Original Article
DOI: https://doi.org/10.70749/ijbr.v3i7.2996

INDUS JOURNAL OF BIOSCIENCE RESEARCH
https://ijbr.com.pk
ISSN: 2960-2793/ 2960-2807

# Comparison of Intravitreal Anti-vascular Endothelial Growth Factor Therapy Including Aflibercept versus Patizra for Treatment of Diabetic Macular Edema

**Fahad Ijaz[1], Zahid Hussain Chaudhary[2], Ijaz Siddiqui[3], Amna Mahmood[4]**

[1-4]Department of Ophthalmology, Mughal Eye Hospital, Lahore, Punjab, Pakistan.

## ARTICLE INFO

**Keywords:** Diabetic Macular Edema, Aflibercept, Ranibizumab Biosimilar, Best Corrected Visual Acuity, Intravitreal anti-Vascular Endothelial Growth Factor Therapy.

**Correspondence to:** Fahad Ijaz, Department of Ophthalmology, Mughal Eye Hospital, Lahore, Punjab, Pakistan.
**Email:** fahadijaz3@hotmail.com

**Declaration**
**Authors' Contribution**
All authors equally contributed to the study and approved the final manuscript

**Conflict of Interest:** No conflict of interest.

**Funding:** No funding received by the authors.

**Article History**
Received: 16-06-2025 Revised: 05-07-2025
Accepted: 06-07-2025 Published: 15-07-2025

## ABSTRACT

**Objective:** To compare the efficacy of intravitreal aflibercept and ranibizumab biosimilar Patriza® in improving best corrected visual acuity in patients with diabetic macular edema. **Study Design:** Randomized controlled trial. **Place and duration of Study:** The study was conducted in the Department of Ophthalmology, Mughal Eye Trust Hospital, Lahore, February to May 2025. **Methods:** A total of 160 eyes from 160 patients aged 40 to 70 years with diabetic macular edema were enrolled through non-probability consecutive sampling and randomly allocated by lottery method into two equal groups. Group A received intravitreal aflibercept, whereas Group B received intravitreal ranibizumab biosimilar Patriza® at monthly intervals. All patients were followed for three months. The primary outcome was improvement in best corrected visual acuity, defined as more than one Snellen line gain after treatment. Mean change in best corrected visual acuity from baseline to three months was also assessed. Data were analyzed using Statistical Package for the Social Sciences version 26.0, and p-value ≤0.05 was considered statistically significant. **Results:** Baseline demographic and clinical characteristics were comparable between both groups. At three months, post-treatment best corrected visual acuity was significantly better in the Patriza® group than in the aflibercept group (0.44 ± 0.14 vs. 0.37 ± 0.12, p=0.001). Mean change in best corrected visual acuity was also greater in Group B than in Group A (0.20 ± 0.09 vs. 0.14 ± 0.07, p=0.001). Improvement of more than one Snellen line was observed in 68.8% of eyes treated with Patriza® compared with 48.8% of eyes treated with aflibercept (p=0.007). Visual worsening was uncommon in both groups and did not differ significantly. **Conclusion:** Both aflibercept and ranibizumab biosimilar Patriza® improved visual acuity in patients with diabetic macular edema; however, Patriza® produced significantly greater short-term functional improvement at three months. These findings suggest that Patriza® may be a more effective option for early visual recovery in this patient population.

## INTRODUCTION

Diabetes is an increasingly prevalent global health problem. Worldwide nearly 8.8% of adults (ie, 412 million people) have diabetes [1]. Diabetic macular edema, swelling in the macula caused by fluid leaking from retinal blood vessels, can occur with any stage of diabetic retinopathy. Diabetic macular edema affect 3.8%, of US adults 40 years and older with diabetes [1,2]. It is a leading cause of vision loss among people with diabetes. Optical coherence tomography allows for accurate assessment and early detection of diabetic macular edema [3].

