 Black and 928 White patients received ranibizumab and had BCVA data at BL and M24. Mean (95% CI) BCVA was higher at BL in Black versus White patients (Figure 1; 66.7 [65.0, 68.4] vs 62.0 [61.1, 62.8] letters, respectively) but was comparable at M24 (72.8 [70.2, 75.4] vs 72.2 [71.2, 73.1] letters). Mean BCVA change from BL at M24 was higher in White patients (10.2 [9.3, 11.1] letters) versus Black patients

(6.1 [3.6, 8.6] letters). When adjusted for differences in BL BCVA, mean BCVA change from BL remained higher in White versus Black patients (10.0 [9.1, 10.9] vs 7.8 [5.8, 9. 7] letters; P = 0.04). In addition, 27.6% (50/181) of Black and 35.0% (325/928) of White patients gained ≥ 15 letters at M24, while 5.0% (9/181) and 3.2% (30/928) lost ≥ 15 letters, respectively. When groups were propensity matched in RIDE/RISE, mean change from BL BCVA was comparable between Black and White patients (10.6 [7.1, 14.1] vs 10.1 [7.3, 12.9] letters; P = 0.83).

CONCLUSION Assessment of treatment outcomes in racial subgroups, including Black patients, is limited by clinical trial enrollment. Existing data are not conclusive enough to determine the magnitude of impact that race has on DME treatment outcomes. Increased enrollment of racial subgroups in clinical trials will be critical for future analyses. Work is needed to augment enrollment of racial subgroups.

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

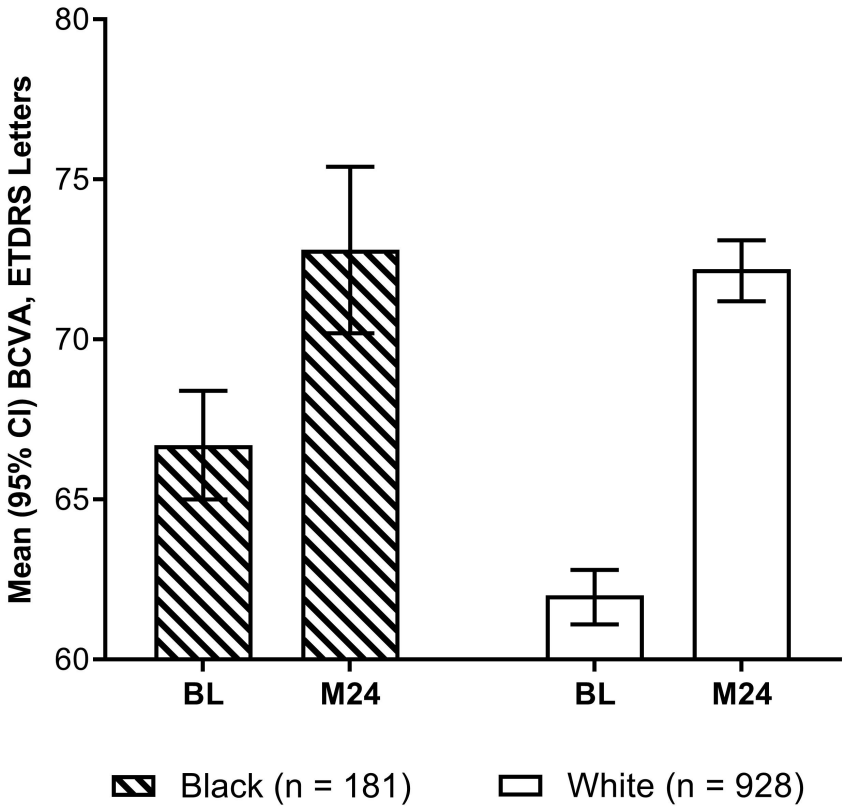


Figure 1. Observed BCVA at BL and M24. Key: BCVA, best-corrected visual acuity; BL, baseline; ETDRS, Early Treatment Diabetic Retinopathy Study; M, month.

