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EVALUATING THE REAL-WORLD EFFICACY AND SAFETY OF INTRAVITREAL FARICIMAB IN THE MANAGEMENT OF NEOVASCULAR AGE-RELATED MACULAR DEGENERATION: A SYSTEMATIC REVIEW

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Abstract

***Introduction*:** *Neovascular age-related macular degeneration (nAMD) is a leading cause of irreversible vision loss in the elderly. Intravitreal anti-vascular endothelial growth factor (anti-VEGF) therapies have revolutionized the treatment of nAMD. Faricimab, a novel bi-specific anti-VEGF and anti-angiopoietin-2 antibody, has shown promise in clinical trials. This comprehensive systematic review aims to evaluate the real-world efficacy and safety of intravitreal faricimab in the management of nAMD.*

***Methods**: A comprehensive search was conducted in major electronic databases to identify studies reporting outcomes related to faricimab treatment for nAMD in real-world settings. A total of 6 studies were included, comprising 800 patients including 874 eyes. The primary outcomes of interest included visual acuity improvements, central subfield thickness of retina, and safety.*

***Result**: The review reveals that intravitreal faricimab is associated with significant visual acuity improvements in patients with nAMD, with outcomes comparable to or better than existing anti-VEGF agents. Furthermore, patients receiving faricimab typically required fewer injections, resulting in a potentially lower treatment burden. The findings also suggest that faricimab may offer a longer treatment interval, which could have a positive impact on patient quality of life.*

***Conclusion**: Regarding safety, faricimab demonstrated a favorable safety profile in the real-world setting, with a low incidence of ocular and systemic adverse events. This suggests that faricimab is well-tolerated by patients, supporting its long-term use in the management of nAMD*

Keywords: Faricimab, efficacy, neovascular age-related macular degeneration, real-world study, safetyCite This Article: BARUS, Dany Petra Pranata; ADRIONO, Gitalisa Andayani. Evaluating the Real-World Efficacy and Safety of Intravitreal Faricimab in the Management of Neovascular Age-Related Macular Degeneration: A Systematic Review. International Journal of Retina, [S.l.], v. 8, n. 2, p. 138, oct. 2025. ISSN 2614-8536. Available at: <https://www.ijretina.com/index.php/ijretina/article/view/329>. Date accessed: 01 oct. 2025. doi: https://doi.org/10.35479/ijretina.2025.vol008.iss002.329...

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INTRODUCTION

Age-related macular degeneration (AMD) is one of the most leading causes of blindness, particularly in people with age older than 60 years and developed countries. It is a chronic and progressive disease of the macula that results in central vision loss. AMD could be classified from early stage into late stage, or known as advanced AMD. Advanced AMD could be further categorized into two types, non-exudative, or atrophic form of AMD (dry AMD) and exudative or neovascular form of AMD (wet AMD or nAMD).[1–3] Neovascular/wet AMD differs mainly from dry AMD due to the presence of new blood vessels from the choroid, called choroidal neovascularization. Those new blood vessels penetrate and proliferate between the subretinal spaces or Bruch's membrane and the retinal pigment epithelium. Imperfect structure of neovascularization will lead to a cascade of pathological changes, including exudation, bleeding, as well as scar which causes rapid decrease of visual acuity.[3,4]

About 196 million people are estimated to have AMD in 2020, more commonly found in Europeans than Asians. The prevalence of people aged 45 to 85 years old with AMD is 8.7%, with 0.4% for advanced AMD. It is estimated that by 2040, the global prevalence of AMD will be 288 million. AMD also holds the third position as the leading cause of blindness after glaucoma and cataract. Despite that about 80% of the AMD patient has dry AMD, nAMD accounts to almost 90% of the severe loss of visual acuity linked with AMD.[1–3,5]

Vascular endothelial growth factor (VEGF) has been identified as one of the main pathophysiological components in neovascular AMD. VEGF has an important part in angiogenesis, permeability of vascular, as well as inflammatory response. It led to the use of anti-VEGF injection as a treatment for nAMD, stopping the pathophysiological action of AMD, restoring the retinal morphology, and maintaining its function. Anti-VEGF injection (Figure 1) has been the main treatment for nAMD due to its safeness, well-tolerated, and few undesirable effects. Currently, there are four main anti-VEGF agents that are widely available in the treatment of nAMD, which are bevacizumab, ranibizumab, brolucizumab and aflibercept. Although anti-VEGF drugs can resolve the exudative signs in most patients, there are some limitations regarding the treatment of nAMD. High-cost of treatment, frequent injections, as well as the decline of visual acuity in long term, attributed to complications such as macular atrophy and fibrosis.[5,6]