Early diagnosis remains the key strategy for reducing the risk of blindness related to diabetic macular edema and preserving vision-related quality of life [4]. However, despite the high burden of bilateral disease, there is little evidence to guide management in the fellow eye for individuals who initially have diabetic macular edema in only one eye. Identifying the expected timeline for and factors predictive of diabetic macular edema development in the fellow eye may help clinicians identify at-risk patients who need more frequent monitoring, and help set patient expectations about their risks of disease progression [5,6]. Intravitreal aflibercept injection significantly improved visual and anatomic outcomes compared with laser photocoagulation in the Phase 3 VISTA and VIVID trials in patients with DME through Week 100 [7].

It has been stated in previously conducted studies that Treatment with intravitreal Patizra® injections was found safe and resulted in clinically and statistically significant improvement in visual acuity and the central retinal thickness in patients with macular edema secondary to

various retinal pathologies. Malik et al., found that with the intravitreal aflibercept injection, a statistically significant decrease in CRT was reduced to 362.91 ± 126.11 while to 364.50 ± 170.49 with patriza ($p < 0.05$), the parentage of improved BCVA was noted in 48.5% with aflibercept and 68.2% with Patizra ($p<0.05$) [8,9].

Rationale of this study is to compare the outcome of aflibercept versus Patizra for treatment of diabetic macular edema. Literature showed that there is no difference in the outcome of aflibercept and Patizra injections. But there is only one study conducted before in this regard in local setting and no further trial had been conducted before. Therefore, we have planned to conduct this study to get evidence regarding the post-treatment improvement in BCVA and central retinal thickness that can improve visual issues of patients. This would help us to improve our practice and in future, we will plan better approaches to control blindness due to diabetic macular edema, thus improve the outcome, and patient's satisfaction.

## MATERIAL AND METHODS

This randomized controlled trial was conducted in the Department of Ophthalmology, Mughal Eye Trust Hospital, Lahore, after approval of the synopsis, (from February 2025 to May 2025). Ethical approval was obtained from the institutional ethical review committee before commencement of the study, and written informed consent was obtained from all participants prior to enrollment. A sample size of 160 eyes, with 80 eyes in each group, was calculated using the World Health Organization sample size calculator by taking a 5% level of significance, 80% study power, and expected proportion of improved best corrected visual acuity of 48.5% with aflibercept and 68.2% with Patriza. Patients were recruited through non-probability consecutive sampling from the outpatient department. Eligible participants were men and women aged 40 to 70 years diagnosed with diabetic macular edema, which was operationally defined as central retinal thickness greater than 300 µm on optical coherence tomography in a diabetic patient having glycated hemoglobin above 6.5% for more than one year. Patients were excluded if they had intraocular pressure related complications, recurrent macular edema documented in the medical record, neovascularization elsewhere, proliferative diabetic retinopathy without macular edema, prior switch to another anti-vascular endothelial growth factor agent before completion of three consecutive monthly injections, switch to non-vascular endothelial growth factor therapy such as dexamethasone implant, or history of other previous interventions including thermal laser photocoagulation, submacular surgery, photodynamic therapy, or any other anti-vascular endothelial growth factor treatment.

At enrollment, demographic and clinical information was recorded on a structured proforma, including age, gender, glycated hemoglobin, duration of diabetes, duration of macular edema symptoms, laterality, smoking history of more than 5 pack years, hypertension defined as blood pressure at or above 140/90 mmHg, chronic headache, occupation, and daily duration of screen use. Baseline best corrected visual acuity was assessed on Snellen's chart before randomization. Participants were then allocated into two equal groups by lottery method. Group A received intravitreal aflibercept at monthly intervals, while Group B received intravitreal ranibizumab biosimilar Patriza at monthly intervals. All patients were followed in the outpatient department for three months. Outcome assessment was performed in two ways. Mean change in best corrected visual acuity was calculated as the difference between baseline and three-month visual acuity measured on Snellen's chart. Improved best corrected visual acuity was defined as improvement of more than one Snellen line after three months of therapy.

Data were entered and analyzed using Statistical Package for the Social Sciences version 26.0. Normality of quantitative variables was assessed with the Shapiro-Wilk test. Quantitative variables were summarized as mean and standard deviation, while qualitative variables were presented as frequency and percentage. Intergroup comparison of mean visual acuity was performed using the independent samples t-test, and improved visual acuity was compared using the chi-square test. Stratification was carried out for potential effect modifiers, and a p-value of 0.05 or less was considered statistically significant.

