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ORIGINAL RESEARCH

Visual Gains with Faricimab vs Aflibercept 8 mg in Naïve Retinovascular Disease: Global Real-World Cases and Literature Review

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Background: To compare the visual gains of faricimab and aflibercept 8 mg as first-line in real-world management of retinovascular diseases.

Methods: Retrospective multicenter interventional case series with retinovascular diseases initiated on faricimab or aflibercept 8 mg till August 30, 2025. Main outcome measure was visual gain in logMAR. Linear mixed-effects model was used to compare vision increase between the two drug groups. In addition, comparative Phase 3 trials were supplemented by a literature review of treatment-naïve eyes using major databases till September 30, 2025.

Results: We collected 500 treated eyes from 35 collaborating centers. The treatment groups included 395 eyes receiving faricimab vs 105 receiving aflibercept 8 mg distributed into neovascular macular degeneration (270 vs 58), diabetic macular edema (97 vs 39) and macular edema associated with retinal vein occlusion (28 vs 8). Adjusted visual gains were comparable between the two drugs in various retinal categories (p=0.672).

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Conclusion: Visual acuity improved significantly and equally in both aflibercept 8 mg and faricimab in several treatment-naïve retinovascular diseases.

Plain Language Summary:

- **What is already known on this topic –** 2 new benchmarks faricimab and aflibercept 8 mg are well known in improving vision in phase 3 trials and extending the interval of treatment in neovascular age-related macular degeneration, diabetic macular edema and macular edema from retinal vein occlusion. No comparison was previously made to detect differences in visual acuity in treatment-naïve eyes and also in real-world settings.
- **What this study adds –** Faricimab and aflibercept 8 mg improved vision significantly and equally when used as first line therapy in real-world management of retinal vascular diseases (neovascular age-related macular degeneration, diabetic macular edema, and macular edema from retinal vein occlusion) in a large global multicenter case series of 500 eyes. Similar conclusions were made after literature review of 6179 treatment-naïve eyes from the real-world literature and 3849 eyes from phase 3 studies.
- **How this study might affect research, practice or policy –** Clinicians have the choice to use between two equally effective drugs in their daily practice.

Keywords: aflibercept 8 mg, faricimab, macular degeneration, diabetic maculopathy, retinal vein occlusion

Introduction

The introduction of faricimab (Vabysmo^{R}, Genentech Inc, South San Francisco, CA, US) and aflibercept 8 mg (Eylea HD^{R}, Regeneron Pharmaceuticals Inc, Tarrytown, New York, US) to treat chorioretinal vascular diseases has garnered significant attention in Ophthalmology. Aflibercept 2 mg (the precursor to 8 mg), a fusion protein that binds all isoforms of vascular endothelial growth factor (VEGF)-A, VEGF-B, galectin-1, and placental growth factor, has an excellent efficacy and safety profile, whereas the recently approved faricimab (2023) is a novel humanized bispecific antibody that targets isoforms of VEGF-A and angiopoietin-2 (Ang-2).

Both faricimab and aflibercept 8 mg were developed to decrease treatment burden by lengthening treatment intervals. Data from pivotal clinical trials[1–6] have demonstrated the long-term efficacy and safety of both drugs in patients with diabetic macular edema (DME) and neovascular age-related macular degeneration (nAMD), with the possibility of interval extension to 16 weeks or longer in nearly 50% of eyes. Preliminary data from real-world nAMD and DME studies support the efficacy of both drugs,[7–57] with excellent stabilization of vision, but no large head-to-head study has compared the visual outcomes and numbers of injections.

In this manuscript, we report the results of a large, multi-center, international comparison cohort to better define the therapeutic abilities of faricimab and aflibercept 8 mg in improving visual outcomes in treatment-naïve eyes. By including a diverse group of patients with different genetic make-ups, backgrounds, medical problems, and environmental influences, we believe that our results are generalizable to clinical practices throughout the world.

Additionally, we performed a comprehensive search of the literature to identify treatment-naïve patients receiving faricimab and aflibercept 8 mg as first line therapy. Finally, we have extracted data from the phase 3 faricimab and aflibercept 8 mg registration trials. We believe that by using data from these three distinct sources, a comprehensive data-driven understanding of the efficacy and safety of faricimab and faricimab can best be attained.