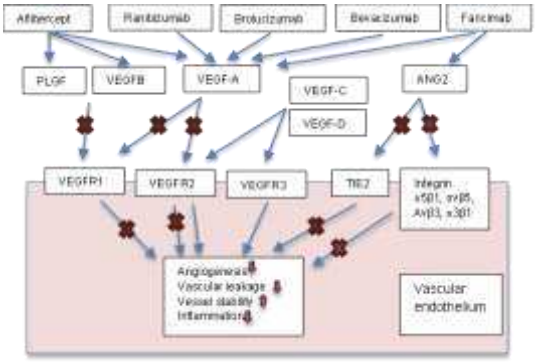

Figure 1. Anti VEGF mechanism of action[7]

A lot of strategies have been used to combat these problems, including altering the dose, researching new anti-VEGF agents, as well as identifying other pathways (Figure 2) which can be used, one of them are angiopoietin (Ang) tyrosine kinase endothelial receptors (Tie) pathway. Ang/Tie is a transmembrane receptor that functions as the binding site for angiopoietin 1 and 2 (Ang-1 and Ang-2), with Ang/Tie pathway playing a role in regulating the vascular homeostasis, modulating vascular permeability, as well as neo angiogenic and proinflammatory processes. Based on preclinical studies, it is shown that dual inhibition of Ang-2 and VEGF-A was superior compared with anti-VEGF-A or anti-Ang-2 alone. Faricimab (Vabysmo™)

is a novel drug which targets both VEGF-A and Ang-Tie pathways.

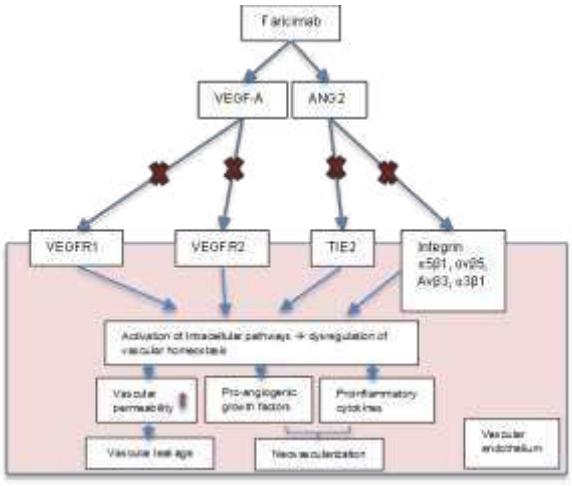

Figure 2. Faricimab mechanism of action

From the clinical studies, TENAYA and LUCERNE are two identical studies conducted over 112 weeks, focusing on faricimab treatment for neovascular AMD. In these studies, patients were randomly assigned to receive either faricimab or aflibercept. The main measure of effectiveness was the average change in best-corrected visual acuity (BCVA) between weeks 40, 44, and 48 from the baseline. Secondary outcomes examined various factors such as the proportion of patients following different faricimab dosing schedules, the number of patients showing significant improvement in vision, and changes in anatomical outcomes from the baseline. Safety aspects were also assessed, including the occurrence and seriousness of adverse events, both ocular and non-ocular. These results are in line with STAIRWAY study, a multicenter study lasting 52 weeks, focused on 76 patients with nAMD. These patients were treated with faricimab after an initial four-month loading period, either every 12 weeks (Q12W) or every 16 weeks (Q16W), and were compared to those receiving ranibizumab 0.5 mg every 4 weeks (Q4W). The study found that faricimab given at Q12W or Q16W intervals, following the loading dose, resulted in similar improvements in both vision and eye structure when compared to ranibizumab administered every 4 weeks. These results suggest a role for simultaneous neutralization of angiopoietin-2 and vascular endothelial growth factor A in providing sustained efficacy through extended durability, warranting further investigation.

Faricimab was recently approved in 2022 to be used in the USA, Japan, and Europe, with approval from both FDA and EMA to treat nAMD. We conducted a review of existing evidence to evaluate the efficacy of faricimab intravitreal injection in treating nAMD patient within real-world clinical settings, as observed in real world studies.[6]

METHOD

Literature search

On August 1st, 2023, a comprehensive search of the literature was performed using online databases such as PubMed, Scopus, Science Direct, and Clinicalkey. Additionally, a secondary search was conducted by examining the reference lists of relevant articles. To structure a focused research question and streamline the identification of pertinent data, the population, intervention, control, and outcomes (PICO) format was employed in the following manner.

