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Evaluating the Impact of Intravitreal Aflibercept on Diabetic Retinopathy Progression in the VIVID-DME and VISTA-DME Studies

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Purpose: To evaluate the impact of intravitreal aflibercept (EYLEA, Regeneron Pharmaceuticals, Tarrytown, NY) versus laser on progression of diabetic retinopathy (DR) severity in Intravitreal Aflibercept Injection in Vision Impairment due to DME (VIVID-DME) and Study of Intravitreal Aflibercept Injection in Patients with Diabetic Macular Edema (VISTA-DME).

Design: Secondary and exploratory analyses of 2 phase 3, randomized, controlled studies.

Participants: All patients with a baseline Diabetic Retinopathy Severity Scale (DRSS) score based on fundus photograph (full analysis), patients who progressed to proliferative DR (PDR) (safety analysis) in VIVID-DME (n = 403) and VISTA-DME (n = 459), or both.

Methods: We randomized patients with diabetic macular edema (DME) to intravitreal aflibercept 2 mg every 4 weeks (2q4), intravitreal aflibercept 2 mg every 8 weeks after 5 initial monthly doses (2q8), or macular laser photocoagulation at baseline and sham injections at every visit.

Main Outcome Measures: Proportions of patients with 2-step or more and 3-step or more improvements from baseline in DRSS score, who progressed to PDR, and who underwent panretinal photocoagulation (PRP).

Results: Among patients with an assessable baseline DRSS score, most showed moderately severe or severe nonproliferative DR. The proportions of patients treated with 2q4, 2q8, and laser with a 2-step or more improvement in DRSS score at week 100 were 29.3%, 32.6%, and 8.2%, respectively, in VIVID-DME and 37.0%, 37.1%, and 15.6%, respectively, in VISTA-DME; the proportions with a 3-step or more improvement in DRSS score were 7.3%, 2.3%, and 0%, respectively, and 22.7%, 19.9%, and 5.2%, respectively. Fewer patients in the 2q4 and 2q8 groups versus the laser group progressed to PDR at week 100 in VISTA-DME (1.5% and 2.2% vs. 5.3%) and VIVID-DME (3.2% and 2.0% vs. 12.3%). The proportions of patients who underwent PRP were 2.9%, 0.7%, and 4.5%, respectively, in VIVID-DME and 1.9%, 0.7%, and 5.2%, respectively, in VISTA-DME. The most frequent serious ocular adverse event at week 100 was cataract (pooled intravitreal aflibercept, 1.7% of patients; laser, 3.5% of patients).

Conclusions: These analyses demonstrate the benefit of intravitreal aflibercept over laser with respect to DR progression, suggesting a benefit on DME, and on underlying DR. *Ophthalmology Retina 2018;2:988-996 © 2018 by the American Academy of Ophthalmology. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).*

See Editorial on page 985.

Diabetic retinopathy (DR) is a progressive dysfunction of the retinal vasculature resulting from chronic hyperglycemia.[1] Diabetic retinopathy has been classified into 4 stages: mild nonproliferative DR (NPDR), moderate NPDR, severe NPDR, and proliferative DR (PDR). Typical management of mild and moderate NPDR involves observation and improved control of diabetes, whereas severe NPDR and PDR require referral to an ophthalmologist. Treatment options for DR in the absence of diabetic macular edema (DME) target only proliferative stages of DR.

Diabetic macular edema may occur at any point in the course of DR, although it is more frequent as the disease progresses. Most vision loss associated with DR is the result of DME.[2] The estimated global prevalence of DME currently is approximately 21 million,[3] and this is expected to increase with the rising diabetes prevalence; diabetes is projected to affect nearly 600 million people worldwide by 2035.[4]

Intravitreal anti−vascular endothelial growth factor (VEGF) agents (aflibercept [EYLEA, Regeneron Pharmaceuticals, Tarrytown, NY] and ranibizumab) are superior to laser for the treatment of center-involved DME.[5−9] Intravitreal aflibercept showed similar sustainable visual acuity (VA) gains with dosing every other month compared with

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ranibizumab given monthly. More recently, the National Institutes of Health–funded Protocol T study conducted by the Diabetic Retinopathy Clinical Research Network compared intravitreal aflibercept, ranibizumab, and non-licensed bevacizumab head to head.[10] At 12 months, VA gains achieved with intravitreal aflibercept, the study's primary end point, were statistically superior to those achieved with ranibizumab or bevacizumab, particularly in patients with baseline VA of 20/50 or worse.[10] After 2 years, the visual gains achieved with intravitreal aflibercept were statistically superior to those with bevacizumab, but not ranibizumab[11]; however, an area under the curve analysis showed that mean change in VA over 2 years was greater with intravitreal aflibercept than with bevacizumab or ranibizumab.[12]

Vascular endothelial growth factor inhibition has been shown not only to influence the course of DME positively, but also to have a positive impact on overall DR severity.[6,13,14] Herein we report on an unplanned retrospective analysis of the impact of intravitreal aflibercept treatment on changes in Diabetic Retinopathy Severity Scale (DRSS) scores, progression of DR to PDR in patients with DME, and use of panretinal photocoagulation (PRP) in the Intravitreal Aflibercept Injection in Vision Impairment due to DME (VIVID-DME) and Study of Intravitreal Aflibercept Injection in Patients with Diabetic Macular Edema (VISTA-DME) studies.