Materials and Methods

Study Approval

A multicenter case series of patients treated from January, 2025 to August 2025 was compiled from 35 retina centers throughout the world (Africa, America, Asia and Europe). The study was approved by the Ethics Committee of the Beirut Eye Specialty Hospital (BESH-EC20-251) and followed the tenets of the Declaration of Helsinki. The need for informed consent was waived because of the anonymous and retrospective nature of the research. The study was exempt from IRB oversight because of its retrospective design and deidentified patient data. Confidentiality was maintained throughout data aggregation and analysis.

Study Design

The study included a consecutive series of patients with treatment-naïve nAMD, DME, or RVO who were primarily treated with either intravitreal aflibercept 8 mg or faricimab depending on commercial availability. Inclusion criteria included the following: active subfoveal neovascular membrane due to nAMD; fovea-involving DME; or diffuse macular edema due to CRVO or BRVO. Exclusion criteria included the following: age under 20 years; previous vitrectomy; cataract surgery within the past 6 months; presence of keratitis, conjunctivitis, blepharitis or systemic infection. Most patients received a loading series of three or four monthly intravitreal injections with additional injections according to treat-and-extend or personalised protocols according to patients needs.

Each patient underwent a comprehensive ocular examination, including measurement of best corrected visual acuity (BCVA) with Snellen charts, which was converted to logMAR for analyses. Spectral domain optical coherence tomography (OCT) or OCT angiography (OCTA) were analysed at baseline and at month four. The primary outcome measures included BCVA at baseline, 1 month, and at last follow-up. Intraocular pressures (IOP) were measured at baseline, 1 minute after the injection, and at follow-up examinations. Participants were scheduled to receive at least three loading doses every four weeks and thereafter at the discretion of the ophthalmologist, based on OCT and/or functional criteria. Complications, as noted during examinations or reported by patients, were recorded.

Aflibercept 8 mg (30.1 mg/0.263 mL) was withdrawn from a vial into a 1 mL sterile syringe and 0.07 mL (8 mg) was injected into the vitreous. Faricimab (28.8 mg/0.24 mL) was withdrawn from a vial into a 1 mL sterile syringe and 0.05 mL (6 mg) was injected into the vitreous. For centers without access to aflibercept 8 mg, the same dose was achieved using multiple doses of aflibercept 2 mg[58] with prior paracentesis to control the anticipated IOP rise.

Literature and Phase 3 Trial Data

Since both drugs were recently approved and only limited data sets had been published, a literature review in the aim to broaden the external validity of the current retrospective case series. We used the PICO framework (Population: treatment naïve eyes with nAMD, DME or RVO-ME, outside controlled studies. Intervention: faricimab or aflibercept 8 mg injections into the vitreous. Comparator: number of injections and period of followup, Outcome: visual gain). We searched the Medline, Scopus, Web of Science, and Cochrane Reviews (from January 1, 2023 to September 30, 2025) databases with the Medical Subject Headings "faricimab AND naïve treatment AND real world" or "8 mg aflibercept AND naïve treatment AND real world". Inclusion criteria included: English, French and Spanish languages; no country restriction; patient age above 18 years; publications that included meeting abstracts and articles in press. Exclusion criteria included: reviews; editorials; letters; Phase 2 or 3 controlled studies; case reports; previous laser therapy; aflibercept 4 mg; and follow-up less than 2 months. The data search was performed by 2 operators (HAM, AMM).

Data were extracted from the phase 3 trials for faricimab (TENAYA and LUCERNE, YOSEMITE and RHINE, BALATON and COMINO) and aflibercept 8 mg (PULSAR, PHOTON, and QUASAR).

Statistical Analysis

Quantitative data were analyzed with mean and standard deviation (SD). For the BCVA analyses, Snellen visual acuity was converted to logMAR and, for consistency, ETDRS letters were also converted into logMAR. Linear Mixed-Effects Model was used to compare BCVA gains between the two drugs. A linear mixed-effects model (LMM) was employed as the primary analytical approach, justified by the large sample size (500 eyes), repeated BCVA measurements across three visits (initial, 1 month and final), unequal follow-up durations, and baseline imbalance between treatment groups. The model included fixed effects for time, retinal disease category, treatment type, number of injections, and follow-up duration. A random intercept for eye was specified to account for within-eye correlation across repeated measures.

Statistical analyses were performed using SPSS 29.0 (IBM SPSS Inc, Armonk, NY, US) software. A P-value equal to or less than 0.05 was considered statistically significant. To analyze the literature review data, missing results were filled using mean imputation. Comparison of two independent means was performed using the *t*-test.