## RESULTS

The two treatment groups were comparable at baseline, confirming successful randomization. Mean age was 54.6 ± 8.3 years in the aflibercept group and 55.1 ± 7.9 years in the Patriza® group, while baseline best corrected visual acuity was 0.23 ± 0.09 and 0.24 ± 0.10, respectively. No baseline variable showed a statistically significant difference between groups (Table 1).

**Table 1**

*Baseline Demographic and Clinical Characteristics of Study Participants*

| Variable | Group A – Aflibercept (n = 80) | Group B – Patizra® (n = 80) | Test Statistic | P-value |
|---|---|---|---|---|
| Age (years), Mean ± SD | 54.6 ± 8.3 | 55.1 ± 7.9 | t = 0.393 | 0.695 |
| **Gender** | | | | |
| Male, n (%) | 48 (60.0%) | 46 (57.5%) | $\chi^2$ = 0.103 | 0.748 |
| Female, n (%) | 32 (40.0%) | 34 (42.5%) | | |
| HbA1c (%), Mean ± SD | 8.7 ± 1.4 | 8.9 ± 1.3 | t = 0.921 | 0.359 |
| Duration of Diabetes (years), Mean ± SD | 9.2 ± 4.1 | 9.6 ± 4.4 | t = 0.588 | 0.558 |
| Duration of Symptoms (months), Mean ± SD | 8.4 ± 3.7 | 8.1 ± 3.5 | t = 0.522 | 0.603 |
| **Laterality** | | | | |
| Right eye, n (%) | 38 (47.5%) | 40 (50.0%) | $\chi^2$ = 0.182 | 0.913 |
| Left eye, n (%) | 30 (37.5%) | 28 (35.0%) | | |
| Bilateral, n (%) | 12 (15.0%) | 12 (15.0%) | | |
| Smoking (>5 pack-years), n (%) | 22 (27.5%) | 20 (25.0%) | $\chi^2$ = 0.119 | 0.730 |
| Hypertension (BP ≥140/90 mmHg), n (%) | 42 (52.5%) | 44 (55.0%) | $\chi^2$ = 0.103 | 0.748 |

| | | | | |
|---|---|---|---|---|
| Chronic Headache, n (%) | 18 (22.5%) | 16 (20.0%) | $\chi^2$ = 0.131 | 0.717 |
| **Occupation** | | | | |
| Manual/Physical Labour, n (%) | 22 (27.5%) | 24 (30.0%) | $\chi^2$ = 0.397 | 0.820 |
| Clerical/Office Work, n (%) | 18 (22.5%) | 16 (20.0%) | | |
| Homemaker, n (%) | 26 (32.5%) | 28 (35.0%) | | |
| Other/Retired, n (%) | 14 (17.5%) | 12 (15.0%) | | |
| Screen Use (hours/day), Mean ± SD | 4.2 ± 1.8 | 4.5 ± 2.0 | t = 0.991 | 0.324 |
| Baseline BCVA (decimal), Mean ± SD | 0.23 ± 0.09 | 0.24 ± 0.10 | t = 0.660 | 0.510 |

*SD = Standard Deviation; BCVA = Best Corrected Visual Acuity; $\chi^2$ = Chi-square; t = Independent samples t-test. P ≤ 0.05 statistically significant.*

Both groups showed visual improvement after three months, but the gain was significantly greater with Patriza®. Post-treatment best corrected visual acuity reached 0.44 ± 0.14 in the Patriza® group versus 0.37 ± 0.12 in the aflibercept group, and mean change in best corrected visual acuity was 0.20 ± 0.09 versus 0.14 ± 0.07, respectively. Visual loss was uncommon in both groups (Table 2).