P (population): nAMD patients

I (intervention): intravitreal injection of faricimab

C (control): no control

O (outcomes): the efficacy and safety of intravitreal injections

The keywords for the literature search included the combination of "Faricimab", "Vabysmo™", "age-related macular degeneration", "wet age-related macular degeneration", "neovascular age-related degeneration", "efficacy and safety" and "real-world" with Boolean operators.

Eligibility criteria

This review encompassed studies that adhered to specific inclusion criteria. Only fully accessible articles published in English within the last 5 years (from 2018 to 2023) were considered. The focus was on real-world studies involving patients with neovascular AMD who underwent intravitreal faricimab injections, encompassing both initial treatment and switch therapy cases. There were no restrictions on study types; observational studies, case series, and individual case studies were all eligible. Studies which use Spectral Domain and Swept Source OCT were included in this study. However, clinical trial reports, commentary, editorial pieces, and conference summaries were excluded from the review.

Study selection and analysis

After conducting a thorough literature search, the findings were examined by reviewing titles, abstracts, and/or full texts. Relevant literature was chosen, and full-text articles that matched the criteria or were uncertain based on titles and abstracts were retrieved. The necessary data were extracted during this process. Two reviewers independently evaluated the full-text studies for this review.

Outcome measures

The focus of this study revolves around several key aspects. Firstly, it assesses the effectiveness by examining alterations in best-corrected visual acuity (BCVA). Additionally, changes in anatomical factors, specifically central subfield thickness (CST) of retina, and the presence of subretinal fluid (SRF), intraretinal fluid (IRF), and pigment epithelial detachment (PED) as measured through optical coherence tomography (OCT), are considered. The study also analyzes the interval between injections. Moreover, it evaluates the safety of faricimab by monitoring adverse events, categorized as intraocular inflammation (IOI), non-inflammatory reactions and systemic reactions.

RESULTS

1. Literature Search Results

For this study, we conducted a literature search through several search engines, such as Pubmed, Clinicalkey, ScienceDirect, and Scopus. We found 990 studies and there are 39 studies that corresponded to the inclusion criteria. Then, we did full text reviews and we found 6 studies were included for critical appraisal. The literature search flowchart is shown in Figure 3.

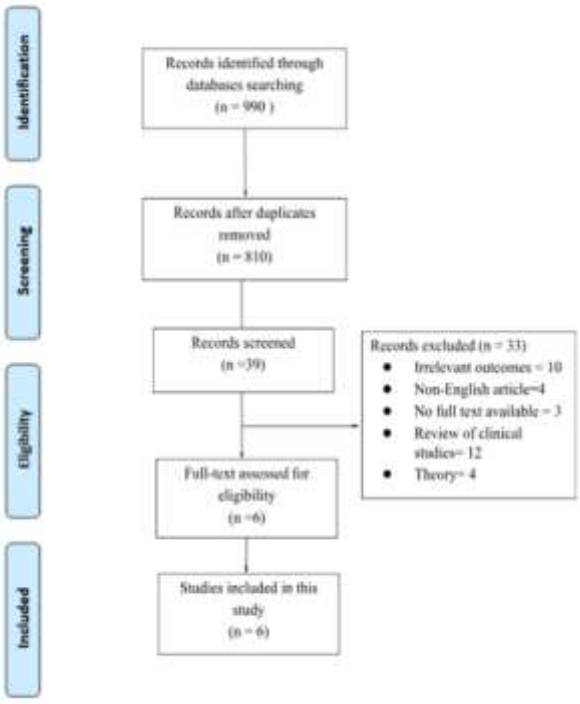

Figure 3. Literature search and selection flowchart

2 Validity Assessment

The assessment of the articles' validity was carried out using the Real-World Observational Studies (known as ArRoWS) critical appraisal tool. From the validity assessment, Matsumoto et al and Khanani et al were not define any confounder. Khanani et al also showed no limitation. Despite that, overall studies showed good validity assessment. The outcomes of this validity assessment are presented in Table 1.

3 Study characteristics

In this review, summary of the studies that were included can be found in Table 2. These 6 studies encompassed a total of 800 patients and 874 eyes, which reported the outcome of intravitreal injection of faricimab. All studies that were included in this review had a retrospective, observational study design. As per the Oxford Center for Evidence-Based Medicine's 2011 Level of Evidence criteria, these studies are categorized as level II evidence. Out of the included studies, two of them were multicenter studies, with the rest being monocenter studies. These studies were conducted in two countries, the United States of America and Japan. Regarding the patient population, three studies enrolled patients who had undergone switch-therapy, while two studies included only treatment-naive patients. Additionally, one study recruited both switch-therapy patients and treatment-naive patients. On average, the patients in these studies were 78 years old. The mean follow-up period across these studies were approximately 21.22 ± 7.59 weeks, with the shortest follow-up period being 16 weeks and the longest being 35 weeks.

