

Intravitreal Aflibercept for Diabetic Macular Oedema; Moorfields' Real-World 12 Month Visual Acuity and Anatomical Outcomes

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Short title: twelve-month real life results in DMO patients treated with aflibercept

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ABSTRACT

Objectives:

To assess structural and functional outcomes of treatment with intravitreal aflibercept (® Eylea) for diabetic macular oedema (DMO) in treatment-naive patients.

Design: This is a retrospective, real-life, cohort study.

Participants and Methods:

Ninety-two diabetic patients (102 eyes) receiving intravitreal anti-VEGF therapy were included. Ninety-nine aflibercept treated eyes were included in the statistical analysis. Each patient had corrected visual acuity in ETDRS letters and OCT central foveal thickness (CFT) and macular volume (MV) performed at baseline and 12 months. Patients were initiated on a loading phase of five one-monthly intravitreal aflibercept injections, followed by injections if needed as per clinicians' discretion.

Results:

The mean number of aflibercept injections received was 6.92. At baseline, the mean VA (SD) (Snellen) was 59.7 (16.1) (20/63) ETDRS letters, the mean CFT (SD) was 431 (129) μm whilst the mean MV (SD) was 9.53 (1.79) mm^3 . At 12 months, the mean VA (SD) (Snellen) was 69.6 (15.2) (20/40) ETDRS letters ($p < .0001$). Mean CFT (SD) was 306 (122) μm ($p < .0001$) and mean MV (SD) was 8.43 (1.58) mm^3 ($p < .0001$) at 12 months. Thirty-three (33.67 %) eyes gained ≥ 15 ETDRS letters at month 12, and 50 (55.55%) eyes had a decrease in CFT of ≥ 100 microns.

Conclusions:

There was a significant improvement in VA and in anatomical outcomes in aflibercept-treated eyes at 12 months after commencing treatment for DME in real life settings.

KEY WORDS: aflibercept, anti-VEGF, diabetic macular oedema, real-life setting, OCT

INTRODUCTION

Diabetic macular oedema (DMO) is a leading cause of visual loss in the working age population. (1) It has been recognized that vascular endothelial growth factor (VEGF) is pivotal to the pathogenesis of DMO. (2,3) The modern approach to DMO treatment therefore relies on the proven safety and efficacy of intravitreal anti-VEGF drugs such as bevacizumab, ranibizumab and aflibercept, all of which have demonstrated functional and anatomical efficacy in clinical trials. (2-7)

Several large randomised controlled studies have established the efficacy of ranibizumab in diabetic macular oedema. The Diabetic Retinopathy Clinical Research (DRCR) network found ranibizumab with or without laser was significantly better than laser alone for visual acuity and anatomical outcomes. (8) Around 30% of eyes in ranibizumab plus deferred laser arm had improvement of ≥ 15 ETDRS (Early Treatment Diabetic Retinopathy Study) letters in year 1. In addition, nearly 50% of eyes of the same arm had improvement of ≥ 10 ETDRS letters. The RISE and RIDE studies showed ranibizumab is significantly more effective than sham for centre-involving DMO. (9) In the RISE and RIDE studies patients received monthly injections of ranibizumab. Our group recently published real-world outcomes of ranibizumab in DMO at our institution, showing comparable outcomes to these clinical trials. (10)

The VIVID and VISTA studies compared the safety and efficacy of intravitreal aflibercept to macular laser, finding a mean 10.7-12.5 letter gain in the aflibercept group compared to 0.2 letters in the laser group at 1 year. (11) The efficacy of aflibercept was further highlighted in DRCR Protocol T, in which aflibercept showed an advantage over ranibizumab at year 1, although there was no significant

difference between ranibizumab and aflibercept at year 2. (12) However, clinical trials select the most motivated of patients and have personnel to ensure efficient attendance and timely trial completion. Trials also have strict exclusion criteria such as very poor glycaemic control. We wanted to investigate the efficacy of intravitreal aflibercept for the treatment of centre-involving DMO in a real-world setting where “all-comers” are seen.