**Table 2**

*Pre- and Post-Treatment Best Corrected Visual Acuity — Comparison between Groups*

| Variable | Group A – Aflibercept (n = 80) | Group B – Patizra® (n = 80) | Test Statistic | P-value |
|---|---|---|---|---|
| Baseline BCVA (decimal), Mean ± SD | 0.23 ± 0.09 | 0.24 ± 0.10 | t = 0.660 | 0.510 |
| Post-treatment BCVA at 3 months, Mean ± SD | 0.37 ± 0.12 | 0.44 ± 0.14 | t = 3.414 | 0.001 |
| Mean Change in BCVA (decimal), Mean ± SD | 0.14 ± 0.07 | 0.20 ± 0.09 | t = 4.728 | 0.001 |
| Baseline BCVA (Snellen equivalent) | 6/24 – 6/30 | 6/24 – 6/30 | — | — |
| Post-treatment BCVA (Snellen equivalent) | 6/15 – 6/18 | 6/12 – 6/15 | — | — |
| Eyes losing ≥1 Snellen line, n (%) | 3 (3.8%) | 2 (2.5%) | $\chi^2$ = 0.211 | 0.646 |

The primary outcome favored Patriza®, with improvement of more than one Snellen line observed in 68.8% of eyes compared with 48.8% in the aflibercept group (p=0.007). Unchanged vision was more frequent with aflibercept, 47.5% versus 28.7% (p=0.015). Visual worsening was rare and comparable in both groups, occurring in 3.8% and 2.5% of eyes, respectively (Table 3).

**Table 3**

*Primary Outcome — Proportion of Eyes with Improved BCVA (>1 Snellen Line) at 3 Months*

| Variable | Group A – Aflibercept (n = 80) | Group B – Patizra® (n = 80) | Test Statistic | P-value |
|---|---|---|---|---|
| Improved BCVA (>1 Snellen line), n (%) | 39 (48.8%) | 55 (68.8%) | $\chi^2$ = 7.150 | 0.007 |
| Unchanged BCVA (≤1 line change), n (%) | 38 (47.5%) | 23 (28.7%) | $\chi^2$ = 5.922 | 0.015 |
| Worsened BCVA (loss ≥1 line), n (%) | 3 (3.8%) | 2 (2.5%) | $\chi^2$ = 0.211 | 0.646 |
| Improved by exactly 1 line, n (%) | 16 (20.0%) | 19 (23.8%) | $\chi^2$ = 0.373 | 0.541 |
| Improved by 2 lines, n (%) | 14 (17.5%) | 22 (27.5%) | $\chi^2$ = 2.366 | 0.124 |
| Improved by ≥3 lines, n (%) | 9 (11.3%) | 14 (17.5%) | $\chi^2$ = 1.236 | 0.266 |

*Improved BCVA defined as >1 Snellen line improvement from baseline. $\chi^2$ = Chi-square test. P ≤ 0.05 statistically significant.*

Stratified analysis of the proportion with improved best corrected visual acuity continued to favor Patriza® across most subgroups. Statistically significant superiority was noted in patients older than 55 years, males, HbA1c ≤8%, diabetes duration ≤10 years, smokers, hypertensive patients, right and left eyes, and screen use ≤4 hours/day. No significant difference was seen in bilateral disease or several smaller strata (Table 4).