Methods

Design

Study design and methods have been published previously.[8,9] Key details are summarized here. Both VIVID-DME (clinicaltrials.gov identifier, NCT01331681) and VISTA-DME (clinicaltrials.gov identifier, NCT01363440) were phase 3, randomized, double-masked, active-controlled, 148-week trials comparing 2 dosing regimens of intravitreal aflibercept with laser for the treatment of DME. The studies were conducted at 127 sites in the Unites States, Europe, Japan, and Australia and in accordance with the principles of the Declaration of Helsinki and International Conference on Harmonisation. All information presented in this study complies with the Health Insurance Portability and Accountability Act for United States sites. Institutional review board or ethics committee approval was obtained at each site before the studies commenced, and all patients provided written consent.

Participants

Adult patients with diabetes mellitus with central DME involvement (defined as retinal thickening involving the 1-mm central OCT subfield [central subfield thickness]) were included if best-corrected VA (BCVA) was between 73 and 24 letters (Snellen equivalent, 20/40–20/320) in the study eye. Only 1 eye per patient was included.

Randomization and Treatment

We randomized patients 1:1:1 to treatment with intravitreal aflibercept 2.0 mg every 4 weeks (2q4), intravitreal aflibercept 2.0 mg every 8 weeks after 5 initial monthly doses (2q8), or macular laser photocoagulation at baseline and sham injections at every visit. Eyes in the 2q8 group received sham injections on nontreatment visits. From week 24 onward, additional active treatment (laser in the intravitreal aflibercept groups or intravitreal aflibercept in the laser group) was allowed if BCVA decreased because of disease reoccurrence or worsening based on prespecified criteria. Panretinal photocoagulation was allowed at any time at the investigator's discretion for PDR.

Outcomes

The primary efficacy end point in VIVID-DME and VISTA-DME was the BCVA change from baseline in Early Treatment Diabetic Retinopathy Study (ETDRS) letter scores at week 52. Results for the primary end point of these studies are reported elsewhere.[8] Herein, we report the proportion of eyes with 2-step or more and 3-step or more improvement in DRSS score at weeks 52 and 100, the proportion of eyes in which PDR developed at weeks 52 and 100, and the proportion of eyes that underwent PRP at weeks 52 and 100. The 2-step or more improvement in DRSS score was a prespecified secondary end point at week 52 and an exploratory end point at week 100 for these studies.

We assessed central subfield thickening using spectral-domain OCT every 4 weeks, and performed fluorescein angiography and color fundus photography at baseline and weeks 24, 52, and 100. Masked graders evaluated images at independent reading centers. For VIVID-DME, readers at the Vienna Reading Center (Vienna, Austria) evaluated OCT images and fundus images. For VISTA-DME, clinicians at the Duke Reading Center (Durham, NC) assessed OCT images and clinicians at the Digital Angiography Reading Center (Great Neck, NY) evaluated fundus images. Although the 2 reading centers used similar methods, the differences in the proportions of ungradable images at baseline were the result of slightly different algorithms used by each center.

Patients were considered to have PDR if their baseline DRSS score was less than 61 and there was at least 1 postbaseline DRSS score of 61 or more. Laser photocoagulation (panretinal or macular) in the study eye within 90 days of day 1 and active PDR in the study eye were exclusion criteria for VIVID-DME and VISTA-DME. Approximately 5% of patients demonstrated PDR at baseline. It was agreed by the reading centers that DRSS level 60 (which indicates prior PRP) would not be used in the study, and therefore patients with prior PRP could still improve on the DRSS scale.

Statistical Analysis

Patients included in the efficacy analyses are those from the full analysis set (FAS) in both studies (VIVID-DME and VISTA-DME). This includes all randomized patients who received any study medication and underwent at least 1 baseline and 1 post-baseline assessment. We analyzed the FAS as randomized. In calculating the percentage of patients with a 2-step or more and 3-step or more improvement in DRSS score, the denominator for VIVID-DME was all patients in the FAS who had a baseline evaluable measurement of DRSS score and at least 1 postbaseline evaluable assessment of DRSS score; the denominator for VISTA-DME was all patients in the FAS. For patients missing a DRSS score at weeks 52 and 100, we imputed missing values using the last observation carried forward method, in which we used the last value before additional treatment for eyes that received additional treatment. The use of these different denominators is consistent with the health authority submission packages for the 2 studies. For the end point of PDR development, we excluded missing and ungradable entries for DRSS score from both studies.

We calculated results for all end points for each treatment group (2q4, 2q8, and laser) for VIVID-DME and VISTA-DME. Additionally, given the low number of cases of incident PDR, we integrated the populations from both studies and calculated the end points for 2 groups from that integrated population: a pooled intravitreal aflibercept group (2q4 and 2q8) and laser group. In the case of the integrated and pooled results, we based *P* values on the Fisher exact test without further adjusting for multiplicities. Patients included in safety analyses are from the safety population in both studies, which includes all randomized patients who received any study treatment.