10/9/2021 8:21AM

Fluctuations in Central Subfield Thickness Associated With Worse Visual Outcomes in Patients With Diabetic Macular Edema in Clinical Trial Setting

- Matthew Starr, MD
- Mirataollah Salabati, MD
- Raziyeh Mahmoudzadeh, MD
- Luv Girish Patel, MD
- Michael Ammar, M.D.
- Jason Hsu, MD
- Sunir J. Garg, MD, FACS, FASRS
- Allen C Ho, MD
- Ajay E Kuriyan, MD, MS

OBJECTIVE Do large fluctuations in central subfield thickness in patients with diabetic macular edema lead to worse vision over time?

PURPOSE This study examines the relationship between fluctuations in central subfield thickness (CST) and visual acuity in patients with diabetic macular edema (DME) using data from two large clinical trials.

METHODS This study was a post-hoc analysis utilizing clinical trial databases from the diabetic retinopathy clinical research (DRCR) Protocols T and V. Eyes with at least 3 CST readings and visual acuity recordings at 1 year were included. Standard deviation (SD) of all recorded CSTs for each patient during the study period were calculated and patients to quantify the fluctuations in CST. Patients from each protocol were grouped into quartiles based on the SD of CSTs. The primary outcomes were visual acuity at 1 and 2 years for each Protocol, stratified based on SD quartile.

RESULTS A total of 1,197 eyes were included in the analysis with 559 eyes (47%) from Protocol T and 638 eyes (53%) from Protocol V. The mean age for all eyes was 59.3 ± 10.2 years with 503 females (42%). There were significant visual acuity differences based on CST SD quartile for both Protocols while adjusting for mean baseline visual acuity, baseline

CST, lens status, hemoglobin A1c, and treatment arm. Quartile 1 had the least fluctuation in CST and quartile 4 had the most fluctuation. At week 104 in Protocol T, the difference between the first and fourth quartiles was -3.59 Early Treatment Diabetic Retinopathy Study (ETDRS) letters (95% CI, -6.17 to -1.00). In Protocol V at week 52 the difference between the first and fourth quartiles was -3.04 ETDRS letters (95% CI, -4.18 to -1.91). At week 104: this difference was -2.35 ETDRS letters (95% CI, -3.58 to -1.13).

CONCLUSION Large fluctuations in CST may portend worse visual acuity outcomes at the 2 year endpoint in patients with DME.

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

10/9/2021 8:39AM

Impact of Nonperfusion and Leakage Areas on Diabetic Macular Edema/Vision-Threatening Complications in Nonproliferative Diabetic Retinopathy (NPDR)

- W. Lloyd Clark, MD

OBJECTIVE To assess impact of baseline angiographic characteristics on center-involved diabetic macular edema (CI-DME) or vision-threatening complication (VTC) rates in the PANORAMA study.

PURPOSE Identification of factors that increase risk of complications in patients with NPDR may help to inform treatment choices. This analysis assessed the impact of baseline retinal non-perfusion (NP) and leakage areas on rates of CI.DME or VTC (PDR/anterior segment neovascularization) in patients receiving intravitreal aflibercept injections (IAI) or sham injections through 100 weeks in PANORAMA.

METHODS This post hoc analysis of the PANORAMA trial included patients with moderately severe to severe NPDR (Diabetic Retinopathy Severity Scale [DRSS] 47–53) without baseline DME who were randomized to receive IAI 2 mg q16 weeks (N=135) or q8 weeks (PRN dosing in year 2; N=134), both after initial loading doses, or sham (N=133). For this analysis, IAI groups were combined. Baseline NP (mm2) was analyzed in 4 groups: G1: =0, n=201; G2: >0–≤0.24, n=52; G3: >0.24–≤0.66, n=53; G4: >0.66, n=51. Baseline leakage area (mm2) was analyzed by quartile: Q1: ≤10.20, n=98; Q2: >10.20–≤19.76, n=97; Q3: >19.76–≤30.41, n=97; Q4: >30.41, n=97.

RESULTS Higher proportions of sham-treated patients, compared with IAI-treated, had CI-DME/VTC as baseline NP/leakage area increased. Risk of CI-DME increased with baseline NP area (per 1 mm2 increase) with sham, hazard ratio: 1.32 (95% confidence interval: 1.04, 1.67), but not with IAI, 0.95 (0.68, 1.33). Results were similar with VTC risk, 1.44 (1.08, 1.92) with sham and 1.10 (0.89, 1.38) with IAI. CI-DME risk with increasing leakage area (per 1 mm2 increase) was 1.02 (0.99, 1.05) with sham and 1.03 (1.00, 1.07) with IAI; risk of

VTC was 1.08 (1.04, 1.12) with sham and 1.00 (0.96, 1.04) with IAI. Sham but not IAI was associated with reduced ≥2-step DRSS improvement and increased ≥2-step DRSS worsening with increasing baseline NP and leakage areas (not significant for NP).