**Table 4**

*Stratified Analysis — Proportion with Improved BCVA (>1 line) by Subgroup*

| Subgroup | Group A – Aflibercept | Group B – Patizra® | $\chi^2$ | P-value |
|---|---|---|---|---|
| **Age Group** | | | | |
| ≤55 years (n = 86) | 21/44 (47.7%) | 26/42 (61.9%) | 1.690 | 0.194 |
| >55 years (n = 74) | 18/36 (50.0%) | 29/38 (76.3%) | 5.575 | **0.018** |
| **Gender** | | | | |
| Male (n = 94) | 23/48 (47.9%) | 33/46 (71.7%) | 5.580 | **0.018** |
| Female (n = 66) | 16/32 (50.0%) | 22/34 (64.7%) | 1.587 | 0.208 |
| **HbA1c** | | | | |
| ≤8% (n = 68) | 20/36 (55.6%) | 25/32 (78.1%) | 3.987 | **0.046** |
| >8% (n = 92) | 19/44 (43.2%) | 30/48 (62.5%) | 3.476 | 0.062 |
| **Duration of Diabetes** | | | | |
| ≤10 years (n = 96) | 24/50 (48.0%) | 34/46 (73.9%) | 6.861 | **0.009** |
| >10 years (n = 64) | 15/30 (50.0%) | 21/34 (61.8%) | 0.937 | 0.333 |
| **Smoking** | | | | |
| Non-smoker (n = 118) | 29/58 (50.0%) | 40/60 (66.7%) | 3.287 | 0.070 |
| Smoker (n = 42) | 10/22 (45.5%) | 15/20 (75.0%) | 4.286 | **0.038** |
| **Hypertension** | | | | |
| Absent (n = 74) | 19/38 (50.0%) | 25/36 (69.4%) | 3.000 | 0.083 |
| Present (n = 86) | 20/42 (47.6%) | 30/44 (68.2%) | 3.976 | **0.046** |
| **Laterality** | | | | |
| Right eye (n = 78) | 18/38 (47.4%) | 29/40 (72.5%) | 5.336 | **0.021** |
| Left eye (n = 58) | 14/30 (46.7%) | 20/28 (71.4%) | 4.009 | **0.045** |
| Bilateral (n = 24) | 7/12 (58.3%) | 6/12 (50.0%) | 0.171 | 0.679 |
| **Screen Use** | | | | |
| ≤4 hours/day (n = 88) | 22/46 (47.8%) | 29/42 (69.0%) | 4.146 | **0.042** |

| | | | | |
|---|---|---|---|---|
| >4 hours/day (n = 72) | 17/34 (50.0%) | 26/38 (68.4%) | 2.925 | 0.087 |

*$\chi^2$ = Chi-square test within each stratum. P ≤ 0.05 statistically significant.*

## DISCUSSION

The present randomized trial demonstrated that both aflibercept and ranibizumab biosimilar Patriza improved visual acuity over three months in eyes with diabetic macular edema, but the magnitude of functional recovery was greater with Patriza. This advantage was seen for both post-treatment best corrected visual acuity and the proportion of eyes achieving more than one Snellen line improvement. Because baseline demographic, metabolic, and ocular characteristics were comparable between the two groups, the observed difference is reasonably attributable to treatment effect rather than baseline imbalance. These findings are particularly important because they provide short-term comparative evidence from a Pakistani tertiary eye care setting where local cost, accessibility, and real-world treatment patterns influence drug choice [10–12].

The pattern observed in this trial is closely aligned with the local comparative study by Malik et al. (2021), in which improved best corrected visual acuity was also reported more frequently in ranibizumab-treated eyes than aflibercept-treated eyes [9]. That concordance strengthens the external relevance of the current findings within the regional context and suggests that the superiority of Patriza in this study was not an isolated observation. From a clinical standpoint, this consistency is useful because locally generated data often carry greater practical value for prescribing decisions than extrapolation from highly selected multinational trials alone. The present study therefore adds confirmatory regional evidence that ranibizumab biosimilar therapy may yield superior early visual recovery in routine practice for diabetic macular edema [5,13,14].

However, the broader international literature has not been entirely uniform. The 1-year Protocol T trial showed greater visual gain with aflibercept than ranibizumab overall, and that advantage was especially marked in eyes with poorer baseline visual acuity, supporting aflibercept as the preferred initial option in more severe presentations at that time point [6,15]. By contrast, the 2-year extension of Protocol T showed substantial narrowing of this difference, with no statistically significant gap between aflibercept and ranibizumab for visual acuity by 24 months, although aflibercept retained some anatomical advantages on optical coherence tomography [13,16]. This apparent discrepancy with the present study may reflect several factors, including different follow-up duration, use of Snellen rather than ETDRS assessment, variation in baseline disease severity, biosimilar use rather than originator ranibizumab, and regional differences in metabolic control or health-seeking behavior. It is therefore reasonable to interpret the current findings as evidence of superior short-term functional response with Patriza rather than a universal declaration of long-term superiority over aflibercept [5,17].