Results

Changes from Baseline in Diabetic Retinopathy Severity Scale Scores

Of 862 patients in the FAS, 748 (86.8%) had a baseline DRSS score (Table 1). The proportions of DRSS images categorized as ungradable were 25%, 28.7%, and 25.2% for the Vienna Reading Center and 2.6%, 0.6%, and 2.0% for the Digital Angiography Reading Center for the laser, 2q4, and 2q8 groups, respectively.

A greater proportion of patients treated with intravitreal aflibercept (both 2q4 and 2q8) in both VIVID-DME and VISTA-DME demonstrated a 2-step or more improvement in DRSS scores at weeks 52 and 100 compared with laser-treated patients (Fig 1). When the data from the studies were integrated, the proportion of patients who showed a 2-step or more improvement was greater in the pooled intravitreal aflibercept group compared with the laser group (week 52: 31.1% vs. 12.0%, $P < 0.0001$; week 100: 34.9% vs. 13.0%, $P < 0.0001$; n = 578 and 287, respectively, for both time points).

The proportion of patients with a 3-step or more improvement in DRSS score at weeks 52 and 100 was greater among the groups treated with intravitreal aflibercept 2q4 and 2q8 than among those treated with laser (Fig 2). When the data from the studies were integrated, the proportion of patients who showed a 3-step or more improvement was greater in the pooled intravitreal aflibercept group compared with the laser group (week 52: 10.7% vs. 3.4%, $P = 0.0008$; week 100: 15.4% vs. 3.3%, $P < 0.0001$; n = 578 and 287, respectively, for both time points). Figure 3 shows a representative example of a fundus photograph from a patient treated with intravitreal aflibercept who experienced a 2-step or more improvement in DRSS score at week 52.

Progression to Proliferative Diabetic Retinopathy

A smaller proportion of patients in the intravitreal aflibercept 2q4 and 2q8 groups demonstrated PDR through weeks 52 and 100 compared with patients in the laser group (Fig 4). When the data from the studies were integrated, the proportion of patients in whom PDR developed was smaller in the pooled intravitreal aflibercept group compared with the laser group (week 52: 1.7% vs. 7.0%, $P = 0.0002$; week 100: 2.2% vs. 9.1%, $P \leq 0.0001$; n = 578 and 287, respectively, for both time points).

Finally, the proportion of patients treated with intravitreal aflibercept 2q4 and 2q8 versus laser who received PRP through weeks 52 and 100 was smaller than the proportion of laser-treated patients who received PRP (Fig 5). When we integrated the data from the studies, the proportion of patients who received PRP developed was smaller in the pooled intravitreal aflibercept group compared with the laser group (week 52: 0.9% vs. 3.5%, $P = 0.0099$; week 100: 1.6% vs. 4.9%, $P = 0.0064$; n = 578 and 287, respectively, for both time points). Not all cases of PDR led to

Table 1. Baseline Diabetic Retinopathy Severity Scale Scores in VIVID-DME and VISTA-DME

		VIVID-DME			VISTA-DME		
	Diabetic Retinopathy Severity Scale Score	*Laser (n = 132)*	*Intravitreal Aflibercept 2 mg Every 4 Weeks (n = 136)*	*Intravitreal Aflibercept 2 mg Every 8 Weeks after 5 Initial Monthly Doses (n = 135)*	*Laser (n = 154)*	*Intravitreal Aflibercept 2 mg Every 4 Weeks (n = 154)*	*Intravitreal Aflibercept 2 mg Every 8 Weeks after 5 Initial Monthly Doses (n = 151)*
None	10	0	0	0	1 (0.6)	4 (2.6)	4 (2.6)
Mild to moderate NPDR	20	1 (0.8)	0	0	3 (1.9)	5 (3.2)	3 (2.0)
	35	2 (1.5)	0	1 (0.7)	5 (3.2)	7 (4.5)	9 (6.0)
	43	36 (27.3)	31 (22.8)	28 (20.7)	60 (39.0)	49 (31.8)	52 (34.4)
Moderately	47	24 (18.2)	18 (13.2)	27 (20.0)	26 (16.9)	26 (16.9)	32 (21.2)
severe/severe NPDR	53	35 (26.5)	44 (32.4)	42 (31.1)	42 (27.3)	53 (34.4)	40 (26.5)
Mild/moderate/high-risk/	61	1 (0.8)	2 (1.5)	2 (1.5)	1 (0.6)	1 (0.6)	2 (1.3)
advanced PDR	65	0	2 (1.5)	1 (0.7)	10 (6.5)	4 (2.6)	5 (3.3)
	71	0	0	0	1 (0.6)	4 (2.6)	1 (0.7)
	75	0	0	0	1 (0.6)	0	0
Cannot grade	90	33 (25)	39 (28.7)	34 (25.2)	4 (2.6)	1 (0.6)	3 (2.0)

NPDR = nonproliferative diabetic retinopathy; PDR = proliferative diabetic retinopathy; VISTA-DME = Intravitreal Aflibercept Injection in Vision Impairment due to DME; VIVID-DME = Study of Intravitreal Aflibercept Injection in Patients with Diabetic Macular Edema.
Full analysis set. Data are no. (%).