Results

Demographics of Cohort

General demographic data on treatment-naïve patients are depicted in Table 1 and Table 2. We included a total of five hundred eyes from 467 patients (bilateral injections were performed in 14 patients with nAMD: 11 faricimab vs 3 aflibercept 8 mg; and 19 patients with DME: 12 faricimab vs 7 aflibercept 8 mg). Mean baseline BCVA was 0.61 ± 0.45 LogMAR. Mean follow-up duration was 11.67 ± 7.61 months, and eyes received a mean of 5.92 ± 4.16 intravitreal injections. The cohort consisted predominantly of age-related macular degeneration (AMD) (65.6%), followed by diabetic macular edema (DME) (27.2%) and retinal vein occlusion (RVO) (7.2%). Most eyes were treated with Faricimab (79.0%), while 21.0% received aflibercept 8 mg. No significant differences in sex (p=0.13 for nAMD and p=0.27 for DME), age and systemic diseases (diabetes mellitus p=0.86 for nAMD and p=1.0 for DME; coronary artery

Table 1 Real World Comparison Between 500 Consecutive Treatment-Naive Eyes Treated with Either Faricimab or Aflibercept 8 mg

Mean±SD	**nAMD FAR**	**nAMD HDA**	**DME FAR**	**DME HDA**	**RVO-ME FAR**	**RVO-ME HDA**
Age	76.6±10.8	78.7±8.6	62.1±12.6	58.3±8.9	67.0±11.5	66.0±11.3
p-value	0.17		0.009		0.8	
Male%	52.5%	41.4%	65.9%	68.0%	60.7%	62.5%
p-value	0.13		0.27		0.96	
DM%	18.9%	17.2%	100%	100%	17.9%	25.0%
p-value	0.86		1.0		0.67	
CAD%	10.4%	13.8%	26.7%	20.0%	10.7%	0.0%
p-value	0.38		0.12		0.35	
HTN%	37.4%	41.8%	52.3%	56.0%	25.0%	12.5%
p-value	0.40		0.73		0.47	
Number of eyes	270	58	97	39	28	8
Right eye %	48.5%	44.8%	50.5%	61.5%	57.1%	87.5%
Phakic %	33.8%	51.7%	56.8%	92.0%	35.7%	50.0%
Number of intravitreal injections	7.1±4.9	5.4±3.1	4.6±2.2	3.8±1.5	3.9±1.2	4.9±3.7
p-value	0.012		0.039		0.22	
Follow-up (months)	14.2±8.4	9.8±6.9	9.7±4.6	5.9±2.3	7.9±4.0	8.3±7.4
p-value	0.001		0.001		0.84	
IOP initial mmHg	14.7±3.5	15.7±3.8	15.0±3.4	15.1±3.4	17.9±3.1	17.9±3.5
IOP 1 minute after injection (mmHg)	16.1±5.4 (n=114)	17.4±8.1 (n=38)	15.9±2.8 (n=23)	16.0±1.1 (n=6)	19.5±3.7 (n=4)	17.3±4.7 (n=7)
Mean IOP rise 1 minute after injection (mm Hg)	1.4	1.7	0.9	0.9	2.0	−0.6
% Aqueous tap before injection	0.0%	31.1%	0.0%	10.3%	0.0%	87.5%
Final IOP (mmHg)	14.3±3.5	14.5±4.1	15.3±3.5	14.9±4.1	17.0±3.6	13.9±1.5
P initial to final IOP	P=0.18	P=0.10	P=0.55	P=0.82	P=0.32	P=0.01

Abbreviations: nAMD, neovascular age-related macular degeneration; FAR, faricimab; HAD, aflibercept 8 mg; DME, diabetic macular edema; RVO-ME, retinal vein occlusion with macular edema; CAD, coronary artery disease; HTN, systemic arterial hypertension; IOP, intraocular pressure; NA, not assessed; SD, standard deviation.