Evidence supporting the efficacy of aflibercept remains robust. The VIVID and VISTA trials showed clear and durable superiority of aflibercept over laser, with meaningful gains in visual acuity and marked reductions in retinal thickness, confirming aflibercept as an effective standard anti-vascular endothelial growth factor option in diabetic macular edema [2,14,18]. Likewise, aflibercept served as the active comparator in later faricimab trials, including YOSEMITE and RHINE, where it delivered strong visual outcomes, although newer agents demonstrated non-inferiority with reduced treatment burden [17,19]. These trials show that aflibercept is far from ineffective; rather, the present findings suggest that in the early three-month interval examined here, Patriza achieved greater functional improvement under the study conditions. This distinction is important because it preserves alignment with established literature while highlighting the specific contribution of the current study.

The ranibizumab literature also supports the biological plausibility of the present results. Protocol I established ranibizumab-based therapy as clearly superior to laser-based management, and showed that prompt laser added little to visual recovery when anti-vascular endothelial growth factor therapy was used [19].

Another notable aspect of the present study was the subgroup pattern. The advantage of Patriza was more evident in older patients, men, patients with glycated hemoglobin of 8% or less, those with diabetes duration of 10 years or less, smokers, hypertensive patients, and unilateral disease. Mean visual improvement also remained significantly greater with Patriza across most examined strata, even where dichotomous improvement did not reach statistical significance. These findings suggest that better systemic control and shorter disease duration may be associated with greater retinal functional reversibility, which is biologically plausible in diabetic macular edema. At the same time, these subgroup findings should be interpreted cautiously because the trial was not primarily powered for interaction testing, and several non-significant subgroup comparisons may simply reflect smaller numbers within strata. Their value lies more in hypothesis generation than in definitive treatment selection rules [1,4,11].

The low frequency of visual worsening in both groups is also noteworthy. Only a small minority of eyes lost one or more Snellen lines over follow-up, and there was no meaningful between-group difference in this regard. Although the study was not designed as a formal safety trial and did not include detailed ocular or systemic adverse event profiling, these results suggest that both regimens were functionally well tolerated during the three-month study interval. This is clinically reassuring, particularly in settings where repeated intravitreal therapy must be balanced against adherence, cost, and follow-up constraints.

The principal new contribution of this study to the medical literature lies in its direct comparison of aflibercept and ranibizumab biosimilar Patriza using clinically interpretable Snellen-based visual outcomes in a local population. Much of the international evidence has compared originator agents, emphasized ETDRS-based outcomes, or focused on anatomical measures alongside vision. The present trial instead provides pragmatic short-term evidence that Patriza may produce greater early visual benefit than aflibercept in this practice

environment. This has clinical significance for ophthalmologists managing diabetic macular edema in resource-sensitive settings, because it supports the consideration of ranibizumab biosimilar therapy not merely as a lower-cost substitute, but as an option capable of strong early functional performance under real-world local conditions.

## CONCLUSION

In this randomized controlled trial, both intravitreal aflibercept and ranibizumab biosimilar Patriza® were effective in improving vision in patients with diabetic macular edema. However, Patriza® achieved a significantly greater gain in best corrected visual acuity and a higher proportion of clinically meaningful visual improvement after three months of treatment. The study therefore showed that ranibizumab biosimilar Patriza® offered superior short-term functional efficacy compared with aflibercept in this setting, while both agents demonstrated a low rate of visual deterioration over follow-up.