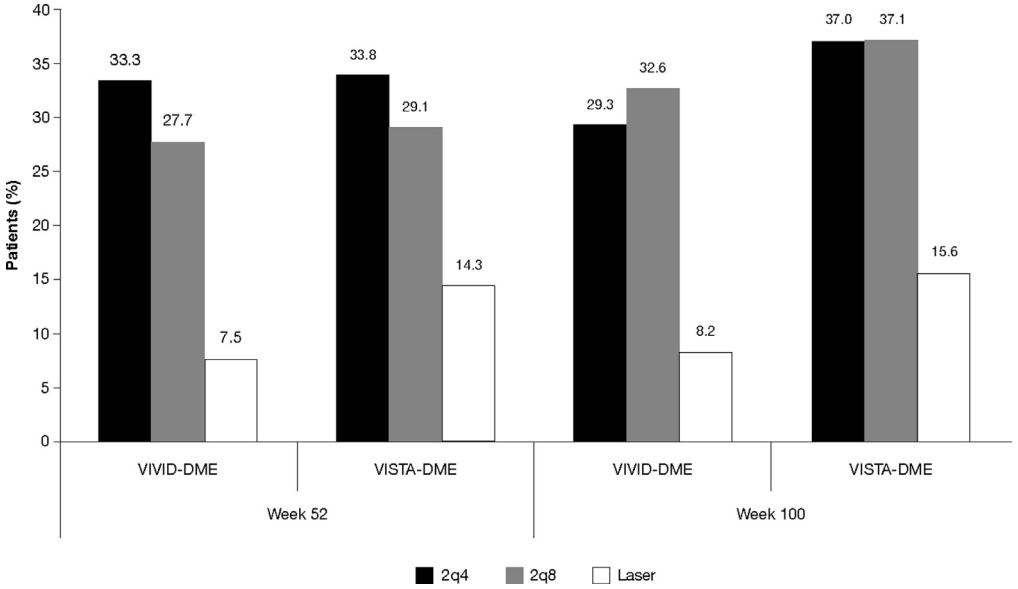

Figure 1. Bar graph showing the proportion of patients with 2-step or more improvement in Diabetic Retinopathy Severity Scale (DRSS) score. For analysis of DRSS, all patients in the full analysis set (FAS) who had a baseline evaluable measurement of DRSS score and at least 1 postbaseline evaluable assessment of DRSS score were included. VIVID-DME: laser, n = 132; 2 mg every 4 weeks (2q4), n = 136; 2 mg every 8 weeks after 5 initial monthly doses (2q8), n = 135; VISTA-DME: laser, n = 154; 2q4, n = 154; 2q8, n = 151.

PRP; it is possible that PRP was administered at time points other than the DRSS reading time points, leading to the different proportions seen in Figures 4 and 5.

Safety

The incidence of adverse events related to the progression of DR was low. The proportions of patients who underwent vitrectomy in the laser, intravitreal aflibercept 2q4, and intravitreal aflibercept 2q8 treatment groups were 0%, 0.7%, and 0%, respectively, in VIVID-DME and 0.6%, 1.9%, and 0.7%, respectively, in VISTA-DME. The proportions of patients in the laser, intravitreal aflibercept 2q4, and intravitreal aflibercept 2q8 treatment groups in whom vitreous hemorrhage developed through week 100 were 4.5%, 2.9%, and 3.0%, respectively, in VIVID-DME and 9.1%, 6.5%, and 2.0%, respectively, in VISTA-DME.