Table 2 Distribution of 500 Eyes Treated with Faricimab of Aflibercept 8 mg. Comparison of Vision is Based on Estimated Marginal Means

Major Characteristics	**Value**
Number of eyes	500
Baseline BCVA, mean±SD	0.61±0.45
Follow-up duration (months), mean±SD	11.67±7.61
Number of injections, mean±SD	5.92±4.16
Disease distribution, n (%)	
1-AMD, n (%)	328 (65.6%)
2-DME, n (%)	136 (27.2%)
3-RVO, n (%)	36 (7.2%)
Treatment distribution, n (%)	
1-Faricimab, n (%)	395 (79.0%)
2- 1Aflibercept 8 mg, n (%)	105 (21.0%)
Visits	**Adjusted Mean BCVA**
1-Baseline adjusted mean BCVA	0.777
2-One-month adjusted mean BCVA	0.550
3-Final adjusted mean BCVA	0.423
Overall adjusted mean gain	
1-Initial BCVA−One-month BCVA	0.777−0.550=0.227 (p<0.001)
2-Initial BCVA−Final BCVA	0.777−0.423=0.353 (p<0.001)
Disease-specific adjusted mean gains	
1-AMD (Gain=Baseline−Final)	0.699−0.474=0.225
2-DME (Gain=Baseline−Final)	0.654−0.420=0.234
3-RVO (Gain=Baseline−Final)	0.977−0.376=0.601
The key comparison (Time×Drug interaction)	**F=0.397 p=0.672**

Note: The adjusted visual gain over time did not differ significantly between Faricimab and 8 mg aflibercept.

Abbreviations: BCVA, best corrected visual acuity in LogMar; AMD, age-related macular degeneration; DME, diabetic macular edema; RVO, retinal vein occlusion; F, F-test.

disease p=0.38 for nAMD and p=0.12 for DME) were noted between the cohorts. Adjusted overall mean initial BCVA (in LogMAR) improved by 0.183 (from 0.719 to 0.536) (95% confidence interval: 0.118–0.247; p<0.001) 1 month after the first injection and by 0.239 (from 0.719 to 0.480) (95% confidence interval: 0.178–0.300; p<0.001) at the end of followup. For eyes with nAMD, DME, or RVO, BCVA at one month was a strong predictor of final BCVA (p=0.001).

Final Results

The final LMM demonstrated a significant effect of time on visual acuity (F=42.12, p<0.001). After adjustment for repeated measurements, retinal disease, follow-up duration, and injection number, the (Treatment × Time interaction) was not significant (F=0.397; p=0.672), indicating that the longitudinal pattern of visual gain over time was comparable between treatment groups. Thus both treatments demonstrated similar visual improvement over the course of follow-up.

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Adverse Events

IOP rise immediately after injections was similar between the two drugs. No drug reflux was noted when aflibercept 8 mg was preceded by paracenteses.

Reported adverse events included death (three months after follow-up and receipt of two faricimab injections), endophthalmitis (two eyes after second injections of aflibercept 8 mg in two patients with severe flu-like diseases), iritis (one faricimab and one aflibercept 8 mg), glaucoma (two faribimab and one aflibercept 8 mg), retinal pigment epithelial tear (one faricimab), subretinal hemorrhage (two faricimab), retinal detachment (two faricimab). Loss to follow-up was due to the following conditions: uremic encephalopathy (one aflibercept 8 mg); macular scars (two faricimab); two aflibercept 8 mg switched to faricimab after third injection; two faricimab switched to aftlibercept 2 mg after 22 months and 24 months on faricimab; one faricimab switched to aflibercept 8 mg after 22 months on faricimab.

Literature Review of Treatment-Naïve Eyes

The database searches yielded 43 papers after deduplication; of these 43 were subjected to full text screen and 32 were judged to be appropriate for inclusion. Additional 21 papers were identified through hand searching and were also deemed suitable for inclusion. In total, the review analyzed 6179 treatment-naïve eyes in 52 studies[7–57] (Table 3): a total of treated with faricimab nAMD (4089), DME (1903), RVO-ME (47) and a total of treated with aflibercept 8 mg for nAMD (140). There was a robust significant visual increase of 1.3 ETDRS line after an average of 4.1 faricimab injections. A marginally significant increase of one ETDRS line was noted in the aflibercept 8 mg group after an average of 3.3 injections. The short follow-up precluded commenting on the difference in the number of injections. Moreover, the faricimab group included worse baseline vision than the aflibercept 8 mg group introducing a bias limiting direct comparison of final outcome.

Phase 3 Trial Data

Phase 3 nAMD trials demonstrated similar one-year improvements in mean BCVA (logMAR) and numbers of injections between faricimab (−0.12, 6.6) and aflibercept 8 mg (−0.13, 5.7) (Table 4). For eyes with DME, one year improvements in mean BCVA and numbers of injections were −0.23, 9.0 for faricimab and −0.17, 5.5 for aflibercept 8 mg. For eyes with RVO-ME, improvements in mean BCVA and numbers of injections were −0.34, 6.0 for faricimab (mean follow-up of 6 months) and −0.36, 6.5 for aflibercept 8 mg (mean follow-up of 8 months).

