

LONG-TERM EFFICACY AND SAFETY OF FARICIMAB *VERSUS* ANTI-VEGF IN NEOVASCULAR AGE-RELATED MACULAR DEGENERATION: A META-ANALYSIS AND SYSTEMATIC REVIEW

KAYLA MARITZA PUTRI SALMA¹, AURIELLE ANNALICIA SETIAWAN¹, REVINA MAHARANI¹, EVIRA RAHMA AYA SOFIA¹ NADIA ARTHA DEWI²

¹Medical Study Program, Faculty of Medicine, Universitas Brawijaya, Indonesia

²Department of Ophthalmology, Faculty of Medicine, Universitas Brawijaya, Indonesia

*corresponding author: nadia_dewi@ub.ac.id

Manuscript received: February 2026

Abstract

Age-related macular degeneration (AMD) is a leading global cause of irreversible vision loss in older adults, primarily affecting the macula. Neovascular Age-related Macular Degeneration (nAMD) is treated with anti-vascular endothelial growth factor (anti-VEGF) agents. Faricimab, a dual inhibitor of VEGF and angiopoietin-2, has been developed to improve durability and anatomical outcomes. This study evaluated the long-term efficacy and safety of faricimab compared with anti-VEGF monotherapy in nAMD. A systematic search of the past 10 years identified five eligible papers, including four randomised controlled trials and one observational study. Data were pooled using Review Manager 5.4, and study quality was assessed using the Joanna Briggs Institute tool. No significant differences were observed in best-corrected visual acuity (BCVA) at one and two years. However, faricimab demonstrated greater reductions in central subfield thickness (CST) (MD = -6.70; $P < 0.001$), choroidal neovascularisation area (CNV) (MD = -0.49; $P < 0.001$) and leakage area (MD = -0.88; $P < 0.001$). Adverse event rates were comparable. Faricimab shows non-inferior efficacy and safety with improved anatomical outcomes in nAMD.

Rezumat

Degenerescenta maculară legată de vârstă (AMD) reprezintă una dintre principalele cauze globale de pierdere ireversibilă a vederii la persoanele vârstnice, afectând în principal macula. Degenerescenta maculară neovasculară asociată vârstei (nAMD) poate fi tratată cu agenți anti-factor de creștere endotelial vascular (anti-VEGF). Faricimab, un inhibitor dual al VEGF și angiopoietinei-2, a fost dezvoltat pentru a îmbunătăți efectul terapeutic și rezultatele anatomice. Acest studiu a evaluat eficacitatea și siguranța pe termen lung a faricimabului comparativ cu monoterapia anti-VEGF în nAMD. O căutare sistematică în literatura publicată în ultimii 10 ani a identificat cinci lucrări eligibile: patru studii clinice randomizate controlate și un studiu observațional. Datele au fost analizate prin meta-analiză utilizând software-ul Review Manager 5.4, iar calitatea studiilor a fost evaluată cu ajutorul instrumentului Joanna Briggs Institute. Nu s-au observat diferențe semnificative în acuitatea vizuală corectată maxim (BCVA) la unul și doi ani. Cu toate acestea, faricimab a determinat reduceri mai mari ale grosimii subfoveale centrale (CST) (MD = -6,70; $P < 0,001$), ale ariei de neovascularizație coroidiană (CNV) (MD = -0,49; $P < 0,001$) și ale ariei de scurgere lezională (MD = -0,88; $P < 0,001$). Astfel, faricimab prezintă eficacitate și siguranță non-inferioare, fiind asociat cu îmbunătățirea parametrilor anatomici în tratamentul nAMD.

Keywords: faricimab, anti-VEGF, angiopoietin-2, age-related macular degeneration

Introduction

Age-related macular degeneration (AMD) is a significant cause of irreversible blindness in the elderly worldwide. It is a progressive chronic eye disease that primarily affects the macula (1). According to a recent Meta-analysis of its disease burden projection, the study estimates that the number of individuals affected by AMD will rise from 196 million in 2020 to 288 million by 2040 (2, 3). Advanced AMD that causes significant cases of vision decline in the elderly includes neovascular AMD (nAMD; Wet AMD) and geographical atrophy (GA, late-stage dry AMD) (1). Anti-vascular endothelial growth factor (anti-VEGF) intravitreal injections is still the current first-line

treatment option for nAMD. However, problems such as the requirement for frequent injections, frequent follow-up visits, long-term treatment and patient-related issues make a significant burden on both patients and the healthcare system (4, 5). Some studies showed that anti-VEGF therapies are not always effective for patients in nAMD and real-world clinical practice data reported that many patients receive fewer anti-VEGF injections than in clinical trials, and many did not gain visual improvements comparable to those documented in clinical studies (6, 7). To address these issues, a new treatment option has been established to improve outcomes and reduce burden for patients with nAMD.

New treatment options have emerged to improve patient outcomes and reduce injection frequency. faricimab (faricimab-svoa; Vabysmo™, Roche, Switzerland) received approval in January 2022 for the treatment of both AMD and diabetic macular oedema (DME) faricimab inhibits both Angiopoietin-2 (Ang-2) and vascular endothelial growth factor (VEGF)-A through its dual-action mechanism (5). Increased Ang-2 expression enhances the effect of VEGF in destabilizing blood vessels by weakening endothelial cell junctions, thereby promoting neo-vascularization and vascular leakage. Endothelial cell homeostasis, survival, integrity and vascular stability depend on its signalling mechanism. To mediate vascular instability, Ang-2 works either independently or in combination with VEGF (8, 9). In the treatment of nAMD, faricimab has shown as a possibly safe therapy (5).

Despite promising early results, concerns remain regarding the long-term efficacy, safety and comparative effectiveness of faricimab relative to established anti-VEGF therapies. Previous Meta-analyses have provided preliminary insights but were largely limited by short follow-up durations (10, 11). The present systematic review and Meta-analyses addresses this gap by integrating 112-week follow-up data and providing a detailed quantitative synthesis of key anatomical parameters, including central subfield

thickness (CST), choroidal neovascularisation (CNV) and lesion leakage. Furthermore, by incorporating evidence from both randomised controlled trials and emerging real-world studies, this study offers a more comprehensive evaluation of faricimab's long-term durability, anatomical impact and clinical safety compared with standard anti-VEGF treatments in neovascular AMD.

Materials and Methods

Literature search

This Meta-analysis was conducted in adherence to the PRISMA guidelines for systematic review and Meta-analysis (12). A comprehensive literature search was done on three databases (PubMed, ScienceDirect and Cochrane Central) and relied on randomised controlled trials that were conducted from January 2014 to November 2024 and published in English. Key-words used were (((faricimab) OR (angiopoietin-2 inhibitor)) AND ((neovascular age-related macular degeneration) OR (nAMD))). The search strategy was presented as in the Figure 1. Previously published reviews were use for bibliographic purposes. This study was exempt from ethical approval as it is a secondary analysis based on previously published studies and does not involve any research with human participants or animals conducted by the authors.