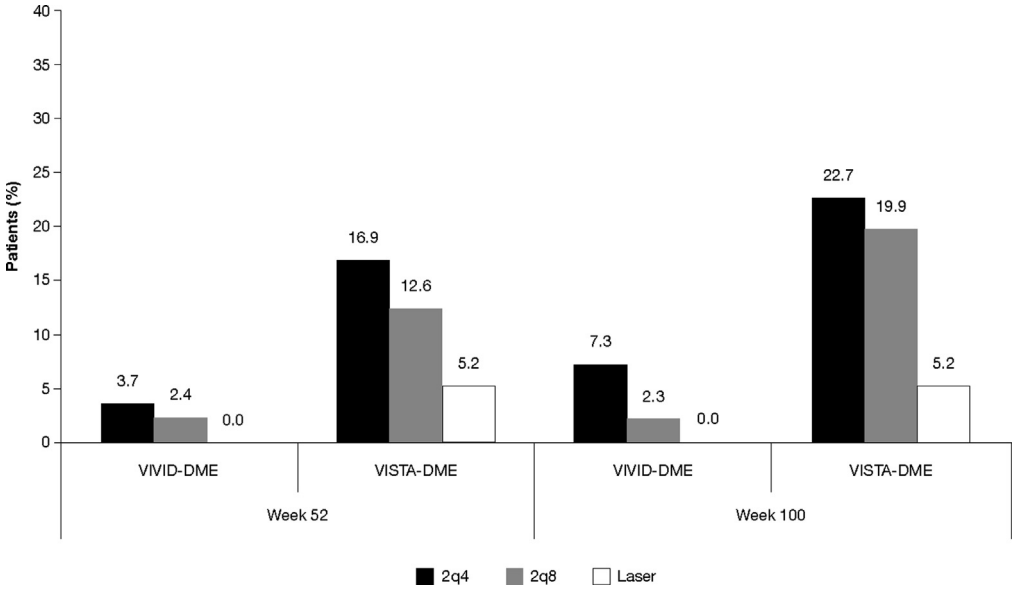

Figure 2. Bar graph showing the proportion of patients with 3-step or more improvement in Diabetic Retinopathy Severity Scale (DRSS) score. For analysis of DRSS, all patients in the full analysis set (FAS) who had a baseline evaluable measurement of DRSS score and at least 1 postbaseline evaluable assessment of DRSS score were included. VIVID-DME: laser, n = 132; 2 mg every 4 weeks (2q4), n = 136; 2 mg every 8 weeks after 5 initial monthly doses (2q8), n = 135; VISTA-DME: laser, n = 154; 2q4, n = 154; 2q8, n = 151.

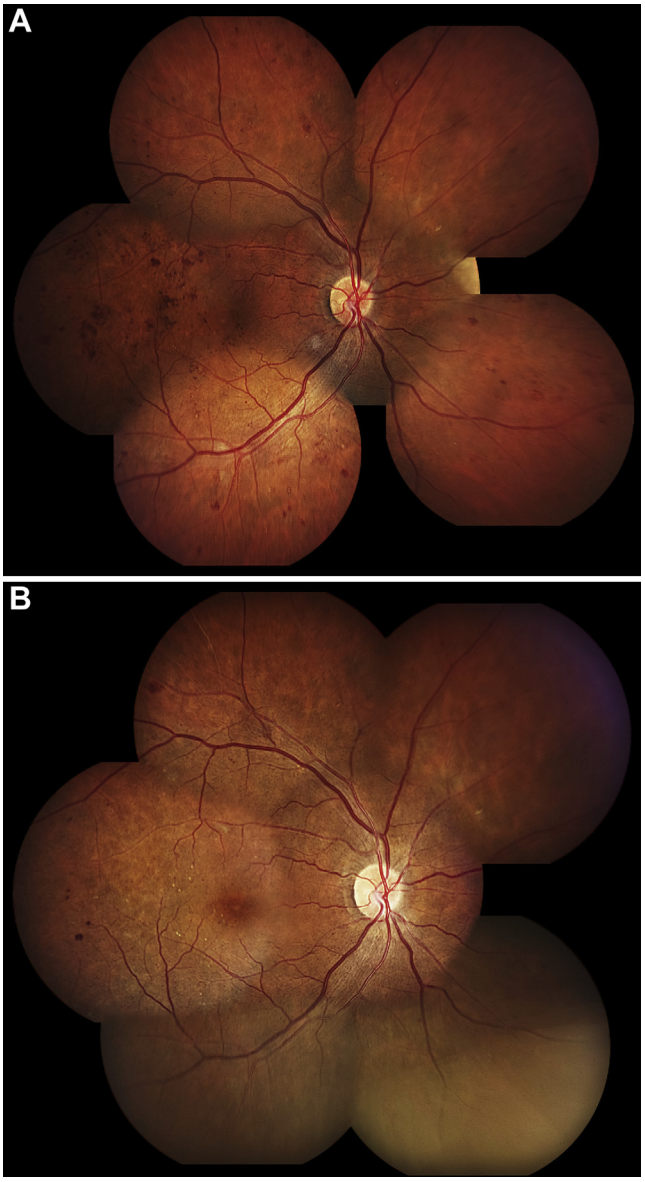

Figure 3. Representative examples of fundus photographs from an intravitreal aflibercept-treated patient from VIVID-DME who experienced a 2-step or more improvement in Diabetic Retinopathy Severity Scale (DRSS) score (**A**) at baseline and (**B**) at week 52.

Discussion

These analyses evaluated the impact of intravitreal aflibercept on DR in patients with DME enrolled in the VIVID-DME and VISTA-DME trials. Compared with laser, the proportion of patients in the intravitreal aflibercept groups who achieved a 2-step or more and 3-step or more improvement in DRSS score was greater, and the proportion of patients in whom PDR developed, who were treated with PRP, or both was smaller. These results were seen in both the 2q4 and 2q8 treatment groups, suggesting that a reduced number of intravitreal aflibercept injections does not decrease the treatment benefit provided.