CONCLUSION Increasing baseline retinal NP and leakage areas were associated with increased rates of CI-DME/VTC in the sham group. This association was not observed in the IAI-treated group. Retinal NP and leakage areas are important variables to consider when managing NPDR patients.

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

10/9/2021 8:43AM

Early Switch to the Dexamethasone Implant After Sub-Optimal Response to Anti-VEGF Therapy for Diabetic Macular Edema

- Shawn Kavoussi, MD
- Seenu M. Hariprasad, MD
- Jay Chhablani, MD
- Joseph Nezgoda, MD, MBA
- Michael A. Singer, MD
- Daniel F. Kiernan, MD, FACS
- Joseph N Martel, MD
- Sonny Caplash

OBJECTIVE Does early treatment with dexamethasone improve visual and antomic outcomes in real world patients with sub-optimal response to anti-vascular endothelial growth factor for diabetic macular edema?

PURPOSE In DRCR Protocol I Early Analysis, 26% of patients were non-responders to anti-vascularendothelial growth factor (AVF) monotherapy, but visual gains with steroid switch therapy in ProtocolU were limited by duration of diabetic macular edema (DME). Study of an earlier multi-factorialapproach is indicated. This study assesses treatment for DME with DEX after limited response to 1-3 monthly AVF.

METHODS This multi-center, retrospective series included 58 consecutive initially treatment-naïve patients with < 200 um reduction in central retinal thickness (CRT) and/or < 5 Early Treatment Diabetic RetinopathyStudy (ETDRS) letters gained after 1-3 intravitreal bevacizumab or aflibercept (AVF), who werethen switched to DEX with ≥ 6 weeks subsequent follow-up. EDTRS visual acuity and CRT were compared from baseline to post-AVF and post-DEX using t-tests.

RESULTS Baseline mean ± standard deviation (SD) best-corrected visual acuity (BCVA) was

55 ± 14letters. CRT was 453 ± 172 microns. After patients received one (26%), two (6%) or three (68%)monthly AVF, mean BCVA was 57 ± 14 letters (p=0.57) and CRT was 412 ± 134 um (p=0.16).After subsequent DEX, BCVA was 65 ± 13 letters (p=0.0001 compared to baseline and p=0.003compared to post-AVF) and CRT was 280 ± 57 um (p<0.0001 compared to both baseline andpost-AVF).

CONCLUSION In this cohort, patients with DME who had a limited visual and anatomic response to 1-3monthly doses of either intravitreal bevacizumab or aflibercept demonstrated significantimprovements after subsequent treatment with the dexamethasone 0.7 mg implant. Earlierintervention with DEX for treating DME may result in more rapid visual and anatomic gainscompared to AVF monotherapy in certain patients.

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

10/9/2021 8:47AM

Amine Oxidase Copper-Containing 3 Inhibitor (BI 1467335) in Non-Proliferative Diabetic Retinopathy: Double-Masked, Randomized, Phase IIa Study (ROBIN)

- Quan Dong Nguyen, MD, MSc, FARVO, FASRS
- Justis P. Ehlers, MD
- Xidong Jin, Ph.D., MBA
- Alison Mackie
- Michael Ehrlich
- David S. Boyer, MD

OBJECTIVE To evaluate the safety, tolerability, and efficacy of BI 1467335 in patients with non-proliferative diabetic retinopathy (NPDR) without center-involved diabetic macular edema (CI-DME).

PURPOSE Amine oxidase copper-containing 3 (AOC3) is involved in leukocyte recruitment, leading to inflammation. AOC3 inhibition may improve or stabilize the retinal pathology of NPDR by correcting the underlying hypoxia, ischemia, and edema. The purpose of this study is to evaluate the safety and potential efficacy of BI 1467335, an oral AOC3 inhibitor in the treatment of NPDR.