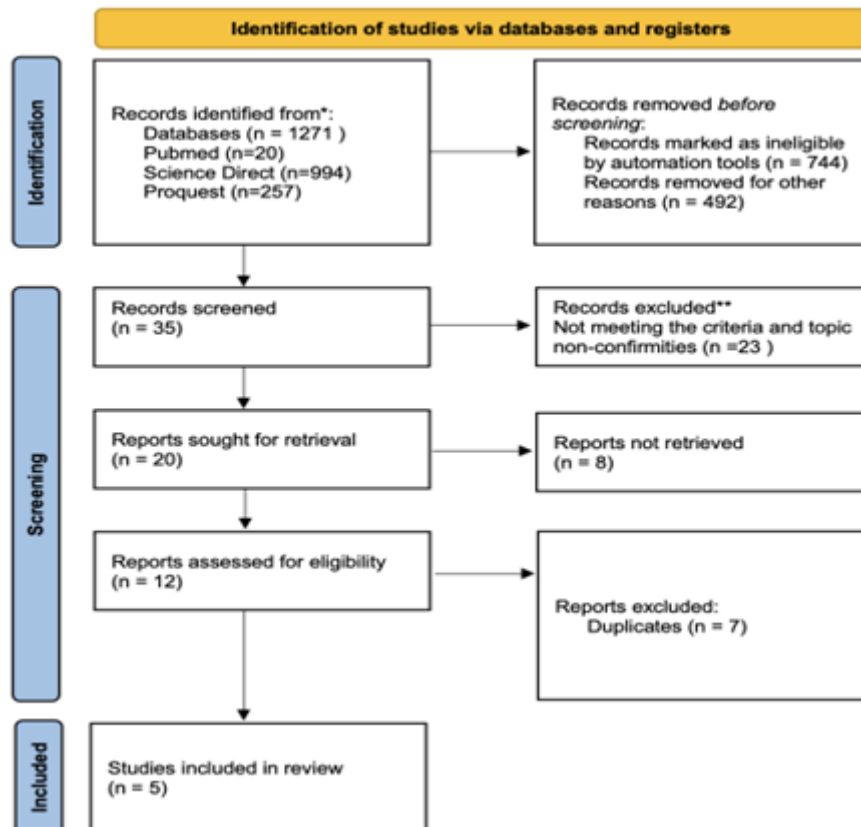


Figure 1.
PRISMA Chart of the study

Literature inclusion and exclusion criteria

The selection criteria for the Meta-analysis are presented in Table I. Inclusion criteria includes (1) Patients that are diagnosed with Wet AMD, (2) Full paper available, (3) Treatment-naïve patients, (4) Out-

come results reported. Papers were excluded based on the following criteria (1) Paper that were written in non-English, (2) conference abstracts, non-experimental studies, (3) data not extractable.

Table I

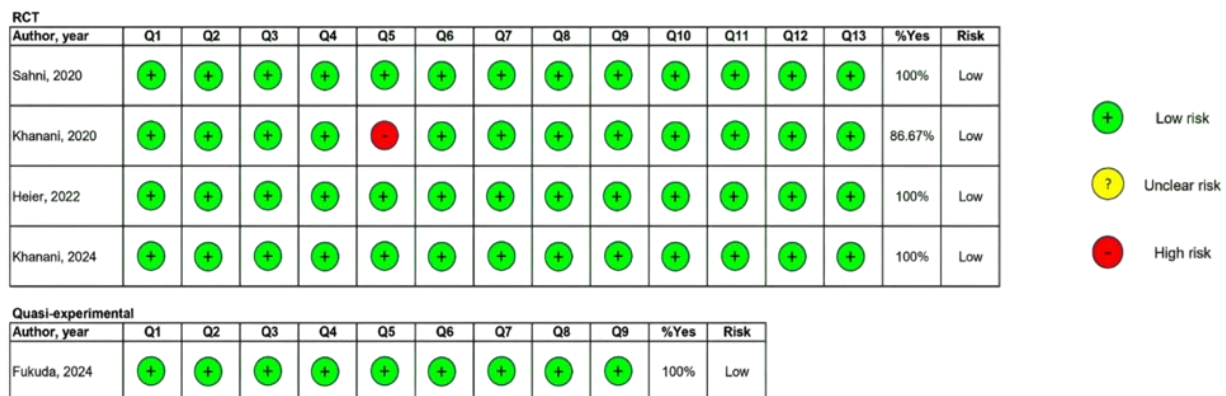
PICO framework for the Meta-analysis

Topic	Description
Population	Patients with nAMD
Intervention	Intravitreal faricimab with Q8W/Q16W interval
Comparison	Intravitreal Anti-VEGF (Ranibizumab/Aflibercept) with Q4W/Q8W interval
Outcomes	Primary: BCVA mean changes and anatomical changes Secondary: Safety profiles

Data extraction and quality assessment

Four reviewers independently conducted the literature search and extracted the data via a standardized Google spreadsheet. All extracted information was then cross-verified to confirm its inclusion in the final dataset. Extracted outcomes divided into two, primary outcomes including BCVA mean changes (MD) and secondary outcomes such as anatomical changes and safety profiles. Data from the included studies were extracted into a predesigned data ex-

traction table in Google Sheets by a primary reviewer and independently verified by a second reviewer. Any discrepancies were resolved through discussion with a third reviewer. Study quality and risk of bias were assessed using the Joanna Briggs Index (JBI). Risk of bias assessment with JBI yielded overall low risk of bias, shown in Figure 2. Formal sensitivity analysis based on study quality was not performed due to the limited number of eligible studies.

**Figure 2.**

Joanna-Briggs Institute risk of bias assessment results

Independent data extraction and quality assessment

Screening through the abstracts and titles were carried out by three reviewers (K.S, E.S and A.S), with a fourth author (R.M) arbitrating any discrepancies. Authors independently extracted data from the included studies. The extraction information was divided as follows: (1) Demographic, (2) Baseline Characteristics, (3) Study outcomes. We ensured a comprehensive systematic collection of relevant data from the studies that met the inclusion criteria. Quality assessments were done using the Joanna Briggs Index where reviewer (A.S) independently performed data extraction and quality assessment. A second author (K.S.) resolved any discrepancies. Studies scoring yes in 70% of the questions were considered high quality and proven to have a low risk of bias.

Statistical analysis

The protocol for this Systematic Review and Meta-analysis was formally registered with the International Prospective Register of Systematic Reviews (PROSPERO: CRD420251051916). Throughout its conduct, the study strictly adhered to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines. Authors use Review Manager 5.4 (RevMan 5.4) to generate the forest plot as our visualisation that were quantitatively presented in Mean Difference (Standard Deviation), effect sizes reported with 95% Confidence Intervals (95% CI), and heterogeneity were presented by I^2 statistics on the application. If I^2 showed less than 50%, a fixed-effects model was used; more than 50%, a random-effects model was used. A p-value of less than 0.05 indicates a significance on different groups.