Only two studies present the subtypes of macular neovascularization in their review. Mukai et al showed that, among the 62 included eyes, there were 32 (52%) eyes with type 1 and/or type 2 macular neovascularization (24 eyes with type 1 macular neovascularization, 4 eyes with type 2 macular neovascularization, and 4 eyes with both), 22 (35%) eyes with polypoidal choroidal vasculopathy (PCV), and 8 (13%) eyes with type 3 macular neovascularization. While Matsumoto et al showed, among the 40 included eyes, macular neovascularization subtypes were as follows: type 1: 14 eyes; polypoidal choroidal vasculopathy (PCV): 17 eyes; mixed type 1 and type 2: 2 eyes; mixed PCV and type 2: 1 eye; type 2: 2 eyes; type 3: 4 eyes. The other studies did not reveal any subtype data of macular neovascularization

Table 1. Validity Assessment of real-world studies

Domains	Questions	Matsumoto et al.	Khanani et al. (TRUCKEE)	Leung et al.	Inoda et al	Mukai et al	Szigiato et al.
Clinical importance of the research question or objective	Is the research question or objective(s) clear?	Yes	Yes	Yes	Yes	Yes	Yes
Representativeness of the sample	Is the study sample representative of its target population?	Yes	Yes	Yes	Yes	Yes	Yes
Reliability of exposure and outcome measures	Has a sample size, power calculation or measure of uncertainty (e.g., confidence intervals, standard errors) been provided?	Yes	Yes	Yes	Yes	Yes	Yes
Reliability of exposure and outcome measures	Are the exposure measures clearly defined and appropriate?	Yes	Yes	Yes	Yes	Yes	Yes

Statistical adjustment for confounders	Is/are the outcome(s) clearly defined and appropriate?	Yes	Yes	Yes	Yes	Yes	Yes
Appropriateness of statistical analyses	Are confounders clearly defined and appropriate?	No	No	Yes	Yes	Yes	Yes
Recognition and minimization of bias	Are the statistical analyses clearly defined and appropriate?	Yes	Yes	Yes	Yes	Yes	Yes
	Are the limitations of the study defined and appropriate?	Yes	No	Yes	Yes	Yes	Yes
Acknowledgment of limits for inferences based on observational data	Have the authors drawn appropriate conclusions from their results?	Yes	Yes	Yes	Yes	Yes	Yes

Table 2. Characteristics of the included studies

Domains	**Questions**	**Matsumoto et al.**	**Khanani et al. (TRUCKEE)**	**Leung et al.**	**Inoda et al**	**Mukai et al**	**Szigiato et al.**
Clinical importance of the research question or objective	Is the research question or objective(s) clear?	Yes	Yes	Yes	Yes	Yes	Yes
Representativeness of the sample	Is the study sample representative of its target population?	Yes	Yes	Yes	Yes	Yes	Yes
Reliability of exposure and outcome measures	Has a sample size, power calculation or measure of uncertainty (e.g., confidence intervals, standard errors) been provided?	Yes	Yes	Yes	Yes	Yes	Yes
Reliability of exposure and outcome measures	Are the exposure measures clearly defined and appropriate?	Yes	Yes	Yes	Yes	Yes	Yes
Statistical adjustment for confounders	Is/are the outcome(s) clearly defined and appropriate?	Yes	Yes	Yes	Yes	Yes	Yes
Appropriateness of statistical analyses	Are confounders clearly defined and appropriate?	No	No	Yes	Yes	Yes	Yes

Recognition and minimization of bias	Are the statistical analyses clearly defined and appropriate?	Yes	Yes	Yes	Yes	Yes	Yes
	Are the limitations of the study defined and appropriate?	Yes	No	Yes	Yes	Yes	Yes
Acknowledgment of limits for inferences based on observational data	Have the authors drawn appropriate conclusions from their results?	Yes	Yes	Yes	Yes	Yes	Yes

4. Study results

The focus of this review centers on assessing how effective faricimab performs in real-world clinical settings. This evaluation is based on several key factors, including improvement in Best-Corrected Visual Acuity (BCVA), changes in Central Subfield Thickness (CST), the presence of retinal fluids (Intraretinal fluid - IRF, subretinal fluid - SRF, and pigment epithelial detachments - PED, dry macula), the injection interval, as well as adverse events, encompassing both intraocular inflammation (IOI) and non-inflammatory complications.