METHODS This Phase IIa, double-masked, randomized study (NCT03238963) included patients with NPDR (Diabetic Retinopathy Severity Scale [DRSS] Level of 47 or ≥53; N=79) without CI-DME. Patients with retinal neovascularization or prior treatment with a macular laser, intraocular injections, or pan-retinal photocoagulation were excluded. Patients received oral BI 1467335 10 mg (n=40) or placebo (PBO; n=39) daily for 12 weeks; post-treatment follow-up was 12 weeks. The primary endpoint was the proportion of patients with ocular events. Secondary endpoints were the proportion of patients with non-ocular events over 24 weeks and those with ≥2-step DRSS improvement from baseline at Week 12.

RESULTS The mean (SD) age of participants was 52.8 (12.1) years, 64.6% were male and 43.0% had severe NPDR. Mean study eye baseline best-corrected visual acuity was 81.8. The proportion of patients with ocular events over 24 weeks was higher in the BI 1467335

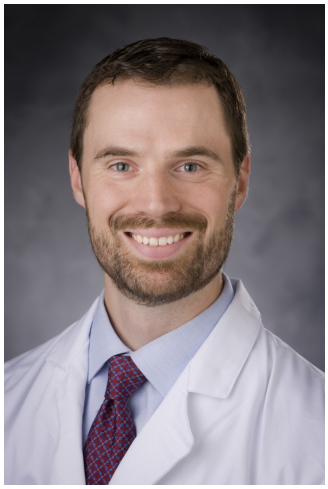
group (35.0%) than in the PBO group (23.1%). No ocular events of CTCAE >3 were reported. Treatment-emergent non-ocular events were reported for more PBO (82.1%) than BI 1467335 patients (55.0%). The large majority of non-ocular events were ≤3 CTCAE grade, while 1 non-drug related assessed non-ocular event (acute cholecystitis) of a BI 1467335 patient was considered Grade 4. 7 patients (BI 1467335, n=5) stopped treatment, none due to ocular events. At Week 12, 5.7% (n=2) of BI 1467335 patients had a 2-step improvement in DRSS (PBO: 0%) from baseline. Most patients had either no change in DRSS, 1-step worsening, or a 1-step improvement. Oscillation of DRSS levels was observed for individual patients over the 24-week study period.

CONCLUSION At 12 weeks, 2 BI 1467335 patients (5.7%) had a 2-step DRSS improvement from baseline vs 0% PBO patients. The risk difference (SE) of BI 1467335 vs PBO was 0.057 (0.039). Most patients had no change or a 1-step worsening/improvement. As high variability of DRSS levels for specific patients over time was noted, DRSS changes from baseline at individual time points should be interpreted with caution.

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

10/9/2021 8:51AM

APX3330, an Oral Drug in Trial for DR and DME, Demonstrated a Favorable Safety and Tolerability Profile in Multiple Phase 1 and 2 Studies



- Michael J Allingham, MD, PhD
- Eliot Lazar, MD
- Mitchell Brigell, PhD
- Curtis J Heisel, B.S.
- Jonah Yousif
- Kavon Rahmani
- Mark Kelley, PhD

OBJECTIVE To report safety data from over 300 subjects receiving oral APX3330 in support of ZETA-1, an ongoing clinical trial evaluating the efficacy of 600mg/day APX3330 for diabetic retinal disease.

PURPOSE APX3330 is a novel, small molecule inhibitor of Ref-1, a transcriptional regulator of key vascular and inflammatory signaling pathways relevant to diabetic retinopathy (DR), diabetic macular edema (DME), and neovascular age-related macular degeneration (AMD). We report systemic and ocular safety and tolerability results from six Phase 1 and five Phase 2 nonophthalmic clinical trials of APX3330.

METHODS Safety data for APX3330 were collected from over 300 healthy volunteers and patients with chronic hepatitis across five Phase 1 and five Phase 2 clinical trials in nonophthalmic indications at doses ranging from 20 mg/day to 600 mg/day. Additionally, safety data was obtained from a sixth phase 1 trial in which 19 patients with solid tumors received twice daily doses of APX3330 of up to 720 mg/day. Notably, many of the subjects received APX3330 for an average of 75 days. Adverse events were recorded for all trial participants in all studies.