Results and Discussion

Study characteristics

We performed an initial screening of 1271 articles identified from the three databases; 1236 studies were excluded based on title and abstract. Further refinement included full text review, which led to 23 studies being excluded due to unrelated topics and not meeting the inclusion and exclusion criteria. After a detailed review, five papers (including one paper with two studies) were selected. The general characteristics of the studies included in this Meta-analysis are shown in Table II. The studies primarily assessed treatment-naïve patients with neovascular age-related macular degeneration (nAMD), comparing faricimab (FAR) with either aflibercept (AFL) or ranibizumab

(RBZ). The sample sizes ranged from 76 (STAIRWAY) to over 1300 participants (TENAYA and LUCERNE), with treatment periods extending from 12 to 112 weeks. In this Meta-analysis, we gathered a total of 2,863 patients. Our analysis focused on the long-term efficacy and safety of intravitreal faricimab for nAMD, providing a comprehensive assessment of its therapeutic potential in this patient population. The included studies demonstrated moderate to high methodological quality according to the Joanna Briggs Institute assessment. The low risk of bias across key domains supports the reliability of the pooled estimates and reduces the likelihood that the observed effects were driven by methodological limitations.

Table II

General characteristics of the studies

No	Study Name	Type of Study	Author (Year)	Period	Treatment(s) and Dose	Regimen	Sample Size	Primary & Secondary Outcome
1	TENAYA and LUCERNE	RCT	Heier <i>et al.</i> (2022)	48 W (Year 1)	FAR/AFL 6.0 mg/2.0 mg	Q8W / Q16W	1329	• BCVA (1st year) • BCVA (2nd year) • Total lesion leakage • Safety profile
2	TENAYA and LUCERNE (Year 2)	RCT	Khanani <i>et al.</i> (2024)	112 W (Year 2)	FAR/AFL 6.0 mg/2.0 mg	Treat-and-extend up to Q16W	1326	• BCVA (1st year) • Safety profile
3	AVENUE	RCT	Sahni <i>et al.</i> (2020)	36 W	FAR/RBZ 1.5 mg; 6.0 mg/ 0.5 mg	Q4W (RBZ, FAR 1.5 mg, FAR 6.0 mg) Q4W → Q8W after W12 (FAR) switch: RBZ → FAR Q4W	263	• BCVA (1st year) • CST (1st year) • Total CNV area • Total lesion leakage • Safety profile
4	STAIRWAY	RCT	Khanani <i>et al.</i> (2020)	52 W	FAR/RBZ 6.0 mg/0.5 mg	Q12W, Q16W/ Q4W	76	• BCVA (1st year) • CST (1st year) • Total CNV area • Total lesion leakage • Safety profile
5	Japanese real-world study	Observational Study	Fukuda <i>et al.</i> (2024)	12 W	FAR/AFL	3 loading doses (monthly)	86	• BCVA (1st year)

Primary outcome analysis

Five studies including one paper with two studies comparing faricimab to anti-VEGF treatments were included in the quantitative Meta-analysis. Five studies were included in the quantitative synthesis of best-corrected visual acuity (BCVA). The pooled first-year analysis demonstrated no statistically significant difference between faricimab and comparator anti-VEGF therapies (mean difference 0.21; 95% CI: - 0.90 to 1.32), indicating comparable short-term visual outcomes. Subgroup comparisons with ranibizumab and aflibercept showed consistent effects with minimal heterogeneity, supporting the stability of the findings (Figure 3).

Long-term analysis based on second-year follow-up also showed equivalent visual acuity outcomes between faricimab and aflibercept (mean difference 0.10; 95% CI: - 1.52 to 1.71), confirming sustained visual efficacy over extended treatment duration (Figure 4). The P-values for heterogeneity indicated minimal between-study variability ($I^2 = 0\%$), further supporting the robustness of these findings. Therefore, it can be concluded that faricimab offers comparable efficacy to standard anti-VEGF therapies in improving visual acuity in patients with wet age-related macular degeneration over the first year of treatment.

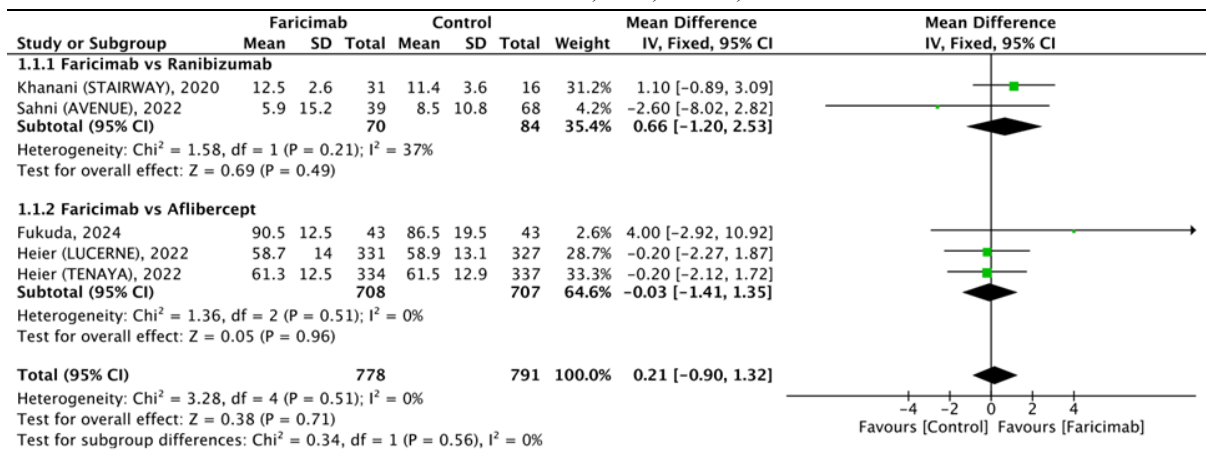


Figure 3.

Forest plot of first-year BCVA outcomes comparing faricimab and anti-VEGF therapies

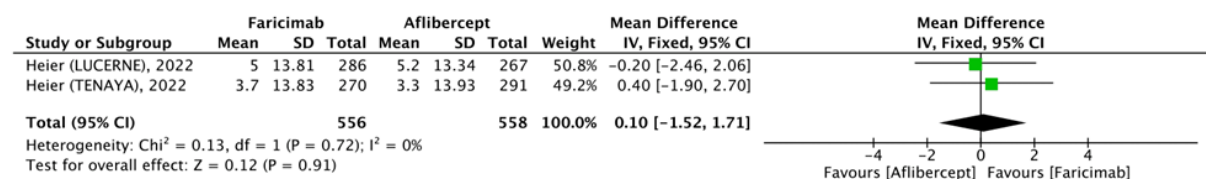


Figure 4.