When combining results of the three analytic models (Tables 1–4) into one (Table 5), complete unadjusted comparative data can be found for nAMD only. Mean unadjusted BCVA improvements were comparable between faricimab and aflibercept 8 mg −0.12 vs −0.13 in phase 3 trials (6.6 vs 5.7 injections over a follow-up of 12 months), −0.13 vs −0.10 in the real-world literature (4.1 vs 3.3 injections over a follow-up of 5.1 vs 3.1 months), and −0.23 vs −0.23 in the current study (7.1 vs 5.4 injections over a follow-up of 14.2 vs 9.8 months).

Discussion

This comparative study of real world treatment-naïve eyes with nAMD, DME, and RVO (Table 1), backed by even larger numbers of real world treatment-naïve eyes from the published world literature (Table 2) and supported by a comparative analysis of phase 3 controlled trials (Table 3), emphasizes the clinical efficacy of faricimab and aflibercept 8 mg with comparable visual gains. The drugs produce similar BCVA gains, comparable final BCVA when initial BCVA is used as a covariate and after matching for follow-up, excellent safety profiles (including minimal IOP rise), and rapid improvments in vision as early as one month post-injection. The unique multifaceted comparison used in this analysis between the two benchmark drugs for three chorioretinal vascular diseases highlights the similarities in safety and efficacy. Because these drugs appear to produce longer dosing intervals with reduced treatment burden compared to previously introduced anti-VEGF drugs, they should become convenient options for real-world practice.[60]

Several lines of evidence point to vision benefits between faricimab and aflibercept 8 mg despite their different mechanisms of action. Faricimab's dual VEGF-A/Ang-2 inhibition and aflibercept's broader VEGF-A/B/PlGF blockade both achieve similar visual outcomes in head-to-head trials, with comparable durability and safety profiles. The similar

Table 3 Systematic Review of 6179 Eyes Through August 30, 2025 for Real-World Treatment Naïve Eyes.[7–57,59] Visual Outcomes with Aflibercept 8 mg or Faricimab are Shown

First Author Year of Publication	FAR HDA	nAMD DME RVO-ME	Vinitial (logMAR) Mean±SD	Vfinal (logMAR) Mean±SD	N. Injection	Follow-Up (Month)	N Eyes	p-value Vision
Matsumoto 2023[7]	FAR	nAMD	−0.64±0.41	−0.47±0.39	3	3	69	0.001
Mukai 2023[8]	FAR	nAMD	−0.40±0.42	−0.32±0.43	3	3	62	0.001
Raslan 2023[9]	FAR	nAMD	−0.46±0.13	NA	2.1	2.1	32	>0.05
Modeste 2024[10]	FAR	nAMD	−0.53±0.29	−0.49±0.42	6.6	10	66	NA
Hara 2024[11]	FAR	nAMD	−0.46±0.41	−0.44±0.45	3	3	30	0.60
Tanaka 2024[12]	FAR	nAMD	−0.29±0.30	−0.18±0.32	3	4	23	0.001
Maruyama-Inoue 2024[13]	FAR	nAMD	−0.36±0.33	−0.28±0.32	3	4	47	0.002
Toto 2024[14]	FAR	nAMD	−0.40	−0.10	4	5	18	0.001
Fukuda 2024[15]	FAR	nAMD	−0.32±0.37	−0.19±0.25	3	3	43	0.001
Grimaldi 2024[16]	FAR	nAMD	−0.40	−0.10	10	15	21	0.01
Quah 2024[17]	FAR	nAMD	−0.52±0.26	−0.46±0.29	4.5	5.1	35	>0.05
Brinkmann 2024[18]	FAR	nAMD	−0.57±0.34	−0.55±0.35	3	4	25	0.57
Cennamo 2024[19]	FAR	nAMD	NA	−0.70±0.30	4	5	12	0.001
Inoda 2024[20]	FAR	nAMD	NA	−0.16 improvement	NA	12	27	0.001
Sim 2024[21]	FAR	nAMD	−0.57	−0.45	5	10.5	151	0.001
Kunzmann 2024[22]	FAR	nAMD	−0.55	−0.30	3	3	5	0.19
Veritti 2024[23]	FAR	nAMD	−0.58±0.24	−0.40±0.24	4	4	22	0.001
Al-Gilgawi 2024[24]	FAR	nAMD	NA	−0.09 improvement	4	4	68	0.07
Han 2025[25]	FAR	nAMD	−0.64±0.41	−0.47±0.39	3	3	69	0.001
Hafner 2025[26]	FAR	nAMD	−0.60	−0.40	4	4	40	0.001
Patwardhan 2025[27]	FAR	nAMD	−1.56±0.30	−0.06±0.29	6.8	12	68	0.001
Scampoli 2025[28]	FAR	nAMD	−0.51±0.23	−0.36±0.26	8	14.1	33	0.03
Sivachandran 2025[29]	FAR	nAMD	NA	Significant improvement	3	3	53	0.001