RESULTS In 5 Phase 1 trials of APX3330 at single doses up to 240 mg and repeat doses up to 600 mg/day, <10% of subjects receiving APX3330 reported mild diarrhea compared to 0% in placebo treated subjects. In the sixth Phase 1 trial 2 patients receiving 720 mg/day exhibited a diffuse skin rash that quickly reversed with 600 mg/day dose, which was defined as the maximum tolerated dose. Four patients took 600 mg/day for over 6 months and 3 longer than 300 days without issue. In 5 Phase 2 trials involving over 200 patients, adverse events occurred in <5% of the patients and at a similar rate between placebo and APX3330, with occasional mild diarrhea seen with APX3330. One patient reported mild orbital discomfort. Based on preclinical data and its clinical safety profile, APX3330 (600 mg/day for 24 weeks) is being tested in a Phase 2 trial for the treatment of subjects with moderately severe to severe NPDR or mild PDR.

CONCLUSION APX3330 demonstrated a favorable safety and tolerability profile across 11 clinical studies at doses of up 600 mg/day. APX3330 has an anti-angiogenic and anti-inflammatory mechanism relevant to the treatment of retinal disease. These safety data support ZETA-1, an ongoing, randomized, placebo-controlled Phase 2 trial evaluating the safety and efficacy of APX3330 in the treatment of DR and DME.

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

10/9/2021 9:03AM

Baseline DR Severity and Time to DME Resolution in Patients Treated With Ranibizumab in the RIDE and RISE Clinical Trials

- Katherine E Talcott, MD
- Rishi P. Singh, MD
- Carolina Carvalho Soares Valentim, MD
- Lauren Hill, BA, MS
- Ivaylo Stoilov, MD

OBJECTIVE To assess the impact of baseline diabetic retinopathy (DR) severity on time to diabetic macular edema (DME) resolution in patients treated with ranibizumab in the RIDE and RISE clinical trials.

PURPOSE This post hoc analysis explored the impact of baseline DR severity on time to DME resolution in patients treated with ranibizumab in the phase 3 RIDE (NCT00473382) and RISE (NCT00473330) clinical trials. Baseline factors associated with time to DME resolution were also evaluated.

METHODS In RIDE/RISE, 759 patients were randomized 1:1:1 to monthly ranibizumab (0.3 mg or 0.5 mg) or sham for 24 months. This analysis included 416 ranibizumab-treated patients (0.3 mg and 0.5 mg arms pooled) with central subfield thickness (CST) > 250 µm and Diabetic Retinopathy Severity Scale (DRSS) score 35–85 at baseline. DME resolution, assessed at set visits (day 7 and months 1, 2, 3, 6, 12, 18, and 24), was defined as first visit with CST ≤ 250 µm. Frequency of DME resolution at months 12/24 and mean time to DME resolution were assessed by baseline DR severity (DRSS score 35/43, 47–53, and 60–85). Baseline predictors of time to DME resolution and DME resolution by month 24 were evaluated.

RESULTS The frequency of patients with DME resolution across baseline DRSS subgroups (35/43, 47–53, and 60–85) was similar at month 12 (52.6%, 55.0%, and 54.6%, respectively) and month 24 (70.7%, 68.9%, and 65.9%, respectively). Time to first DME resolution was shorter in eyes with more severe DR at baseline, with a mean (95% CI) time of 8.6 (6.9, 10.3) months for patients with baseline DRSS score 35/43, 8.0 (6.6, 9.4) months

for those with baseline DRSS score 47–53, and 5.8 (4.3, 7.3) months for those with baseline DRSS score 60–85 (Figure 1; P = 0.03). No other baseline variables were significantly associated with time to DME resolution (all P > 0.05). Baseline lens status was the only factor significantly associated with DME resolution by month 24. Rate of DME resolution by month 24 was higher in patients with phakic versus pseudophakic eyes at baseline (72.1% vs 59.8%; P = 0.01).

CONCLUSION The proportion of ranibizumab-treated patients who achieved DME resolution at months 12/24 of RIDE/RISE was similar across baseline DR severity subgroups. However, there was a significant trend for shorter time to DME resolution in patients with more severe DR at baseline. These findings may guide treatment decisions and patient expectations in clinical practice.