Forest plot of second-year BCVA outcomes comparing faricimab and aflibercept

Secondary outcome and funnel plot analysis

In evaluating the secondary outcomes, our Meta-analysis assessed central subfield thickness (CST), choroidal neovascularization (CNV) and total lesion leakage. Analysis of anatomical outcomes demonstrated a consistent advantage of faricimab in reducing central subfield thickness (CST), particularly in comparisons with aflibercept, suggesting enhanced retinal fluid control (Figure 5). Although subgroup findings with ranibizumab were more variable, the overall pooled effect favoured faricimab (mean difference - 6.86 μm ; 95% CI: - 7.18 to - 6.54; $p < 0.00001$).

Regarding CNV (Figure 6), faricimab was associated with significantly lower lesion size compared to

aflibercept, whereas the comparison with ranibizumab showed no significant difference. The overall effect again favoured faricimab (mean difference - 0.48; 95% CI: - 0.67 to - 0.28; $p < 0.00001$), suggesting its potential superiority in suppressing CNV progression over time.

Similarly, in terms of total lesion leakage (Figure 7), faricimab significantly reduced leakage compared to aflibercept, while the ranibizumab subgroup did not show a statistically significant difference. The pooled analysis confirmed the benefit of faricimab with a mean difference of - 0.85 (95% CI: - 1.07 to - 0.62; $p < 0.00001$), underscoring its efficacy in reducing retinal fluid leakage in nAMD patients over the long term.

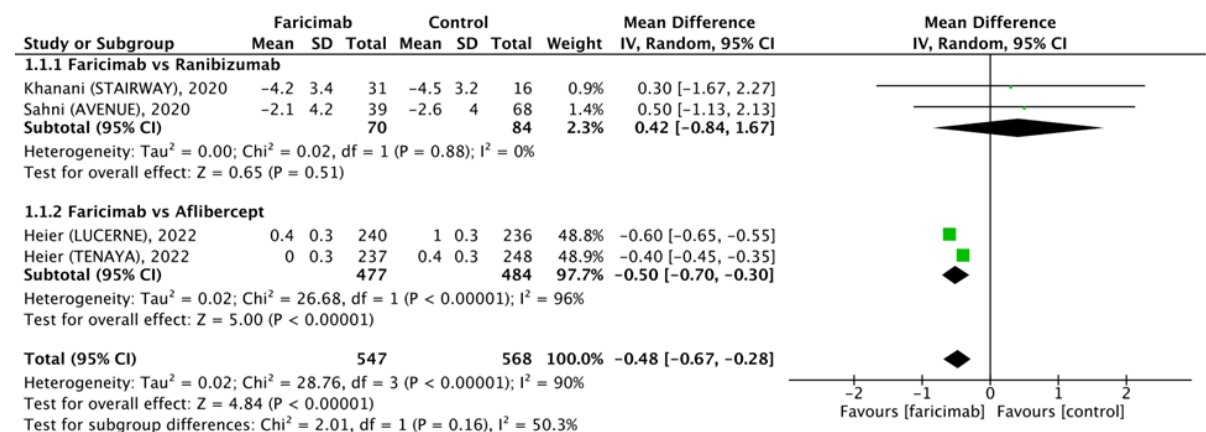


Figure 5.

Forest plot of CST changes comparing faricimab and anti-VEGF therapies

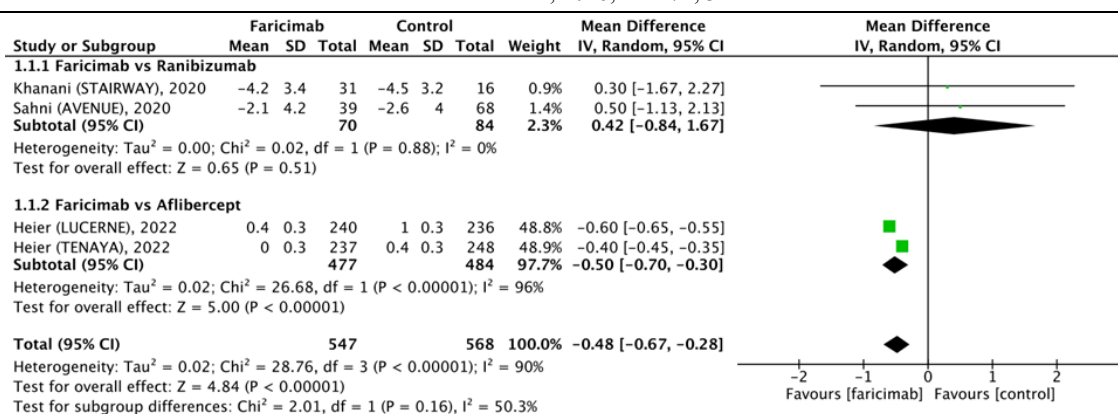


Figure 6.

Forest plot of CNV outcomes comparing faricimab and anti-VEGF therapies

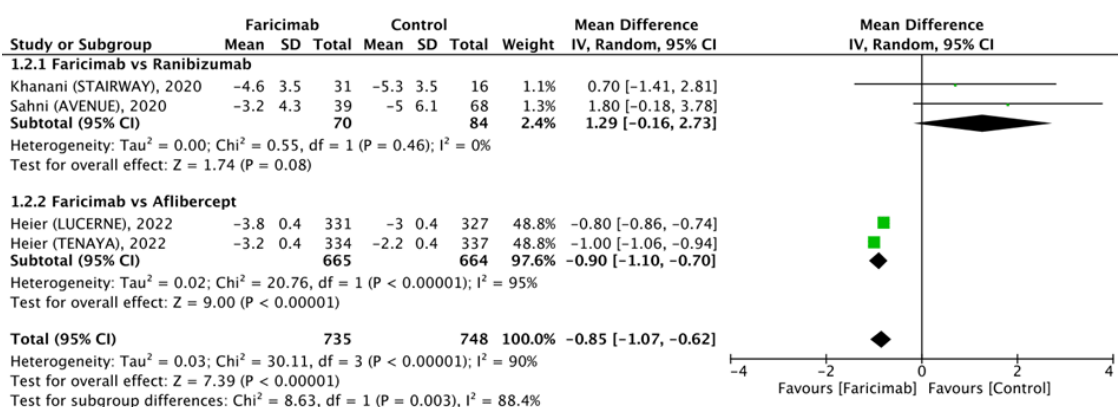


Figure 7.

Forest plot of total lesion leakage comparing faricimab and anti-VEGF therapies

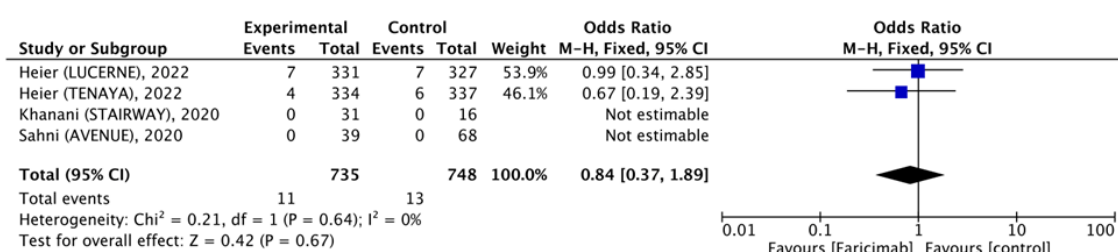


Figure 8.