The Diabetic Retinopathy Clinical Research Network Protocol S study demonstrated that, in eyes with PDR, ranibizumab 0.5 mg administered as needed was noninferior to PRP with respect to BCVA outcomes at 2 years, and the cumulative benefit of ranibizumab over the study period was superior to PRP.[15] In the Clinical Efficacy of Intravitreal Aflibercept versus Panretinal Photocoagulation for Best Corrected Visual Acuity in Patients with Proliferative Diabetic Retinopathy at 52 weeks (CLARITY) study, intravitreal aflibercept administered as needed (after 3 initial monthly doses) was noninferior and superior to PRP in terms of mean change in BCVA at 52 weeks.[16] The Diabetic Anti-VEGF study compared ranibizumab 0.3-mg monotherapy with combination ranibizumab plus targeted retinal photocoagulation and found no differences between groups in visual improvement or decreases in central retinal thickness (Brown DM et al. Unpublished observations, 2015). These studies suggest a beneficial effect of anti-VEGF on the underlying diffuse DR in eyes with DME, which also was seen in the current analyses.

The VIVID-DME and VISTA-DME trials were the first anti-VEGF studies to examine the improvement of DR as a prespecified end point; however, progression of DR has been evaluated in other studies. The A Study of Ranibizumab Injection in Subjects With Clinically Significant Macular Edema (ME) With Center Involvement Secondary to Diabetes Mellitus (RISE) and A Study of Ranibizumab Injection in Subjects With Clinically Significant Macular Edema (ME) With Center Involvement Secondary to Diabetes Mellitus (RIDE) studies found a trend similar to those seen in VIVID-DME and VISTA-DME, with a greater proportion of ranibizumab-treated patients experiencing a 2-step or more or 3-step or more improvement in DRSS score compared with sham-treated patients and a smaller proportion in whom PDR developed or who underwent PRP.[17] However, the results in RISE and RIDE were achieved with monthly injections of ranibizumab (median of 24 injections over 2 years),[5] whereas in the 2q8 group of VIVID-DME and VISTA-DME, the total number of injections received from baseline to week 100 was lower (mean, 13.5 injections in VISTA and 13.6 injections in VIVID over 2 years[9]). Additionally, the distribution of baseline DRSS scores was different in RISE and RIDE compared with VIVID-DME and VISTA-DME. In RISE and RIDE, the distribution of patients with mild to moderate NPDR, moderately severe to severe NPDR, and PDR was roughly equal (approximately one third of patients in each group).[17] In VIVID-DME and VISTA-DME, nearly half of patients demonstrated moderately severe to severe NPDR at baseline, and less than 10% demonstrated PDR (Table 1).

The Diabetic Retinopathy Clinical Research Network conducted an exploratory analysis of the Protocol I study to evaluate the effects of intravitreal ranibizumab or triamcinolone on the progression of DR, which was defined as (1) worsening from no PDR to PDR, (2) worsening of 2 or more severity levels on reading center assessment of fundus photographs in eyes without PDR at baseline, (3) having PRP, (4) having vitreous hemorrhage, or (5) requiring vitrectomy for treatment of PDR. Intravitreal ranibizumab was associated with a reduced risk of DR worsening in eyes with

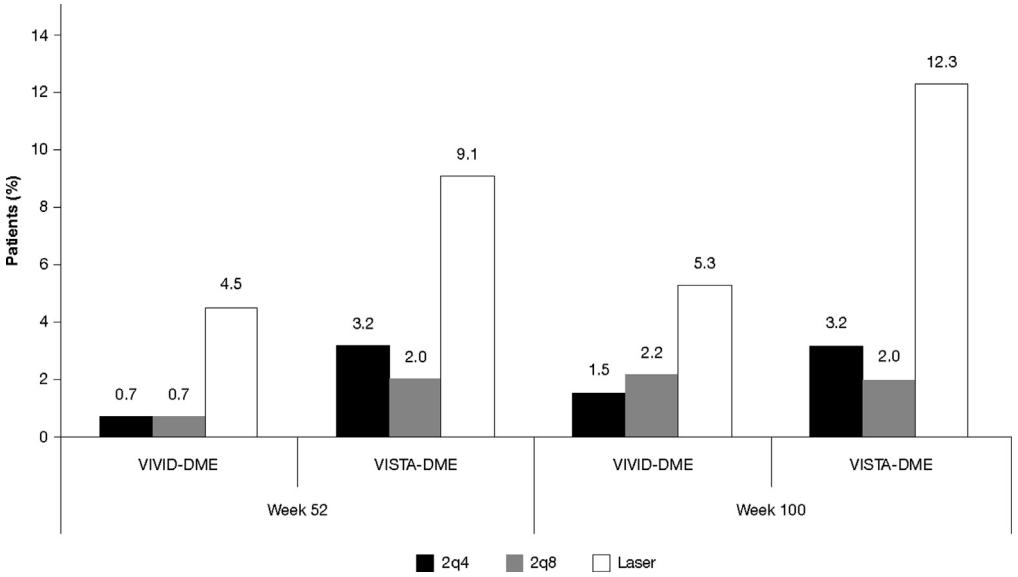

Figure 4. Bar graph showing the proportion of patients in whom proliferative diabetic retinopathy (PDR) developed, safety analysis set. For both studies, PDR development was defined as patients with baseline Diabetic Retinopathy Severity Scale (DRSS) value of less than 61 and at least 1 postbaseline DRSS value of 61 or more. VIVID-DME: laser, n = 133; 2 mg every 4 weeks (2q4), n = 136; 2 mg every 8 weeks after 5 initial monthly doses (2q8), n = 135; VISTA-DME: laser, n = 154; 2q4, n = 155; 2q8, n = 152.