4.1 Visual acuity

BCVA was measured with a visual acuity chart in four studies, which converted into the logarithm of the minimal angle of resolution (logMAR) units. The other two studies use Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity chart and we convert to LogMAR units. The comparison of BCVA was made between the baseline measurement and the final follow-up assessment.

There was notable improvement in the Best-Corrected Visual Acuity (BCVA) in most of the studies, with improvement deemed to be statistically significant ($p<0.05$) in four of them. Detailed information regarding the changes in visual acuity following the administration of faricimab can be found in Table 3 and 4.

Table 3. Visual acuity at baseline and at last follow-up of the Treatment-naive studies

Author	Baseline BCVA (logMAR)	Last BCVA	Δ (D)	P-value of BCVA changes
Khanani et al.	0.58	0.49	0.09	0.076
Matsumoto et al.	0.33 ± 0.41	0.22 ± 0.36	0.11 ± 0.05	<0.01
Mukai et al.	0.4 ± 0.42	0.32 ± 0.43	0.08 ± 0.01	<0.01

Treatment-naive eyes

There are three studies that focused on treatment-naive patients conducted by Matsumoto et al., Mukai et al., and Khanani et al. In all three of these studies, it was shown there was an improvement in BCVA, with two of them being statistically significant ($p<0.05$). In the studies conducted by Matsumoto et al., and Mukai et al., it was shown that there was an increase from 0.33 to 0.22 and 0.4 to 0.32, with follow-up periods 16 weeks and 3 months respectively. Similar results can be found in studies conducted by Khanani et al. regarding the treatment-naive patients, with an improvement of visual acuity from 0.58 to 0.49 letters during the last follow up, with a follow up period of 6 months. In general, there is an improvement in BCVA after therapy (treatment-naïve patients).

Table 4. Visual acuity at baseline and at last follow-up of the Switch-therapy studies

Author	Baseline BCVA (logMAR)	Last BCVA	Δ (D)	P-value of BCVA changes
Khanani et al.	0.51	0.49	0.02	0.035
Szigato et al.	0.44	0.45	0.01	0.42
Leung et al.	0.33±0.32	0.27±0.32	0.06	0.0022
Inoda et al.	0.34 ± 0.37	0.36 ± 0.40	0.02 ± 0.03	0.29

Switch-therapy eyes

There was a total of four studies that focused on eyes undergoing switch therapy. Half of these studies observed an improvement in BCVA by the end of the follow-up period, with both being statistically significant ($p<0.05$). Leung et al. and Khanani et al. studies showed that there was an improvement of BCVA from 0.33 to 0.27 and from 0.51 to 0.49. The other half could be found in the studies by Szigato et al. and Inoda et al., with a mean visual acuity did not change during treatment 0.44 to 0.45 ($p=0.42$) and 0.34 to 0.36 ($p=0.29$) respectively. Thus, in switch-therapy studies, there are 2 studies with increase in BCVA and 2 other studies with relatively unchanged in BCVA.

4.2 Central Subfield Thickness

Anatomical parameters were assessed using Optical Coherence Tomography (OCT), both through quantitative and qualitative methods. In terms of quantitative measurements, we detected statistically significant alterations in Central Subfield Thickness (CST) as shown in Table 5. In general, there is a decrease in CST after therapy.

Table 5. Central retinal thickness at baseline and at last follow-up of the included studies.

Author	Type of patients	Baseline CST (µM)	Last CST (µM)	Δ (D)	p-value
Khanani et al.	TN	388.1±11.38	308.0±11.12	80.1±22.5	0.204
Matsumoto et al	TN	278 ± 116	173 ± 48	105± 164	0.01
Mukai et al	TN	357 ± 165	175 ± 91	182± 256	p < 0.0001
Khanani et al.	ST	356.0±1.81	317.9±1.24	38.1± 3.05	<0.001
Leung et al.	ST	312±87	287± 71	25±16	<0.0001
Inoda et al.	ST	242±72	242± 82	0±10	0.99
Szigato et al.	ST	266.8±64.7	249.8±58.6	17±123.3	**0.02**

TN= Treatment-naive patients; ST: Switch-therapy patients

Treatment-naive eyes

All studies that assessed treatment-naive patients reported changes in central subfield thickness (CST). Studies conducted by Khanani et al. reported changes in Central Subfield Thickness (CST) from the baseline measurement to the last follow-up assessment which are not statistically significant. Matsumoto et al and Mukai et al found that CST was significantly reduced between the baseline and the last follow up after the administration of faricimab.