Forest plot of first-year serious adverse events comparing faricimab and anti-VEGF therapies

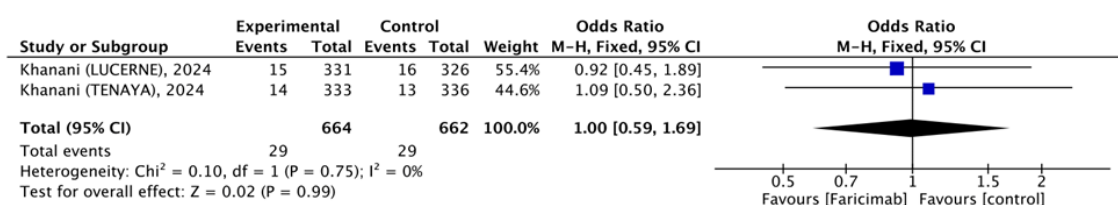


Figure 9.

Forest plot of second-year serious adverse events comparing faricimab and anti-VEGF therapies

Safety outcomes were comparable between treatment groups across all evaluated endpoints. The incidence of serious adverse events did not differ significantly between faricimab and anti-VEGF therapies during the first year (OR 0.84; 95% CI: 0.37 to 1.89) or second year of follow-up (OR 1.00; 95% CI: 0.59 to 1.69), with consistent findings

across studies (Figure 8 and Figure 9). Similarly, overall adverse event rates were equivalent between groups in both the first year (OR 1.03; 95% CI: 0.84 to 1.27) and second year (OR 1.08; 95% CI: 0.87 to 1.34), supporting stable long-term tolerability (Figure 10 and Figure 11). The pooled risk of intraocular inflammation remained low and showed

no significant difference between treatments during the first year (OR 1.48; 95% CI: 0.68 to 3.18) or second year (OR 1.34; 95% CI: 0.68 to 2.63), indi-

cating a comparable ocular safety profile over extended treatment (Figure 12 and Figure 13).

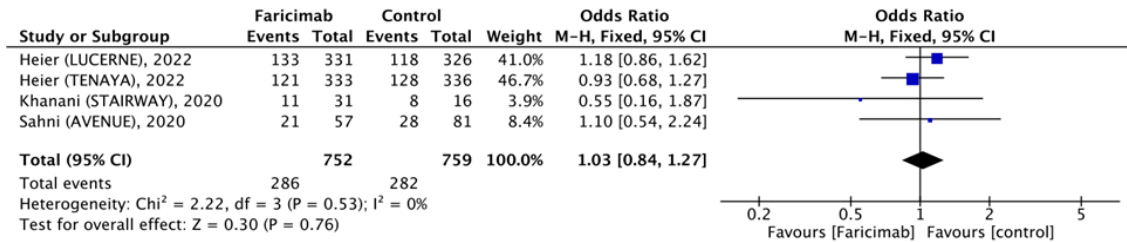


Figure 10.

Forest plot of first-year overall adverse events comparing faricimab and anti-VEGF therapies

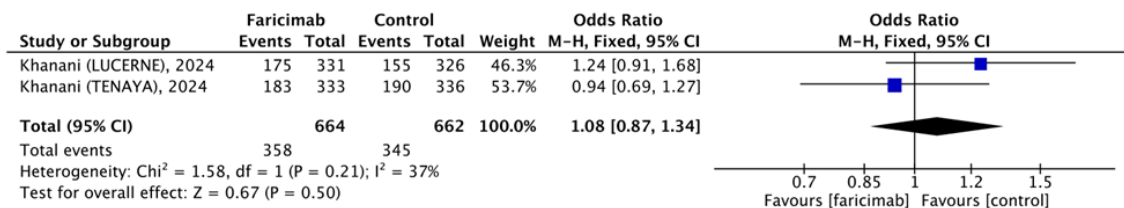


Figure 11.

Forest plot of second-year overall adverse events comparing faricimab and anti-VEGF therapies

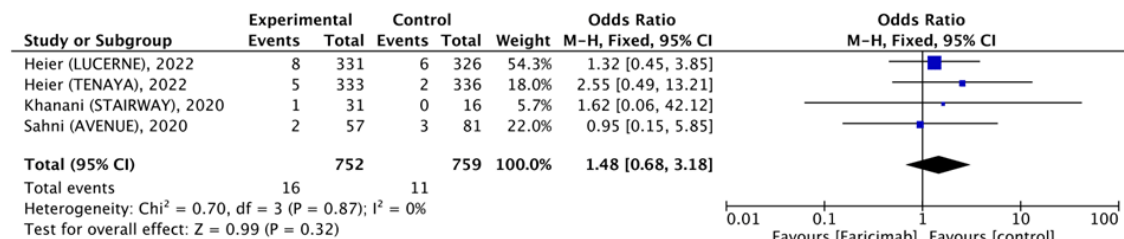


Figure 12.

Forest plot of first-year intraocular inflammation comparing faricimab and anti-VEGF therapies

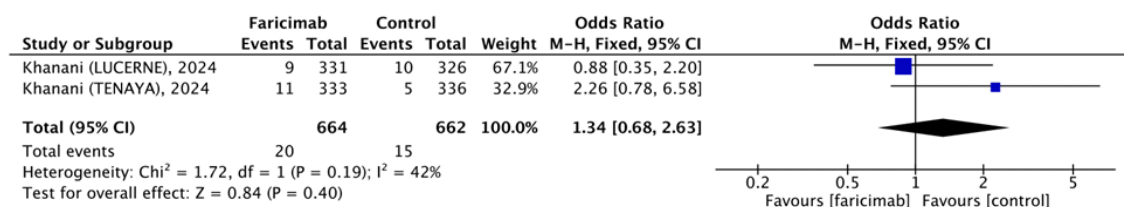


Figure 13.

Forest plot of second-year intraocular inflammation comparing faricimab and anti-VEGF therapies

A funnel plot analysis was performed to assess potential publication bias in the pooled analysis of first-year best-corrected visual acuity (BCVA) outcomes comparing faricimab with anti-VEGF therapies. The plot demonstrated a generally symmetrical distribution of studies around the pooled effect estimate, with most points falling within the funnel boundaries, suggesting no significant publication bias among the included studies. The funnel plot evaluating publication bias is presented in Figure 14.

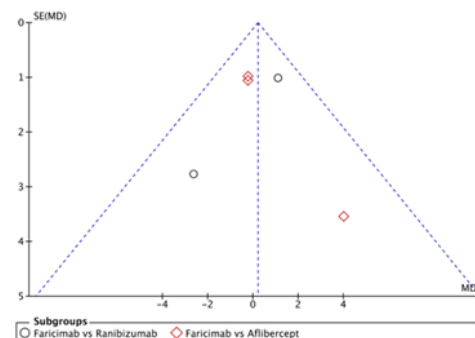


Figure 14.