METHODS

This retrospective cohort study included 102 eyes (of 92 diabetic patients) with centre-involving diabetic macular oedema (≥ 400 microns as per National Institute of Care and Excellence (NICE) criteria). This study entered only treatment naïve eyes which were funded for intravitreal aflibercept treatment for DMO between November 2015 and May 2016. Patients older than 18 years of age with either diabetes mellitus (DM) type 1 or type 2 were included. All grades of diabetic retinopathy (DR) were included. DMO and DR were graded by using the modified Early Treatment Diabetic Retinopathy Study (ETDRS) classification system based on clinical appearance. HBA1c was recorded but did not influence treatment decisions at onset of treatment. Patients with hypertension, other comorbidities and patients with vitreoretinal conditions such as epiretinal membrane were not excluded. Each patient prior initiation of treatment had FFA and/or OCTA imaging done which is part of the Moorfields’ guidelines. We defined severe macular ischaemia using ETDRS criteria by using FAZ size, FAZ outline and capillary loss in central subfield. Patients who had FAZ greater than 1500 microns GLD in size, capillary outline completely destroyed and who had severe capillary loss were considered as severe macular ischaemia. None of the patient had severe macular ischaemia or were excluded.

The study was approved prospectively by the Clinical Audit and Assessment Committee of Moorfields Eye Hospital and registered with the trust clinical audit department (reference no: CA17/MR/06). Patients who had consented to imaging and anonymised data collection and analysis of outcomes as part of their clinical care were included and the study followed the tenets of the Declaration of Helsinki. All patients were under the care of Moorfields Eye Hospital (MEH) National Health Service (NHS) Trust, London, United Kingdom.

All eyes included in the study were treatment naïve at baseline and were treated with intravitreal aflibercept injections. Patients were initiated on a loading phase of five one-monthly intravitreal aflibercept injections, followed by injections if needed as per clinicians' discretion. Clinical decision on further injections following the loading phase was on the basis of treating towards Visual Acuity and OCT scan stability i.e. if there was potential for further VA and/or OCT improvement (e.g. persistent fluid) after the loading phase, further injections were given. Visual acuity (VA) measurements expressed in Early Treatment Diabetic Retinopathy Study (ETDRS) letters and Optical Coherence Tomography (OCT) (Topcon, Tokyo, Japan) scans were performed at each visit.

Primary outcomes were visual acuity (VA), central foveal thickness (CFT) and macular volume (MV) 12 months after commencing treatment. Secondary outcomes were percentage of eyes that achieved visual acuity gain of ≥ 10 and ≥ 15 ETDRS letters as well as percentage of eyes achieved reduction in CFT of 100 microns or more. Additionally, we carried out subgroup analysis according to the baseline VA (worse than 69 ETDRS letters or ≥ 69 ETDRS letters) and mean change in VA, CFT and MV at month 12.

Key exclusion criteria included a history of an acute coronary event or cerebrovascular accident in the previous 3 months, pregnancy or lactation, active infection or intraocular inflammation in either eye, poor view of the fundus, severe macular ischaemia, other pathologies contributing towards macular oedema, anti-VEGF treatment received for any other condition and other macular diseases present at baseline that might confound the outcomes such as a coexistent retinal vein occlusion.

We assessed the primary and secondary outcomes at 12 months. The t-paired sample test was used to determine statistical significance (<https://www.graphpad.com/quickcalcs/ttest1.cfm>) . A P value of <0.05 was interpreted as statistically significant.

RESULTS

Ninety-nine aflibercept treated eyes (89 patients) entered the statistical analysis. Three eyes out of 102 were excluded as they were switched to other treatment over 12 - month follow up period. The mean number of aflibercept injections received was 6.92 (Figure 1). Fourteen percent of included eyes had less than 5 monthly loading doses (minimum 3) due to either clinicians' discretion or patients did not attend or cancelled their appointments. Thirty percent of included eyes did not have further injections after the loading phase. Two patients (two eyes from the cohort) did not complete the follow up of 12 months. 33% of patients were pseudophakic and 67% were phakic at baseline.

Aflibercept cohort outcomes

At baseline, the mean VA (SD) (Snellen) was 59.7 (16.1) (20/63) ETDRS letters, the

mean CFT (SD) was 431 (129) μm whilst the mean MV (SD) was 9.53 (1.79) mm^3 . (Table 1) At 12 months, the mean VA (SD) (Snellen) was 69.6 (15.2) (20/40) ETDRS letters ($p < .0001$). The mean CFT (SD) was 306 (122) μm ($p < .0001$) and the mean MV (SD) was 8.43 (1.58) mm^3 ($p < .0001$) at 12 months. Thirty-three (33.67 %) eyes gained ≥ 15 ETDRS letters at month 12, and 50 (55.55%) eyes had a decrease in CFT of ≥ 100 microns (Table 2). Three (3.06 %) eyes lost ≥ 15 ETDRS letters and 6 (6.66 %) eyes had an increase in CFT of ≥ 100 microns at the end of follow up period. Forty-seven (46.53%) eyes achieved 10 ETDRS letters or more gain at month 12, whilst 5 (4.95%) eyes lost 10 ETDRS letters or more at the end of follow up.