Switch therapy eyes

In the case of studies that included only switch therapy eyes, four of them reported changes in the Central Subfield Thickness (CST) from the baseline measurement to the last follow-up assessment, three of them are statistically significant ($p<0.05$). The magnitude of these changes varied, with the mean changing from 0.13 to 38.1 µM.

4.3 Subretinal fluid, intraretinal fluid, pigment epithelial detachment, and dry macula

The assessment of improvements in the retina involved evaluation of the presence of Intraretinal Fluid (IRF), Subretinal Fluid (SRF), Pigment Epithelial Detachments (PED), and whether dry macula is achieved. The information regarding the quantitative assessment was presented in Table 6. One study was not included in the analysis since the studies did not provide data regarding SRF, IRF, PED, or dry macula.

There were three studies that showed the percentage of eyes that showed complete resolve of SRF and IRF by the end of their respective studies, which were Khanani et al, Leung et al, and Szigiato et al. Although those studies did not provide any statistical significance data. Studies by Khanani et al, and Mukai et al. also reported a complete resolution of PED, with the number of 40% in treatment-naive patients, 14.9% in switch-therapy patients, and 54% in the studies conducted by Mukai et al. Like the data of SRF and IRF, there is no information regarding the statistical significance data. The number of dry maculae that was achieved was also reported in the studies by Matsumoto et al and Mukai et al., with the number being 79.5% and 82% respectively.

Table 6. Retinal fluids at baseline and at last follow-up of the included studies

Author	Type of patients	Complete resolve of			Dry Macula Achieved (%)
		SRF (%)	IRF (%)	PED (%)	
Matsumoto et al.	TN	NA	NA	NA	79.5
Khanani et al. (TRUCKEE)	TN	25	45.5	40	NA
Khanani et al. (TRUCKEE)	ST	20.8	21.4	14.9	NA
Leung et al.	ST	38*		NA	NA
Mukai et al.	TN	NA	NA	54	82
Szigiato et al.	ST	24,6	16,7	NA	NA

TN= Treatment-naive patients ; ST: Switch-therapy patients
* Complete resolve of SRF and IRF

4.4 Safety

In terms of safety outcomes, this review considered both Intraocular Inflammation (IOI) and other adverse events unrelated to inflammation. Out of the 874 eyes included in the review, 16 eyes (approximately 1.83%) developed adverse events, of which 7 of them developed intraocular inflammation (approximately 0.8%) and 9 of them (approximately 1%) developed other adverse events. Notably, studies by Inoda et al. did not report any instance of intraocular inflammation during their investigations. Table 7 in the review provides a list of adverse events that is reported in all the studies included in this review.

Table 7. List of adverse events reported in all included studies.

Adverse Events	n (eyes/percentage)
IOI (0.875%)	
Vitritis	1 (0.11%)
Endophthalmitis	3 (0.34%)
Anterior chamber inflammation	1 (0.11%)
Unspecified IOI	2 (0.23%)
Non-inflammation (1.125%)	
Subretinal hemorrhage	3 (0.34%)
Pigment epithelial tear	4 (0.46%)
Corneal edema	2 (0.23%)
RPE tears	2 (0.23%)
Systemic (0.11%)	
Death*	1 (0.11%)
Total	**19 (2.17%)**

Treatment of the adverse effect varies depending on the adverse event that happens. In the event of intraocular inflammation, most of the studies observed that it is resolved after the administration of corticosteroids, both topical and intravitreal. These studies include those conducted by Khanani et al and Szigato et al, as well as Matsumoto et al. But in the case of vitritis without any visual loss that is observed in the studies by Matsumoto et al, more intensive interventions were necessary, such as the use of sub tenon injection of triamcinolone acetonide. Intravitreal antibiotics were also given to patients with endophthalmitis in studies by Khanani et al. Adverse effects were observed to develop in 16 weeks, or after the fourth injection of the intravitreal faricimab in these studies. Table 8 in the review provides a comprehensive list of adverse events that were reported in all the studies included in this review.