## REFERENCES

1. Graue-Hernandez, E. O., Rivera-De-La-Parra, D., Hernandez-Jimenez, S., Aguilar-Salinas, C. A., Kershenobich-Stalnikowitz, D., & Jimenez-Corona, A. (2020). Prevalence and associated risk factors of diabetic retinopathy and macular oedema in patients recently diagnosed with type 2 diabetes. *BMJ Open Ophthalmology*, *5*(1), e000304. https://doi.org/10.1136/bmjophth-2019-000304
2. Heier, J. S., Korobelnik, J.-F., Brown, D. M., Schmidt-Erfurth, U., Do, D. V., Midena, E., Boyer, D. S., Terasaki, H., Kaiser, P. K., Marcus, D. M., Nguyen, Q. D., Jaffe, G. J., Slakter, J. S., Simader, C., Soo, Y., Schmelter, T., Vitti, R., Berliner, A. J., Zeitz, O., & Metzig, C. (2016). Intravitreal Aflibercept for Diabetic Macular Edema: 148-Week Results from the VISTA and VIVID Studies. *Ophthalmology*, *123*(11), 2376–2385. https://doi.org/10.1016/j.ophtha.2016.07.032
3. Im, J. H., Jin, Y., Chow, R., & Yan, P. (2022). Prevalence of diabetic macular edema based on optical coherence tomography in people with diabetes: A systematic review and meta-analysis. *Survey of Ophthalmology*, *67*(4), 1244-1251. https://doi.org/10.1016/j.survophthal.2022.01.009
4. Cantrell, R. A., Lum, F., Chia, Y., Morse, L. S., Rich, W. L., Salman, C. A., & Willis, J. R. (2020). Treatment patterns for diabetic macular edema: An intelligent research in sight (IRIS®) registry analysis. *Ophthalmology*, *127*(3), 427-429. https://doi.org/10.1016/j.ophtha.2019.10.019
5. Massin, P., Bandello, F., Garweg, J. G., Hansen, L. L., Harding, S. P., Larsen, M., Mitchell, P., Sharp, D., Wolf-Schnurrbusch, U., Gekkieva, M., Weichselberger, A., & Wolf, S. (2010). Safety and efficacy of Ranibizumab in diabetic macular edema (Resolve study). *Diabetes Care*, *33*(11), 2399-2405. https://doi.org/10.2337/dc10-0493
6. Wells, J. A., Glassman, A. R., Ayala, A. R., Jampol, L. M., Bressler, N. M., Bressler, S. B., Brucker, A. J., Ferris, F. L., Hampton, G. R., Jhaveri, C., Melia, M., & Beck, R. W. (2016). Aflibercept, Bevacizumab, or Ranibizumab for Diabetic Macular Edema. *Ophthalmology*, *123*(6), 1351–1359. https://doi.org/10.1016/j.ophtha.2016.02.022
7. Dhoot, D. S., Moini, H., Reed, K., Silva, F. Q., Berliner, A., Du, W., & Sharma, S. (2022). Incidence of new diabetic macular edema in fellow eyes of patients in the vista and vivid studies. *Retina*, *43*(2), 254-262. https://doi.org/10.1097/iae.0000000000003658
8. Malik, H. A., Sabih, R., Khan, H., Asrar, A., & Asif, M. (2021). Comparison of Intravitreal Bevacizumab versus Intravitreal Ranibizumab in treatment naive macular edema patients (Real world evidence in Pakistan). *Pakistan Journal of Ophthalmology*, *37*(2). https://doi.org/10.36351/pjo.v37i2.1194
9. Malik, H. A., Sabih, R., Khan, H., Muhammad Umair, Muhammad Asif, Asrar, A., & Asrar, M. (2022). Short-term efficacy of INTRAVITREAL PATIZRA® (RANIBIZUMAB) in treatment naive patients- Real world evidence in Pakistan. *Journal of Ayub Medical College Abbottabad*, *34*(3 (SUPPL 1)). https://doi.org/10.55519/jamc-03-s1-9562
10. Ali, M. A. A., Saied Hegazy, H., Othman Abdelkhalek Elsayed, M., Tharwat, E., Nabeh Mansour, M., Hassanein, M., Ramadan Ezzeldin, E., Mohammed GadElkareem, A., Mahmoud Abd Ellateef, E., A. Elsayed, A., Hassan Elabd, I., H Abd Rbu, M., Saleh Amer, R., Ali El Gabbar, A. G., Mahmoud, H., Mohamed Abdelhameed, H., & Mohammed Elsayed Abdelkader, A. (2024). Aflibercept or ranibizumab for diabetic macular edema. *Medical hypothesis discovery and innovation in ophthalmology*, *13*(1), 16-26. https://doi.org/10.51329/mehdiophthal1490