(*Continued*)

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Table 3 (Continued).

First Author Year of Publication	FAR HDA	nAMD DME RVO-ME	Vinitial (logMAR) Mean±SD	Vfinal (logMAR) Mean±SD	N. Injection	Follow-Up (Month)	N Eyes	p-value Vision
Guymer 2025[30]	FAR	nAMD	NA	−0.08±0.29 improvement	4.7	6	120	NA
Hoshino 2025[31]	FAR	nAMD	−0.28±0.41	−0.18±0.32	10.1	24	25	0.06
Ali 2025[32]	FAR	nAMD	−0.57	−0.47	4	4	1982	0.01
Sreekala 2025[33]	FAR	nAMD	−0.54	Group 1 −0.45	3	4	324	NA
	FAR	nAMD	–0.54	Group 2 −0.43	4	5		
Lupidi 2025[34]	FAR	nAMD	NA	NA	6.9	15.6	24	NA
Doi 2025[35]	FAR	nAMD	−0.39±0.41	−0.16±0.32	4	5	24	0.01
Doi 2025[35]	FAR	nAMD	−0.34±0.32	−0.21±0.32	3	4	25	0.01
Cho 2025[36]	FAR	nAMD	−0.43±0.41	−0.36±0.27	6.1	12	30	0.013
Cattaneo 2025[37]	FAR	nAMD	−0.32	−0.18	6.0	12	13	0.053
Yanai 2025[38]	FAR	nAMD	−0.39±0.37	−0.29±0.34	4.0	6	126	0.001
Augustin 2025[39]	FAR	nAMD	NA	Improvement 0.2–0.3 decimals	3.0	3.0	205	0.001
Bartolomeo 2025[40]	FAR	nAMD	−0.29±0.2.5	−0.22±0.25	4.6	6.0	51	0.010
Obana[41]	FAR	nAMD	0.21±0.23	0.08±0.14	6.4	15.0	47	0.001
Carlà 2025[42]	FAR	nAMD	NA	NA	9.1	12	18	NA
Kamao 2025[59]	FAR	nAMD	−0.07	−0.02	3	4	28	0.003
Kamao 2025[59]	FAR	nAMD	−0.42	−0.38	3	4	28	0.001
TOTAL	FAR	nAMD	−0.56±0.33	−0.43±0.33	4.1	5.1	4089	0.001
Cattaneo 2025[37]	HDA	nAMD	−0.54±0.74	−0.11±0.37	3	3	10	0.25
Bala 2025[43]	HDA	nAMD	−0.74±1.14	−0.81±1.07	4	5.4	10	1.00
Hosoda 2025[44]	HDA	nAMD	−0.31±0.38	−0.25±0.38	3	3	21	0.035
Mizukami 2025[45]	HDA	nAMD	−0.22±0.23	−0.18±0.20	3	3	12	0.07
Sambhara 2025[46]	HDA	nAMD	−0.69±0.25	−0.60±0.27	NA	6	4	>0.05