or without PDR, and intravitreal triamcinolone was associated with a reduced risk of PDR worsening.[18]

A post hoc analysis of the Protocol T study evaluated the proportion of patients with DR improvement at 1 and 2 years and the cumulative probabilities for DR worsening through 2 years without adjustment for multiple outcomes. In eyes with NPDR at baseline, anti-VEGF treatment resulted in improvement in DR severity for 22.1% to 37.7% at year 1 and 22.1% to 31.0% at year 2; less improvement was observed with bevacizumab compared with intravitreal aflibercept or ranibizumab. Among eyes with PDR at baseline, intravitreal aflibercept was associated with more DR improvement at 1 and 2 years. Use of all 3 anti-VEGF agents was associated with low rates of DR worsening.[14]

In the ETDRS, 1 eye of each patient was assigned to early photocoagulation, whereas the other was assigned to

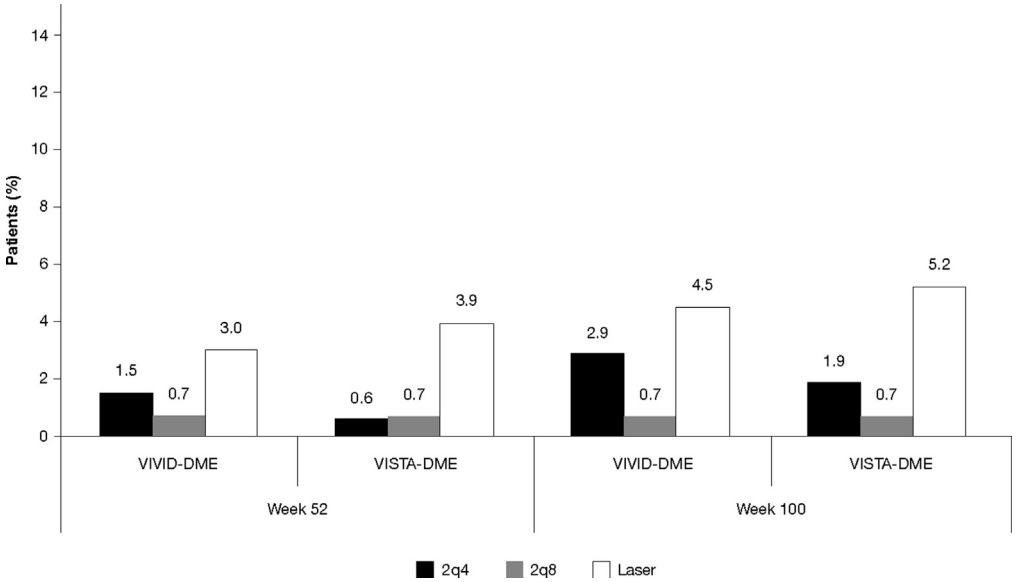

Figure 5. Bar graph showing the proportion of patients who underwent panretinal laser photocoagulation, safety analysis set. VIVID-DME: laser, n = 133; 2 mg every 4 weeks (2q4), n = 136; 2 mg every 8 weeks after 5 initial monthly doses (2q8), n = 135; VISTA-DME: laser, n = 154; 2q4, n = 155; 2q8, n = 152.

deferred photocoagulation, allowing observation of the natural course of DR in the initially untreated eye. The proportions of eyes with progression to PDR were 22.8%, 40.2%, and 54.7%, at 1, 3, and 5 years of follow-up, respectively.[19] These proportions are substantially higher than the proportions of patients in whom PDR developed, who underwent PRP, or both in any of the treatment groups of VIVID-DME and VISTA-DME. The lower rates seen in the current studies may be the result of temporal improvements in glycemic control made possible by advances in diabetes treatment over the last 25 years, shown to reduce progression of DR.[20–24] Mean baseline hemoglobin A1c levels for patients in VIVID-DME and VISTA-DME ranged from 7.6% to 7.9% and did not change over the course of the study; in contrast, 42.0% of patients enrolled in the ETDRS before 1983 had a baseline hemoglobin A1c of 10% or more.[25]

The current analysis has some limitations. The relative infrequency of DRSS measurements (at baseline, weeks 24, 52, 72 [VISTA-DME] or 76 [VIVID-DME], and 100) means that it is possible that there are patients in any treatment group who did progress to PDR, but that this resolved spontaneously during continued treatment and was not captured. Additionally, investigators administered PRP at their discretion, a clinical decision that likely was driven by multiple factors. There was no specific guidance indicating when PRP should be performed, and therefore some investigators may have chosen to wait for high-risk PDR to develop. Others may have deferred PRP because of the expectation of a positive treatment effect on the condition. Finally, images for the 2 studies were graded by 2 different reading centers. The reading centers used different criteria to grade images; however, both approaches are considered valid per the ETDRS DRSS protocol. The overall similarity of the results between the 2 studies suggests that the different grading criteria did not impact the outcomes.