Mean changes and sub-group analysis according to baseline VA and CFT

We calculated the changes in VA, CFT and MV after 12 months. The mean change in VA was + 9.9 ETDRS. The mean change in MV was -1.08 mm^3 whilst the mean change in the CFT was -128 μm .

We sub-divided the included eyes into two subgroups according to the baseline visual acuity; < 69 ETDRS letters ($< 20/50$ Snellen) and ≥ 69 ETDRS letters ($\geq 20/40$ Snellen) and according to the baseline CFT; 400- 499 microns or ≥ 500 microns. Sixty-six percent of eyes had baseline visual acuity less than 69 ETDRS letters ($< 20/50$ Snellen). The mean change in visual acuity in the subgroup with baseline VA less than 69 letters ($< 20/50$ Snellen) was +13.8 ETDRS letters (Figure 2). Thirty-four percent of eyes had baseline visual acuity ≥ 69 ETDRS letters ($\geq 20/40$ Snellen) and the mean change in the visual acuity after 12 months in that subgroup was + 2.6 ETDRS letters. The subgroup of eyes with initially worse visual acuity ($< 20/50$ Snellen) had mean 7.4 intravitreal injections of aflibercept over 12 months whilst the

subgroup with initial visual acuity of $\geq 20/40$ Snellen had mean 6.6 injections over same follow up period ($p = .07$) Twenty-seven percent of included eyes had baseline CFT of 500 microns or more. The mean change in CFT in that subgroup was -265 microns. In the subgroup where the baseline CFT was between 500 and 400 microns the mean change in CFT was -86 microns.

DISCUSSION

Clinical trials generally produce results above what would be expected to occur in a normal patient population, with real world evidence rarely indicating equivalence. There are myriad reasons for this, including tight inclusion and exclusion criteria, a well-motivated patient population, more injections given and a mandated tight appointment schedule. The DRCR.net Protocol T study demonstrated a 13.3 letter gain with aflibercept therapy, with the mean VA at baseline being 64.8 ETDRS letters. (12) The major trials examining anti-VEGF effect in DMO (VIVID, VISTA, RESOLVE, RESTORE, RISE, RIDE, RETAIN, Da VINCI) had a baseline VA that ranged from 56.9 letters to 64.8 ETDRS letters with VA gain ranging from 6.8 to 13.1 letters over the first year of the study.(13-16) An inverse correlation was noted whereby patients with the higher baseline VA demonstrated the lower improvement in acuity.

Real-world results have not displayed the same amount of improvement in visual acuity with anti VEGF treatment in DMO, with the frequency of injections being the factor that tends to be cited in order to explain this finding. (17) There are no large-scale real-world data looking at aflibercept therapy for DMO. However, it was previously hypothesised based on diminished number of injections in a real world setting that the results would be inferior to the major trials. Our study is look at real

world evidence of aflibercept use and with an average of 6.92 injections, significantly less than the 9-10 observed in DRCR.net protocol T, with around 10 ETDRS letters of improvement noted. In those eyes with VA of less than 69 letters, the improvement in acuity was markedly greater than in those with higher baseline visual acuity scores, thus confirming the ceiling effect seen when treating patients with good initial baseline acuity. The ceiling effect was noted when divided our cohort based on degree of foveal thickening. Our results indicate that despite a significantly lower number of injections over a 12-month period than those observed in the landmark trials, good visual and anatomical outcomes are attainable.

The number of injections was less than those used in the large clinical studies. We believe this is a significant collection of real-world outcomes that show very good results with aflibercept therapy for diabetic macular oedema in a real-world setting. Regardless to the limitations of this study, which are number of patients included, and lack of more detailed analysis of macular perfusion, we believe that the reporting of real-world outcomes is of benefit to clinicians who are treating patients in the real world, rather than a clinic trial setting and thus do not see this as a limitation.