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Matsumoto 2025[47]	HDA	nAMD	−0.33±0.45	−0.22±0.38	3	3	83	<0.01
TOTAL	HDA	nAMD	−0.37±0.49	−0.27±0.41	3.3	3.1	140	0.065
P	FAR-HDA	nAMD	P=0.001	P=0.001				
Kusuhara 2023[48]	FAR	DME	−0.23±0.26	−0.22±0.32	1.6	6	14	>0.05
Al-Rufayie 2024[49]	FAR	DME	−0.86±0.31	−0.23±0.26	3	6	35	<0.05
Quah 2024[17]	FAR	DME	−0.48±0.26	−0.24±0.23	4.4	5.3	33	>0.05
Al-Gilgawi 2024[24]	FAR	DME	NA	−0.15 improvement	4	4	77	0.001
Guymer 2025[30]	FAR	DME	NA	−0.14 improvement	4.7	6	67	NA
Śpiewak 2025[50]	FAR	DME	−0.38	−0.02	4	4	20	0.001
Peto 2025[51]	FAR	DME	−0.38	−0.20	4.5	12	690	NA
Lupidi 2025[34]	FAR	DME	NA	NA	6.1	12.4	9	NA
Hirakata 2025[52]	FAR	DME	−0.24±0.31	−0.16±0.26	2.7	5.1	15	0.03
Chakraborty 2025[53]	FAR	DME	−0.43±0.13	−0.21±0.09	4.9	6	16	0.001
Esteban-Floría 2025[54]	FAR	DME	−0.23±0.11	−0.12±0.29	5.7	8	28	0.003
Borkar 2025[55]	FAR	DME	−0.49±0.40	−0.42±0.37	4.9	10.0	851	<0.01
Augustin 2025[39]	FAR	DME	NA	Improvement 02.–0.3 decimals	4.0	4.0	48	0.001
TOTAL	FAR	DME	−0.44±0.33	−0.30±0.29	4.6	9.9	1903	0.001
Hikichi 2025[56]	FAR	RVO-ME	−0.38	−0.09	1.96	6	25	0.001
Hirakata 2025[52]	FAR	RVO-ME	−0.30±0.37	−0.11±0.20	1.40	3.7	17	0.01
Inokuchi 2025[57]	FAR	RVO-ME	−0.37	−0.12	1	3	5	0.068
TOTAL	FAR	RVO-ME	−0.35±0.37	−0.10±0.20	1.66	4.8	47	0.001

Abbreviations: nAMD, neovascular age-related macular degeneration; FAR, faricimab; HAD, aflibercept 8 mg; DME, diabetic macular edema; RVO-ME, retinal vein occlusion with macular edema; NA, not assessed.

Table 4 The Table Includes 3849 Treatment-Naïve Eyes in Phase 3 Faricimab and Aflibercept 8 mg Registration Trials with Data Captured at Approximate One Year (Depending on the Primary Endpoints) Except for Retinal Vein Occlusion Trials Which Terminated Earlier

Trial Name (First Author)	FAR vs HDA	Visual Gain (logMAR)	N. Injections	Follow-Up (Month)	N. Eyes
nAMD					
TENYA/LUCERNE (London)[1]	FAR	−0.12 (−0.10 to −0.14)	6.6	12	665
Total	FAR	−0.12 (−0.10 to −0.14)	6.6	12	665
PULSAR (Lanzetta)[2]	HDA	−0.13±0.25	6.1	12	316
PULSAR (Lanzetta)[2]	HDA	−0.12±0.23	5.2	12	312
TOTAL	HDA	−0.13±0.24	5.7	12	628
DME					
YOSEMITE (Wong, Wykoff)[3,4]	FAR	−0.23 (−0.20 to −0.26)	10.0	12	238
YOSEMITE (Wong, Wykoff)[3,4]	FAR	−0.23 (−0.20 to −0.26)	8.0	12	245
RHINE (Wong, Wykoff)[3,4]	FAR	−0.23 (−0.21 to −0.26)	10.0	12	254
RHINE (Wong, Wykoff)[3,4]	FAR	−0.22 (−0.20 to −0.25)	8.0	12	255
TOTAL	FAR	−0.23 (−0.20 to −0.26)	9.0	12	992
PHOTON (Brown)[5]	HDA	−0.18±0.18	6.0	12	164
PHOTON (Brown)[5]	HDA	−0.16±0.17	5.0	12	167
TOTAL	HDA	−0.17±0.17	5.5	12	331
RVO-ME					
BALATON (Tadayoni)[6]	FAR	−0.34 (−0.31 to −0.36)	6.0	6	276
COMINO (Tadayoni)[6]	FAR	−0.34 (−0.31 to −0.37)	6.0	6	366
TOTAL	FAR	−0.34 (−0.31 to −0.37)	6.0	6	642
QUASAR	HDA	−0.34	6.1	8	293
QUASAR	HDA	−0.38	6.9	8	298
TOTAL	HDA	−0.36	6.5	8	591

Notes: Values between parentheses represent the 95% confidence interval. Note that all visual gains were significant.
Abbreviations: FAR, faricimab; HAD, aflibercept 8 mg; N., number; nAMD, neovascular age-related macular degeneration; DME, diabetic macular edema; RVO-ME, retinal vein occlusion with macular edema.

intravitreal half-lives (faricimab: 7.5 days; aflicercept 8 mg: 7.2 days)[61,62] further support similar clinical efficacies, since both drugs maintain therapeutic intraocular concentrations over extended periods of time.