Funnel plot of first-year BCVA comparing faricimab and anti-VEGF therapies

Visual outcomes of faricimab compared with anti-VEGF therapy

In our study, faricimab visual outcome improvement was found to be non-inferior compared to anti-VEGF agents for both short- and long-term outcomes. From TENAYA and LUCERNE 2-year outcome, it had clinically meaningful improvements in best-corrected visual acuity (BCVA), with faricimab achieving an average gain of + 4.4 letters and aflibercept + 4.3 letters. The akin result was also shown in the STAIRWAY trial, that faricimab given every 12 or 16 weeks sustained the initial visual and anatomical benefits, comparable to those achieved with monthly ranibizumab at week 52 (13, 14).

Faricimab also showed a greater improvement in anatomic changes than control in this study. A significant reduction of central subfield thickness (CST) was shown to favour faricimab compared to aflibercept, while no significant difference was observed between faricimab and ranibizumab. The efficacy of faricimab in reducing CST is well-supported by several studies. Indirect treatment comparisons revealed that faricimab led to a significantly greater CST reduction within one year. This showed consistent results for both short- and long-term outcome (15). Faricimab demonstrated a greater significant reduction in CNV compared to aflibercept, whereas its effect was comparable to ranibizumab. From the AVENUE trial, it was shown that faricimab effectively improved CNV-related anatomical parameters comparable to monthly injections of ranibizumab (16). In retrospective studies, faricimab demonstrated encouraging results in resolving choroidal neovascularization (CNV) among patients with nAMD who had received prior treatment (17).

Anatomical outcomes and clinical significance of CST reduction

The clinical relevance of central subfield thickness (CST) reduction with faricimab lies primarily in its association with decreased injection frequency and overall treatment burden. Large-scale trials and real-world studies have shown that sustained CST reduction permits extended dosing intervals of up to 12 or even 16 weeks in a substantial proportion of patients without compromising visual outcomes (13, 15). This translates into fewer required injections compared with aflibercept, particularly within treat-and-extend regimens and reflects faster and more complete retinal fluid resolution that supports earlier and sustained interval extension (13). However, the absolute reduction of approximately 6 - 7 μm remains modest, and differences of this magnitude may not independently mirror clinical improvements in visual acuity, as structural changes do not always proportionally correspond to functional gains (18-20). Nonetheless, improved retinal morphology may indicate enhanced fluid control and disease stability, which are critical for maintaining long-term dura-

bility and extended treatment intervals (21, 22). Therefore, the anatomical advantages associated with faricimab are best interpreted in the context of sustained disease control and reduced treatment burden rather than immediate visual acuity improvement (21, 23).

The nonsignificant CST difference in the ranibizumab subgroup (mean difference = 3.77 μm , $P = 0.47$) may be due to several factors. Ranibizumab, given monthly, could already be approaching a ceiling effect, where the retina has limited potential for further thinning because maximal anatomical improvement has been achieved. Additionally, patient characteristics, disease severity and treatment history can affect the response. This suggests faricimab provides comparable CST reduction, not superiority, but still offers clinical value by maintaining similar outcomes with less frequent dosing. Therefore, the results should be interpreted in the context of both anatomical effects and patient-centred benefits (24, 25).

Interestingly, although greater CST reduction was observed in the faricimab group compared with aflibercept, this was not accompanied by a corresponding significant improvement in BCVA. This discrepancy may reflect the weak correlation between anatomical and functional outcomes. A study by Nanegrungsunk *et al.* reported only weak or no correlation between changes in CST and BCVA in patients with nAMD receiving anti-VEGF therapy (26). This weak correlation can be linked to the lack of consistency of BCVA as a measure for disease progression and criteria for extending injection intervals. According to a study by Patel *et al.*, patients with late AMD had greater variability of BCVA measures compared to patients with small or intermediate drusen (27). Other factors such as the patients' preferred retinal locus can also affect this intersession variability (28). However, in real world settings, other than BCVA, CST is also often used as a measure to determine disease progression (29). This could be a more reliable and objective measure to base extending injection intervals compared to BCVA, which had more variability.

Mechanistic basis of faricimab: dual VEGF-A and Ang-2 inhibition

Faricimab's dual mechanism of action targeting both VEGF-A and Ang-2 may allow better anatomical changes compared to anti-VEGF agents alone, but the visual acuity improvements might not be directly correlated. The relationships between retinal thickness, leakage/fluid reduction and CNV and visual acuity is complex, as there are other factors influencing anatomical changes. For instance, decreased retinal thickness caused by decreased leakage may lead to visual gains, while retinal thinning from retinal pigment epithelium loss may cause the opposite results (30). Anatomical improvements are

not always in line with visual gains (31). Patients with more advanced or longer disease duration might experience less visual improvement despite anatomical changes. Patient response to treatment can vary significantly, and there are some factors affecting the efficacy of the outcome, such as genetics, disease subtype and treatment history (32).

VEGF-A pathway induces development of abnormal retinal angiogenesis and permeabilization of blood vessels, which frequently makes it a target for nAMD therapy. VEGF-A pathway inhibition reduces angiogenesis, vascular permeability and neovascularization (10). The Ang-2 pathway, which competes with Ang-1 to bind with the Tie2 transmembrane receptor, plays a role in angiogenesis, vascular destabilization, inflammation and increases sensitivity to VEGF-A in blood vessels. Dual Ang2/VEGF inhibition, enhances vascular stability beyond VEGF monotherapy (33). By blocking Ang-2, faricimab further reduces neovascularization and vascular leakage. By targeting both pathways, faricimab reduces CNV in nAMD, decreases vascular permeability and slows disease progression. This dual mechanism of action may provide benefits compared to anti-VEGF alone, potentially leading to improved outcomes in patients with nAMD (34).

Safety profile and clinical implications of extended dosing with faricimab

From a safety perspective, this study found that faricimab demonstrated a comparable adverse event (AE) profile to other anti-VEGF agents. In the phase 3 TENAYA and LUCERNE trials, the incidence of ocular AEs was similar between faricimab and aflibercept at both one-year and two-year follow-up (35). Similarly, phase 2 trials such as STAIRWAY and AVENUE reported comparable ocular AE rates between faricimab and ranibizumab treatment groups (16, 36). These findings support faricimab as a well-tolerated and effective treatment option that reduces the burden of frequent injections while maintaining visual and anatomical outcomes.