Real world evidence is important in making decisions about how to treat patients with DMO in an efficient and cost-effective manner. Modern healthcare systems may not be able to provide injections at the same frequency for sustained periods of time as was observed in the major studies. This is the largest published dataset examining aflibercept therapy provided in a real world setting and our observed improvement could potentially be explained in theory by the pharmacokinetic advantages of aflibercept in its increased binding affinity for VEGF, its longer duration of action and ability to bind placental growth factor. Whatever the reason we

have demonstrated that it is possible to deliver very good visual acuity and anatomical outcomes in a real-world setting using less injections than those used in the published literature. Diabetic maculopathy is a major cause of sight impairment amongst working age people and the prevalence of type 2 diabetes is rapidly increasing in both the developed and less well-developed world economies. We demonstrate that good outcomes can be achieved in the real world away from clinical trials and this should support doctors and patients together in managing diabetic macular oedema.

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Conflict of Interest Statement:

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Authors' contribution:

Marko Lukic: Drafted the study, acquired, analysed and interpreted data, drafted the manuscript, gave final approval and is accountable for all aspects of the work

Gwyn Williams: Drafted the study, acquired, analysed and interpreted data, drafted the manuscript, gave final approval and is accountable for all aspects of the work

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Praveen J. Patel: Drafted the study, acquired, analysed and interpreted data, drafted the manuscript, gave final approval and is accountable for all aspects of the work

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FIGURE LEGENDS

Figure 1. Number of eyes per number of injections of the cohort in 12 months follow-up

Figure 2. Visual acuity change over 12 months in the main cohort and two subgroups (< 69 ETDRS letters at baseline and > 69 ETDRS letters at baseline)

REFERENCES

1. Yau JW, Rogers SL, Kawasaki R, Lamoureux EL, Kowalski JW, Bek T, et al. Global prevalence and major risk factors of diabetic retinopathy. *Diabetes care*. 2012;35(3):556-64.
2. Wells JA, Glassman AR, Ayala AR, Jampol LM, Bressler NM, Bressler SB, et al. Aflibercept, Bevacizumab, or Ranibizumab for Diabetic Macular Edema: Two-Year Results from a Comparative Effectiveness Randomized Clinical Trial. *Ophthalmology*. 2016;123(6):1351-9.
3. Bressler SB, Glassman AR, Almkhatar T, Bressler NM, Ferris FL, Googe JM, Jr., et al. Five-Year Outcomes of Ranibizumab With Prompt or Deferred Laser Versus Laser or Triamcinolone Plus Deferred Ranibizumab for Diabetic Macular Edema. *American journal of ophthalmology*. 2016;164:57-68.
4. Heier JS, Korobelnik JF, Brown DM, Schmidt-Erfurth U, Do DV, Midenas E, et al. Intravitreal Aflibercept for Diabetic Macular Edema: 148-Week Results from the VISTA and VIVID Studies. *Ophthalmology*. 2016;123(11):2376-85.
5. Boyer DS, Nguyen QD, Brown DM, Basu K, Ehrlich JS. Outcomes with As-Needed Ranibizumab after Initial Monthly Therapy: Long-Term Outcomes of the Phase III RIDE and RISE Trials. *Ophthalmology*. 2015;122(12):2504-13.e1.

6. Rajendram R, Fraser-Bell S, Kaines A, Michaelides M, Hamilton RD, Esposti SD, et al. A 2-year prospective randomized controlled trial of intravitreal bevacizumab or laser therapy (BOLT) in the management of diabetic macular edema: 24-month data: report 3. *Arch Ophthalmol*. 2012;130(8):972-9.
7. Virgili G, Parravano M, Evans JR, Gordon I, Lucenteforte E. Anti-vascular endothelial growth factor for diabetic macular oedema: a network meta-analysis. *Cochrane Database of Systematic Reviews*. 2017(6).
8. Elman MJ, Aiello LP, Beck RW, Bressler NM, Bressler SB, Edwards AR, et al. Randomized trial evaluating ranibizumab plus prompt or deferred laser or triamcinolone plus prompt laser for diabetic macular edema. *Ophthalmology*. 2010;117(6):1064-77.e35.
9. Brown DM, Nguyen QD, Marcus DM, Boyer DS, Patel S, Feiner L, et al. Long-term outcomes of ranibizumab therapy for diabetic macular edema: the 36-month results from two phase III trials: RISE and RIDE. *Ophthalmology*. 2013;120(10):2013-22.
10. Patrao NV, Antao S, Egan C, Omar A, Hamilton R, Hykin PG, Sivaprasad S, Rajendram R, Moorfields Diabetic Macular Oedema Study Group. Real-World Outcomes of Ranibizumab Treatment for Diabetic Macular Edema in a United Kingdom National Health Service Setting. *Am J Ophthalmol*. 2016; 172:51-57.