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

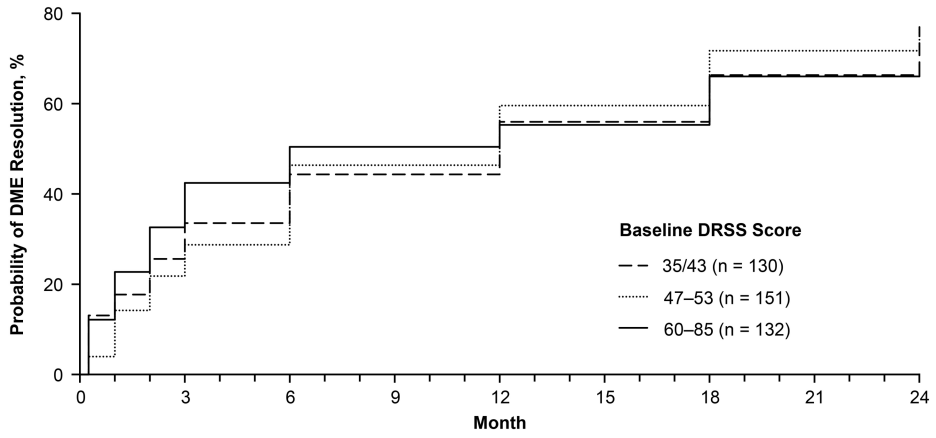


Figure 1. Kaplan-Meier plot of time to DME resolution over 24 months, stratified by baseline DR severity. DME, diabetic macular edema; DR, diabetic retinopathy; DRSS, Diabetic Retinopathy Severity Scale.

10/9/2021 9:07AM

Characteristics and the Need for Supplementation Following 0.19mg Fluocinolone Acetonide (FAc) in Diabetic Macular Edema (DME) Patients

- Victor Hugo Gonzalez, MD

OBJECTIVE To Evaluate the impact of a durable therapy on the need of supplemental treatments based on patient characteristics

PURPOSE Real-world studies show that non-adherence to treatment occurs at higher rates in patients with DME. This is problematic as DME patients are at risk for vision loss due to treatment delay. The FAc 0.19mg implant provides delivery of uninterrupted anti-inflammatory treatment of DME for up to 36 months. This data evaluates the impact of a durable treatment on the need of supplemental treatments.

METHODS PALADIN study is a US based, prospective real world observational study to evaluate the ILUVIEN implant in patients diagnosed with DME treated according to the US label. The patient population was divided into 4 groups based on the number of supplemental treatment events (including laser, intravitreal anti-VEGF and steroid) per year post FAc. These groups were stratified for ocular and non-ocular characteristics at baseline. Final outcomes of BCVA (best corrected visual acuity), CST (central subfield thickness) and treatment burden were reported amongst the treatment groups.

RESULTS PALADIN 24 month data included 115 eyes. A subset of 83 eyes based on 24 months pre and post FAc was divided into groups based on post FAc supplementation: Group A–Treatment Free (n=24), Group B >0-1 treatment per year (n=18), Group C >1-4 treatments per year (n=28) and Group D > 4 treatments per year (n=13). Baseline characteristics of Group A & B included mean VA 63.7 ETDRS letters and mean CST 374.7 µm. Prior to FAc, the mean number of treatments in Group A&B was 5.2 treatments per year. At 24 months, ~50.6% of patients received 1 or less supplemental treatment per year.

This was an 80% reduction in treatments per year. At 24 months, this group had stable vision (+0.7 BCVA letters). CST improved to 343.3µm. In contrast, Group C&D received 7.07 treatments per year prior to FAc. Baseline characteristics of Group C&D were 56.7 ETDRS letters and 403 µm. VA and CST improved to 60.4 BCVA letters and 367.8 µm post FAc. There was a 37.2% reduction in treatments per year in group C&D.

CONCLUSION Patients with highest treatment efficiency following FAc had mean BCVA Snellen equivalent of 20/63 and less edema at baseline (~374.7µm) compared to eyes that had worse BCVA (mean of 56.7 ETDRS letters) and greater edema (403 µm) at baseline. Preserving vision whilst utilizing fewer treatments can be optimized by patient selection particularly those with less edema and better vision at baseline.

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