DISCUSSION

Neovascular Age-Related Macular Degeneration (nAMD) is a complex and debilitating eye disease characterized by the growth of abnormal blood vessels in the macula, leading to central vision loss. Intravitreal anti-VEGF therapy has been a cornerstone of nAMD treatment, revolutionizing patient outcomes in clinical trials. Faricimab, as a novel anti-VEGF agent, has generated substantial interest in the field due to its unique bispecific mode of action targeting both VEGF-A and Ang-2 pathways. However, the translation of promising clinical trial results into real-world clinical practice poses distinct challenges and uncertainties. In this discussion, we synthesize the key findings of our systematic review and contextualize them within the broader landscape of nAMD management.[14]

A statistically significant improvement in visual acuity was evident in three studies of naive-eyes. Matsumoto et al., Mukai et al., and Khanani et al. collectively demonstrated an enhancement in Best-Corrected Visual Acuity (BCVA) in their respective investigations, with statistical significance observed in two of them ($p<0.05$).[8,9,12] There are some adverse events that can occur, such as vitritis, endophthalmitis, anterior chamber inflammation, subretinal hemorrhage, pigment retinal tear, and corneal edema. These adverse events can be resolved by treatment.

This is in accordance with both TENAYA and LUCERNE trials. These trials showed improvement from the initial visual acuity was comparable when administering faricimab at fixed intervals of up to 16 weeks, which proved non-inferior to aflibercept administered every 8 weeks. In these trials, faricimab consistently displayed long-lasting effectiveness, with nearly half of the patients on faricimab treatment (around 45%) able to extend their treatment intervals to every 16 weeks by week 48, and a significant proportion (approximately 80%) achieving intervals of every 12 weeks or longer. These findings collectively highlight faricimab's potential, achieved through its dual inhibition of Ang-2 and VEGF-A, to extend treatment intervals for nAMD patients, addressing a critical need for more durable and effective therapies that optimize clinical benefits while reducing the overall burden of visits and treatments.[15]

Another clinical trial also showed similar results. The subgroup analysis of the TENAYA study in Japan indicated that faricimab, when administered at intervals of up to 16 weeks, maintained its effectiveness while maintaining a safe profile. These results align with the overall findings from the TENAYA and LUCERNE studies on a global scale.[16]

Table 8. Overview of safety outcomes of the included studies.

Author	Follow-up period	Type of eyes with AEs	Adverse events	Timing	Presenting symptoms and signs	Treatment	Outcomes
Matsumoto et al.	16 weeks	Treatment-naive patients	One eye (2.5%) with Vitritis development without visual loss One patient (2.6%) died due to acute exacerbation of heart failure	Week 16 Week 12	NA	Combination therapy with sub tenon injection of triamcinolone acetonide (30 mg/0.75 ml) and 0.1% betamethasone eye drops	NA
Khanani et al.	6 months	Treatment-naive and Switch-therapy patients	One patient with Infectious endophthalmitis, one patient with mild anterior chamber inflammation	NA, fourth injection of faricimab	Vision loss	Intravitreal antibiotics, topical steroid	Three-weeks post treatment, vision returning to baseline.
Leung et al.	35 weeks	Switch-therapy patients	Two patients (1%) with presumed endophthalmitis, four patients (2%) with retinal pigment epithelial (RPE) tears, three patients (1.6%) developed subretinal hemorrhages	Fourth doses of intravitreal faricimab, after 5.25±2.06 injections, after 7.33±2.08 injections	NA	NA	NA
Inoda et al.	71.0 ± 46.9 months	Switch-therapy patients	None	NA	NA	NA	NA
Mukai et al.	3 months	Treatment-naive	Two eyes from two patients (3%) with RPE tears	NA	NA	NA	NA
Szigato et al.	24.3±5.2 weeks	Switch-therapy	Two eyes (1.6%) from 1 patient with intraocular inflammation (IOI).	NA	Corneal edema, increased IOP (36 and 43 mg), and panuveitis	High dose oral steroids on a gradual taper over several weeks, topical steroids, IOP lowering medications, discontinuation of intravitreal vitreous faricimab.	VA returned to 20/40 OD 20/50 OS 3 months after the episode of IOI

Real-world evidence regarding faricimab's efficacy in the management of nAMD is promising. The real-world evidence analyzed in this review indicates that faricimab has demonstrated effectiveness in maintaining or improving visual acuity in patients with nAMD. Studies indicate that faricimab effectively preserves or improves visual acuity in patients. Most patients experience gains in vision, supporting its potential as an effective therapeutic option. It is important to note that the variability in study designs, endpoints, and follow-up durations makes direct comparisons challenging. To further refine our understanding, longer-term studies with larger sample sizes are necessary. Comparative analyses with other anti-VEGF agents in real-world settings indicate similar efficacy, suggesting that faricimab performs at least as well as established treatments.