Currently, nAMD patients are subjected to the need for frequent visits and injections. This leads to difficulty to follow through with the regimen, and loss to follow-up, which causes suboptimal results. According to a study, in patients undergoing three monthly ranibizumab injections followed by PRN variable-dosing and mandatory monthly visits, there was a 2-year loss to follow-up rate of 28% and a 5-year loss to follow-up rate of 57% (37). Differences in dosing regimens are an important consideration when interpreting long-term efficacy outcomes. Conventional anti-VEGF therapies are often administered at fixed intervals such as every 4 weeks (Q4W) or every 8 weeks (Q8W), which can impose a substantial treatment burden on patients and healthcare systems (23, 28). In contrast, faricimab has demonstrated the ability to maintain disease control with

extended dosing intervals of up to every 16 weeks (Q16W) in a significant proportion of patients (38). The intervals per injection of faricimab can alleviate the burden of frequent injections and lead to greater adherence and optimising its benefits.

Its similar mechanism of action to anti-VEGF agents, which already has an established safety profile, also supports its similar safety profile to anti-VEGF agents. With its less frequent injection schedule compared with anti VEGF alone, faricimab has been optimised to minimize adverse events while maintaining efficacy. Real-world long-term follow-up studies back up these outcomes, demonstrating ongoing BCVA improvements in patients who transitioned to faricimab from other anti-VEGF treatments, further establishing its value as a reliable therapy for neovascular age-related macular degeneration (nAMD) (2). Treat-and-extend strategies, commonly used in real-world practice, aim to individualize injection intervals based on disease activity, balancing efficacy with reduced visit frequency (38, 39). The extended durability observed with faricimab may therefore translate into fewer injections and clinic visits, potentially improving adherence and patient quality of life without compromising visual outcomes (38).

Limitation of the study

One of the limitations we acknowledged in this study was the high heterogeneity of the results due to differences in the duration of treatment, number of patients and different dosing techniques. Epidemiological variability in AMD progression, as evidenced by a recent systematic review (3), may contribute to observed between-study differences in baseline characteristics and treatment response. Additionally, although all studies assessed anatomical outcomes using optical coherence tomography (OCT), variability in devices, segmentation algorithms and measurement protocols may have further contributed to inter-study heterogeneity. Another limitation was the shorter duration of some studies (*e.g.*, one 12-week trial), preventing optimal examination of full treatment effects. Additionally, few studies reported long-term outcomes. More studies with longer follow-up, especially up to two years, are needed to better assess faricimab's long-term efficacy and safety. However, ongoing monitoring and real-world experience will continue to provide valuable insight into faricimab's safety and efficacy.

Conclusions

Intravitreal faricimab, a bispecific agent with extended injection intervals, provides comparable visual outcomes and superior anatomical recovery compared to standard anti-VEGF therapies in neovascular age-related macular degeneration (nAMD), without an increased risk of safety concerns. The possi-

bility of longer dosing intervals may reduce treatment burden for both patients and healthcare providers, potentially improving adherence and quality of life. However, large, well-designed randomised controlled trials with longer follow-up are warranted to confirm the long-term benefits and safety of extended faricimab regimens in diverse patient populations.

Acknowledgement

Not applicable.

Funding

Not applicable.

Availability of data and materials

The data generated in the present study are included in the figures and/or tables of this article.

Ethics approval and consent to participate

Not applicable.

AI use disclosure

Not applicable.

Conflict of interest

The authors declare no conflict of interest.

References

1. Chaudhuri M, Hassan Y, Bakka Vemana PPS, Bel-lary Pattanashetty MS, Abdin ZU, Siddiqui HF. Age-related macular degeneration: an exponentially emerging imminent threat of visual impairment and irreversible blindness. *Cureus*. 2023;15:e39624.
2. Wong WL, Su X, Li X, Cheung CMG, Klein R, Cheng CY, et al. Global prevalence of age-related macular degeneration and disease burden projection for 2020 and 2040: a systematic review and meta-analysis. *Lancet Glob Health*. 2014;2(2):e106-16.
3. Dascalu AM, Alexandrescu C, Vancea G, Stana D, Costea DO, Zgura A, et al. The relationship between statin therapy and age-related macular degeneration – a systematic review. *Farmacia*. 2024;72(2):285-93.
4. Nasimi N, Nasimi S, Grauslund J, Vergmann AS, Subhi Y. Real-world efficacy of intravitreal faricimab for neovascular age-related macular degeneration: a systematic review. *Int J Retina Vitreous*. 2024;10:66.
5. Weber C, Schipper P, Stasik I, Weinhold L, Bulirsch L, Thiele S, et al. Early real-world experience with intravitreal faricimab for neovascular AMD: FAN study. *AJO Int*. 2024;1(4):100074.
6. Zou W, Jiang Q, Wang Y, Wei W, Sun X, Basu K, et al. Efficacy, durability and safety of faricimab for patients with neovascular age-related macular degeneration: 48-week results from the phase 3 LUCERNE China subpopulation. *Asia Pac J Ophthalmol (Phila)*. 2025;14(1):100142.
7. Agostini H, Abreu F, Baumaal CR, Chang DS, Csaky KG, Demetriades AM, et al. Faricimab for neovascular age-related macular degeneration and diabetic macular edema: from preclinical studies to phase 3 outcomes. *Graefes Arch Clin Exp Ophthalmol*. 2024;262:3437-51.
8. Hara C, Suzue M, Fujimoto S, Fukushima Y, Sanyanagi K, Nishida K, et al. Comparison of loading dose between aflibercept and faricimab for neovascular age-related macular degeneration. *J Clin Med*. 2024;13(2):385.
9. Chaudhary V, Guymer R, Artignan A, Downey A, Singh RP. Real-world evidence for faricimab in neovascular age-related macular degeneration and diabetic macular edema: a scoping review. *Ophthalmol Sci*. 2025;5(4):100744.
10. Yen WT, Wu CS, Yang CH, Chen YH, Lee CH, Hsu CR. Efficacy and safety of intravitreal faricimab for neovascular age-related macular degeneration: a systematic review and meta-analysis. *Sci Rep*. 2024;14(1):2485.
11. Samacá-Samacá D, Hernández-Castillo C, Prieto-Pinto L, Rodríguez F, Sardi C, Ocampo H, et al. Efficacy and safety of faricimab for neovascular age-related macular degeneration: a systematic review and network meta-analysis. *BMJ Open Ophthalmol*. 2024;9:e001702.
12. Jeong A, Liang H, Baek SC, Sagong M. Real-World Efficacy and Durability of Faricimab in Aflibercept-Resistant Neovascular Age-Related Macular Degeneration. *J Clin Med*. 2025;14(15):5412.
13. Panos GD, Lakshmanan A, Dadoukis P, Ripa M, Motta L, Amoaku WM. Faricimab: transforming the future of macular diseases treatment – a comprehensive review of clinical studies. *Drug Des Devel Ther*. 2023;17:2861-73.
14. Wijesingha N, Kotecha A, Margaron P, Sivaprasad S. Infographic: 2-year efficacy, durability and safety of intravitreal faricimab with treat-and-extend dosing up to 16 weeks in neovascular age-related macular degeneration (pooled results from TENAYA and LUCERNE). *Eye (Lond)*. 2025;39(Suppl 1):186-7.
15. Galeone C, Turati F, Nicolò M, Parravano M, Vujosevic S, Bianchino L, et al. Faricimab versus the standard of care for neovascular age-related macular degeneration in Italy: an indirect treatment comparison. *Drug Target Insights*. 2024;18(1):105-11.
16. Sahni J, Dugel PU, Patel SS, Chittum ME, Berger B, Del Valle Rubido M, et al. Safety and efficacy of different doses and regimens of faricimab vs ranibizumab in neovascular age-related macular degeneration: the AVENUE phase 2 randomized clinical trial. *JAMA Ophthalmol*. 2020;138(9):955-63.
17. Hang A, Ngo T, Virk JS, Moussa K, Moshiri A, Emami-Naeini P, et al. Intravitreal faricimab for previously treated neovascular age-related macular degeneration. *Clin Ophthalmol*. 2024;18:3781-9.
18. Cheung CMG, Lim JJ, Priglinger S, Querques G, Margaron P, Patel S, et al. Anatomic outcomes with faricimab vs aflibercept in head-to-head dosing phase of the TENAYA/LUCERNE trials in neovascular