11. Brown, D. M., Emanuelli, A., Bandello, F., Barranco, J. J., Figueira, J., Souied, E., Wolf, S., Gupta, V., Ngah, N. F., Liew, G., Tuli, R., Tadayoni, R., Dhoot, D., Wang, L., Bouillaud, E., Wang, Y., Kovacic, L., Guerard, N., & Garweg, J. G. (2022). Kestrel and KITE: 52-Week results from two phase III pivotal trials of Brolucizumab for diabetic macular edema. *American Journal of Ophthalmology*, *238*, 157-172. https://doi.org/10.1016/j.ajo.2022.01.004
12. Gardner, T. W. (2011). The restore study. *Evidence-Based Ophthalmology*, *12*(4), 206-207. https://doi.org/10.1097/ieb.0b013e31822faded
13. Isik, P., Sizmaz, S., Esen, E., Uysal, A., & Demircan, N. (2023). Comparison of intravitreal ranibizumab and aflibercept for the treatment of diabetic macular edema: A real-world study. *International Ophthalmology*, *43*(11), 4171-4180. https://doi.org/10.1007/s10792-023-02820-0
14. Korobelnik, J.-F., Do, D. V., Schmidt-Erfurth, U., Boyer, David S., Holz, F. G., Heier, J. S., Midena, E., Kaiser, Peter K., Terasaki, H., Marcus, D. M., Nguyen, Q. D., Jaffe, G. J., Slakter, J. S., Simader, C., Soo, Y., Schmelter, T., Yancopoulos, G. D., Stahl, N., Vitti, R., & Berliner, A. J. (2014). Intravitreal Aflibercept for Diabetic Macular Edema. *Ophthalmology*, *121*(11), 2247–2254. https://doi.org/10.1016/j.ophtha.2014.05.006
15. Shimizu, N., Oshitari, T., Tatsumi, T., Takatsuna, Y., Arai, M., Sato, E., Baba, T., & Yamamoto, S. (2017). Comparisons of efficacy of Intravitreal Aflibercept and Ranibizumab in eyes with diabetic macular edema. *BioMed Research International*, *2017*, 1-7. https://doi.org/10.1155/2017/1747108
16. Fouda, S. M., & Bahgat, A. M. (2017). Intravitreal aflibercept versus intravitreal ranibizumab for the treatment of diabetic macular edema. *Clinical Ophthalmology*, *11*, 567-571. https://doi.org/10.2147/opth.s131381
17. Wykoff, C. C., Abreu, F., Adamis, A. P., Basu, K., Eichenbaum, D. A., Haskova, Z., Lin, H., Loewenstein, A., Mohan, S., Pearce, I. A., Sakamoto, T., Schlottmann, P. G., Silverman, D., Sun, J. K., Wells, J. A., Willis, J. R., Tadayoni, R., Aaberg, T., Abbey, A., & Abdulaeva, E. (2022). Efficacy, durability, and safety of intravitreal faricimab with extended dosing up to every 16

weeks in patients with diabetic macular oedema (YOSEMITE and RHINE): two randomised, double-masked, phase 3 trials. *The Lancet*. https://doi.org/10.1016/s0140-6736(22)00018-6

18. Lundeen, E. A., Andes, L. J., Rein, D. B., Wittenborn, J. S., Erdem, E., Gu, Q., Saaddine, J., Imperatore, G., & Chew, E. Y. (2022). Trends in prevalence and treatment of diabetic macular edema and vision-threatening diabetic retinopathy among Medicare part B fee-for-Service beneficiaries. *JAMA Ophthalmology*, *140*(4), 345. https://doi.org/10.1001/jamaophthalmol.2022.0052
19. Elman, M. J., Bressler, N. M., Qin, H., Beck, R. W., Ferris, F. L., Friedman, S. M., Glassman, A. R., Scott, I. U., Stockdale, C. R., & Sun, J. K. (2011). Expanded 2-Year follow-up of Ranibizumab plus prompt or deferred laser or Triamcinolone plus prompt laser for diabetic macular edema. *Ophthalmology*, *118*(4), 609-614. https://doi.org/10.1016/j.ophtha.2010.12.033