In conclusion, these analyses through week 100 demonstrated the benefits of intravitreal aflibercept over laser in terms of DR progression, improvement, and outcomes, suggesting that intravitreal aflibercept has a beneficial impact not only on localized DME, but also on the underlying DR.

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Footnotes and Financial Disclosures

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Analysis and interpretation: Mitchell, McAllister, Larsen, Staurenghi, Korobelnik, Boyer, Do, Brown, Katz, Berliner, Vitti, Zeitz, Metzig, Lu, Holz

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Abbreviations and Acronyms:
BCVA = best-corrected visual acuity; **DME** = diabetic macular edema; **DR** = diabetic retinopathy; **DRSS** = Diabetic Retinopathy Severity Scale; **ETDRS** = Early Treatment Diabetic Retinopathy Study; **FAS** = full analysis set; **NPDR** = nonproliferative diabetic retinopathy; **PDR** = proliferative diabetic retinopathy; **PRP** = panretinal photocoagulation; **RIDE** = A Study of Ranibizumab Injection in Subjects With Clinically Significant Macular Edema (ME) With Center Involvement Secondary to Diabetes Mellitus; **RISE** = A Study of Ranibizumab Injection in Subjects With Clinically Significant Macular Edema (ME) With Center Involvement Secondary to Diabetes Mellitus; **VA** = visual acuity; **VEGF** = vascular endothelial growth factor; **VISTA-DME** = Study of Intravitreal Aflibercept Injection in Patients with Diabetic Macular Edema; **VIVID-DME** = Intravitreal Aflibercept Injection in Vision Impairment due to DME; **2q4** = 2 mg every 4 weeks; **2q8** = 2 mg every 8 weeks after 5 initial monthly doses.

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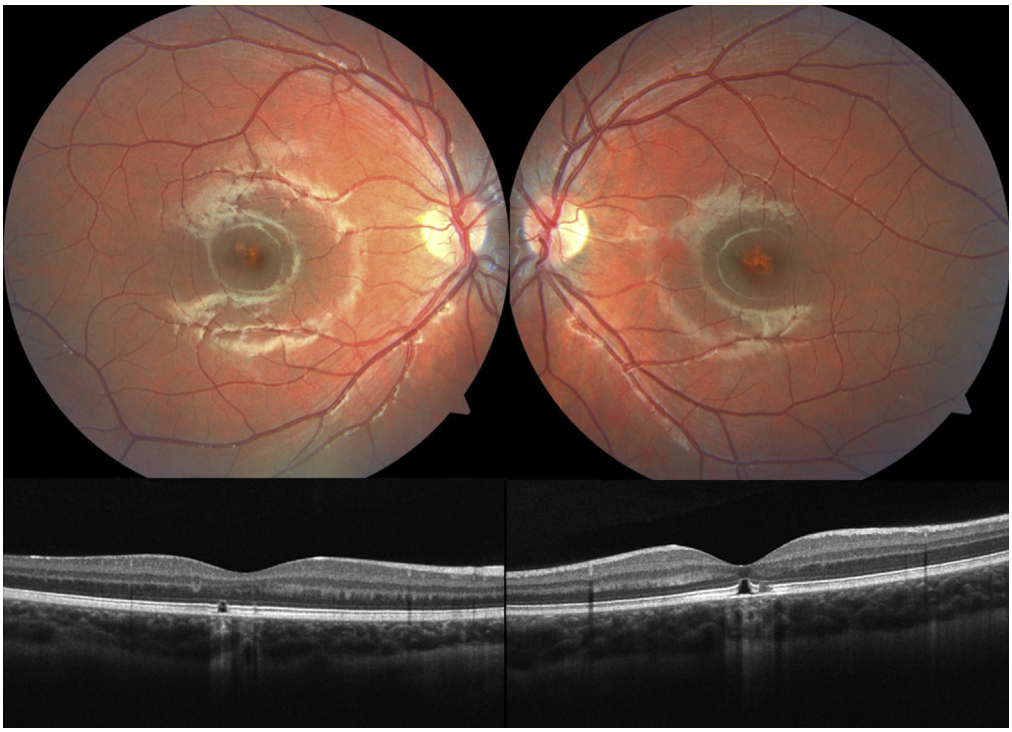
Pictures & Perspectives



Laser Pointer Maculopathy

An 11-year old Caucasian boy was referred for loss of vision for 1 year concerning for inherited retinal dystrophy. Best-corrected visual acuity was 20/30 in the right eye and 20/80 in the left. No family history of early vision loss was noted. Anterior segment examination was unremarkable. Dilated fundus examination showed irregular areas of foveal atrophy in both eyes. OCT shows a focal, well-circumscribed area of photoreceptor loss subfoveally in the left eye and parafoveally in the right eye. Upon further questioning, he admits that before noticing the vision changes a friend had shined a laser pointer in his eyes for a prolonged period of time.

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