- age-related macular degeneration. *Ophthalmology*. 2025;132(5):519-26.
19. Savant SV, Kwan JT, Barouch F, Chang J, Ramsey DJ, Marx J, et al. Durability and efficacy of faricimab in treatment-resistant retinal edema utilizing real-world dosing regimens. *J Ophthalmol*. 2024;2024:8583348.
20. Watkins C, Paulo T, Bührer C, Holekamp NM, Bagijn M. Comparative efficacy, durability and safety of faricimab in the treatment of diabetic macular edema: a systematic literature review and network meta-analysis. *Adv Ther*. 2023;40(12):5204-21.
21. Goodchild C, Bailey C, Soto Hernaez J, Ahmed E, Salvatore S. Real-world efficacy and durability of faricimab in patients with neovascular AMD who had sub-optimal response to prior anti-VEGF therapy. *Eye (Lond)*. 2024;38(16):3059-64.
22. Jeong A, Liang H, Baek SC, Sagong M. Real-world efficacy and durability of faricimab in aflibercept-resistant neovascular age-related macular degeneration. *J Clin Med*. 2025;14(15):55412.
23. Daien V, Finger RP, Talks JS, Mitchell P, Wong TY, Sakamoto T, et al. Evolution of treatment paradigms in neovascular age-related macular degeneration: a review of real-world evidence. *Br J Ophthalmol*. 2021;105:1475-9.
24. Khanani AM, Kotecha A, Chang A, Chen SJ, Chen Y, Guymer R, et al. TENAYA and LUCERNE: two-year results from the phase 3 neovascular age-related macular degeneration trials of faricimab with treat-and-extend dosing in year 2. *Ophthalmology*. 2024;131(8):914-26.
25. Bressler SB, Qin H, Beck RW, Chalam KV, Kim JE, Melia M, et al. Factors associated with changes in visual acuity and central subfield thickness at 1 year after treatment for diabetic macular edema with ranibizumab. *Arch Ophthalmol*. 2012;130(9):1153-61.
26. Nanegrungsunk O, Gu SZ, Bressler SB, Du W, Amer F, Moini H, et al. Correlation of change in central subfield thickness and change in visual acuity in neovascular AMD: post hoc analysis of VIEW 1 and 2. *Am J Ophthalmol*. 2022;238:97-102.
27. Patel PJ, Chen FK, Rubin GS, Tufail A. Intersession repeatability of visual acuity scores in age-related macular degeneration. *Invest Ophthalmol Vis Sci*. 2008;49(10):4347-52.
28. Crossland MD, Culham LE, Kabanarou SA, Rubin GS. Preferred retinal locus development in patients with macular disease. *Ophthalmology*. 2005;112(9):1579-85.
29. Bhatia B, Sim SY, Chalkiadaki E, Koutsocheras G, Nicholson L, Selvam S, et al. The impact of disease activity criteria on extending injection intervals in real-world patients with neovascular age-related macular degeneration. *Ophthalmol Ther*. 2025;14(4):773-86.
30. Jaffe GJ, Ying GS, Toth CA, Daniel E, Grunwald JE, Martin DF, et al. Macular morphology and visual acuity in year five of the comparison of age-related macular degeneration treatments trials. *Ophthalmology*. 2019;126(2):252-60.
31. Seguin-Greenstein S, Lightman S, Tomkins-Netzer O. A meta-analysis of studies evaluating visual and anatomical outcomes in patients with treatment-resistant neovascular age-related macular degeneration following switching to treatment with aflibercept. *J Ophthalmol*. 2016;2016:4095852.
32. Ma C, Bai L, Lei C, Wu C, Shi Q, Hu F, et al. Predictors of visual and anatomical outcomes for neovascular age-related macular degeneration treated with bevacizumab. *Biomed Rep*. 2015;3(4):503-8.
33. Dascalu AM, Cherecheanu AP, Serban D, Alexandrescu C, Stana D, Costea AC, et al. Combined anti-ANG2/TIE and anti-VEGF intravitreal therapy in age-related macular degeneration – a systematic review. *Farmacia*. 2023;71(6):1120-8.
34. Nair AA, Finn AP, Sternberg P. Spotlight on faricimab in the treatment of wet age-related macular degeneration: design, development and place in therapy. *Drug Des Devel Ther*. 2022;16:3395-400.
35. Heier JS, Khanani AM, Quezada Ruiz C, Basu K, Ferrone PJ, Brittain C, et al. Efficacy, durability, and safety of intravitreal faricimab up to every 16 weeks for neovascular age-related macular degeneration (TENAYA and LUCERNE): two randomised, double-masked, phase 3, non-inferiority trials. *Lancet*. 2022;399(10326):729-40.
36. Khanani AM, Patel SS, Ferrone PJ, Osborne A, Sahni J, Grzeschik S, et al. Efficacy of every four-monthly and quarterly dosing of faricimab vs ranibizumab in neovascular age-related macular degeneration: the STAIRWAY phase 2 randomized clinical trial. *JAMA Ophthalmol*. 2020;138(9):964-72.
37. Boulanger-Scemama E, Querques G, About F, Puche N, Srouf M, Mane V, et al. Ranibizumab for exudative age-related macular degeneration: a five-year study of adherence to follow-up in a real-life setting. *J Fr Ophtalmol*. 2015;38(7):620-7.
38. Luu KT, Seal J, Green M, Winskill C, Attar M. Effect of anti-VEGF therapy on the disease progression of neovascular age-related macular degeneration: a systematic review and model-based meta-analysis. *J Clin Pharmacol*. 2022;62(5):594-608.
39. Rosenberg D, Deonarain DM, Gould J, Sothivannan A, Phillips MR, Sarohia GS, et al. Efficacy, safety, and treatment burden of treat-and-extend versus alternative anti-VEGF regimens for nAMD: a systematic review and meta-analysis. *Eye (Lond)*. 2023;37:6-16.