The current study found small, similar IOP rises one minute post-injection, consistent with published observations.[63] Ocular and systemic complications were infrequent and mild, which closely matched the phase 3 trials safety profiles.[64]

Limitations of our real-world case study included its retrospective design, short follow-up, heterogeneous subcategories, inclusion of advanced maculopathy, variable retreatment strategies, missing anatomic markers, and selection bias for most difficult scenarios that collectively limit clinical interpretability between the faricimab and the aflibercept cohorts. Additionally, one must be cautious when comparing data from different studies (multicenter real-world study, compendium of world literature, and phase 3 trials) because of the differences in study designs and populations. Also, we did not compare the behavior of the two drugs in refractory cases.[65,66] However, the major strength of this study is the

Table 5 Summary of Head to Head Comparison Between First Line Therapy with Faricimab or Aflibercept 8 mg in the Phase 3 Clinical Controlled Trials, Real World Published Studies, and Current Real World Retrospective Study

	Controlled Phase 3 Trials[1–6]	Real-World Literature[7–56]	Current real- world study
nAMD FAR vs HDA			
Visual gain (logMar)	−0.12 vs −0.13	−0.13 vs −0.10	−0.23 vs −0.23
N. injections	6.6 vs 5.7	4.1 vs 3.3	7.1 vs 5.4
Followup (month)	12 vs 12	5.1 vs 3.1	14.2 vs 9.8
N. eyes	665 vs 628	4033 vs 140	270 vs 58
DME FAR vs HDA			
Visual gain (logMar)	−0.23 vs −0.17	−0.14 vs NA	−0.56 vs −0.26
N. injections	9.0 vs 5.5	4.6 vs NA	4.6 vs 3.8
Followup (month)	12 vs 12	9.9 vs NA	9.7 vs 5.9
N. eyes	992 vs 331	1903 vs NA	97 vs 39
RVO FAR vs HDA			
Visual gain (logMar)	−0.34 vs −0.36	−0.25 vs NA	−0.25 vs −0.73
N. injections	6.0 vs 6.5	1.7 vs NA	3.9 vs 4.9
Followup (month)	6 vs 8	4.8 vs NA	7.9 vs 8.3
N. eyes	642 vs 591	47 vs NA	28 vs 8

Note: All values represent unadjusted means.
Abbreviations: nAMD, neovascular age-related macular degeneration; FAR, faricimab; HAD, aflibercept 8 mg; DME, diabetic macular edema; RVO-ME, retinal vein occlusion with macular edema; NA, not assessed.

comprehensive accumulation of a large volume of data from several sources, all of which point to quite similar results. It is still unknown if the two drugs keep their therapeutic efficacy and safety profile in the long-range.

Conclusions

In conclusion, comparable, robust, rapid, and durable BCVA gains were achieved across different disease processes (nAMD, DME and possibly RVO-ME) with very low rates of ophthalmic or systemic adverse effects in clinical trials (long-term), real world literature (midterm), and our large-cohort multicenter real world study (short term) when using faricimab or aflibercept 8 mg as first-line therapies.

Abbreviations

Ang-2, angiopoietin-2; BCVA, best corrected visual acuity; BRVO, branch retinal vein occlusion; CRVO, central retinal vein occlusion; DME, diabetic macular edema; nAMD, neovascular age-related macular degeneration; VEGF, vascular endothelial growth factor.

Data Sharing Statement

Data are available on reasonable request to corresponding author AMM. The original contributions presented in the study are included in the article. Further inquiries can be directed to the corresponding authors.

Ethics Approval and Informed Consent

The study was approved by the Ethics Committee of the Beirut Eye Specialty Hospital (BESH-EC20-251) and followed the tenets of the Declaration of Helsinki. The need for informed consent was waived because of the anonymous and

retrospective nature of the research. The study was exempt from IRB oversight because of its retrospective design and deidentified patient data. Confidentiality was maintained throughout data aggregation and analysis.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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