11. Korobelnik JF, Do DV, Schmidt-Erfurth U, Boyer DS, Holz FG, Heier JS, et al. Intravitreal aflibercept for diabetic macular edema. *Ophthalmology*. 2014;121(11):2247-54.
12. Wells JA, Glassman AR, Ayala AR, Jampol LM, Aiello LP, Antoszyk AN, et al. Aflibercept, bevacizumab, or ranibizumab for diabetic macular edema. *The New England journal of medicine*. 2015;372(13):1193-203.
13. Massin P, Bandello F, Garweg JG, Hansen LL, Harding SP, Larsen M, et al. Safety and efficacy of ranibizumab in diabetic macular edema (RESOLVE Study): a 12-month, randomized, controlled, double-masked, multicenter phase II study. *Diabetes care*. 2010;33(11):2399-405.
14. Nguyen QD, Brown DM, Marcus DM, Boyer DS, Patel S, Feiner L, et al. Ranibizumab for diabetic macular edema: results from 2 phase III randomized trials: RISE and RIDE. *Ophthalmology*. 2012;119(4):789-801.
15. Do DV, Nguyen QD, Boyer D, Schmidt-Erfurth U, Brown DM, Vitti R, et al. One-year outcomes of the da Vinci Study of VEGF Trap-Eye in eyes with diabetic macular edema. *Ophthalmology*. 2012;119(8):1658-65.
16. Dugel PU, Hillenkamp J, Sivaprasad S, Vögeler J, Mousseau M-C, Wenzel A, et al. Baseline visual acuity strongly predicts visual acuity gain in patients with diabetic macular edema following anti-vascular endothelial growth factor treatment across trials. *Clinical Ophthalmology (Auckland, NZ)*. 2016;10:1103.

17. Kiss S, Liu Y, Brown J, Holekamp NM, Almony A, Campbell J, et al. Clinical utilization of anti-vascular endothelial growth-factor agents and patient monitoring in retinal vein occlusion and diabetic macular edema. *Clinical ophthalmology (Auckland, NZ)*. 2014;8:1611.

Table 1 Aflibercept cohort: General data; CFT = Central Foveal Thickness, MV = Macular Volume, SD = Standard Deviation, VA = Visual Acuity

	AFLIBERCEPT COHORT
TREATED EYES	99
MEAN VA BASELINE (SD) (Snellen) ETDRS letters	59.66 (16.11) (20/63)
MEAN VA 5 MONTHS (SD) (Snellen) ETDRS letters	66.5 (13.65) (20/40)
MEAN VA 12 MONTHS (SD) (Snellen) ETDRS letters [p value]	69.56 (15.24) (20/40) [p < .0001]
MEAN VA CHANGE ETDRS letters	+ 9.9
MEAN CFT BASELINE (SD) microns	431 (129)
MEAN CFT 5 MONTHS (SD) microns	298 (101)
MEAN CFT 12 MONTHS (SD) microns [p value]	306 (122) [p < .0001]
MEAN CFT CHANGE microns	-128
MEAN MV BASELINE (SD) mm³	9.53 (1.79)
MEAN MV 5 MONTHS (SD) mm³	8.5 (2.03)
MEAN MV 12 MONTHS (SD) mm³ [p value]	8.43 (1.58) [p < .0001]
MEAN MV CHANGE mm³	-1.08
MEAN NUMBER OF INJECTIONS	6.92

Table 2 Changes in VA and CFT; CFT = Central Foveal Thickness, MV = Macular Volume, SD = Standard Deviation, VA = Visual Acuity

VA	COHORT (eyes)	%
≥ 15 letters gain	33	33.67 %
< 15 letters gain	47	47.95 %
≥ 15 letters loss	3	3.06 %
< 15 letters loss	15	15.30 %
≥ 10 letters gain	46	46.66 %
≥ 10 letters loss	5	5.05 %
CFT		
≥ - 100 microns	50	50.50 %
< - 100 microns	21	21.21 %
≥ 100 microns	6	6.06 %
< 100 microns	13	13.13 %

Table 3 Macular oedema appearance at baseline; DMO = Diabetic Macular Oedema, CSMO = Clinically Significant Macular Oedema

TYPE OF MACULAR OEDEMA	PERCENTAGE (%)
FOCAL, CENTRE-INVOLVING DMO	29
DIFFUSE CSMO, INVOLVING FOVEA	64
FOCAL CSMO, INVOLVING FOVEA	7
PRESENCE OF SUBRETINAL FLUID	18
PRESENCE OF EPIRETINAL MEMBRANE	13
VITREO-MACULAR TRACTION	2