Moreover, the comparison of faricimab with other established anti-VEGF agents in real-world settings has provided insights into its comparative efficacy. While some studies suggest no significant differences, more extended observational periods and larger sample sizes may be necessary to detect subtle distinctions in outcomes and injection frequency. This finding underscores the need for more robust comparative studies to better inform treatment decisions.

The CST parameter is a significant clinical outcome measure in the management of nAMD, as it provides insights into the anatomical changes within the macula, a key determinant of visual function and disease progression. Based on the studies, it is found that there are changes in the central subfield thickness in treatment-naive eyes as well as switch therapy eyes. This is also like the results in the BOULEVARD trials, which shows reduction in the central subfield thickness. In the BOULEVARD trial, faricimab led to numerically greater reductions in central subfield thickness (CST) when compared to another anti-VEGF agent, namely ranibizumab. In patients who had received prior anti-VEGF treatments, the degree of central subfield thickness (CST) reduction favored eyes treated with faricimab over ranibizumab. This suggests that faricimab has the potential to reduce the treatment burden for individuals with diabetic macular edema (DME) who are currently undergoing anti-VEGF monotherapy. In both TENAYA and LUCERNE, treatment with faricimab dosed up to every 16 weeks resulted in CST reductions from baseline at all timepoints up to week 48, starting at 4 weeks after treatment initiation, and was comparable with aflibercept every 8 weeks. Adjusted mean CST change from baseline at primary endpoint visits was −136·8 µm (95% CI −142·6 to −131·0) with faricimab and −129·4 µm (−135·2 to −123·5) with aflibercept in TENAYA (treatment difference −7·4 µm [−15·7 to 0·8]), and −137·1 µm (−143·1 to −131·2) with faricimab and −130·8 µm (−136·8 to −124·8) with aflibercept in LUCERNE (treatment difference −6·4 µm [−14·8 to 2·1]). The dual inhibition of Ang-2 and VEGF-A likely contributes to enhanced vascular stability compared to VEGF inhibition alone, which may explain the increased durability of the treatment effect. This extended durability seen with faricimab could translate to sustained effectiveness with fewer injections, thereby helping to maintain and protect visual improvements in a real-world clinical practice setting.[17]

Real-world studies on various anti-VEGF medications, such as faricimab, Aflibercept, and Bevacizumab, offer invaluable insights into their effectiveness and practical implications outside controlled clinical settings. Faricimab, an emerging treatment, demonstrates promise due to its unique dual mechanism of action targeting VEGF-A and Ang-2 pathways. In comparison to more established medications like Aflibercept and Bevacizumab, these real-world analyses provide a comprehensive view of their respective efficacy, safety, and real-world outcomes in conditions like age-related macular

degeneration. American nAMD patients undergo fewer anti-VEGF injections (regularly repeating monthly injections for ranibizumab or bevacizumab, or bimonthly injections for aflibercept) and encounter poorer visual results compared to clinical trial participants, aligning with findings from studies outside the US. Individuals starting with better vision face a heightened risk of vision decline. Patients who drop out before completion exhibit even worse visual outcomes at or before their final visit, hinting that dropout might inflate visual success in clinical nAMD studies.[18]

Our analysis of real-world safety data concerning Faricimab in nAMD patients suggests a favorable safety profile. Few serious ocular and systemic adverse events were reported, consistent with the known safety profile from clinical trials. The infrequency of serious safety events is reassuring, although long-term safety assessments are crucial, given that nAMD often requires chronic treatment. However, this review's findings are consistent with the understanding that Faricimab exhibits a safety profile like other anti-VEGF agents, thereby supporting its potential as a safe treatment option for nAMD in real-world settings. Table 9 show common Adverse Reaction from TENAYA and LUCERNE trials, compared faricimab and aflibercept.

Table 9. The common adverse reaction of faricimab vs aflibercept.

Adverse Reaction	Faricimab (N=664)	Aflibercept (N=625)
Conjunctival hemorrhage	7%	8%
Vitreous floaters	3%	2%
Retinal pigment epithelial tear	3%	1%
Intraocular pressure increased	3%	2%
Eye pain	3%	3%
Intraocular inflammation	2%	1%
Eye irritation	1%	< 1%
Ocular discomfort	1%	< 1%
Vitreous hemorrhage	< 1%	1%

This review reveals variability in faricimab dosing regimens in clinical practice. While the flexibility of Faricimab's dosing schedule is one of its appealing features, it raises questions about the optimal dosing interval. The recommended dose for faricimab by FDA is 6 mg (0.05 mL of 120 mg/mL solution) administered by intravitreal injection every 4 weeks (approximately every 28 ± 7 days, monthly) for the first 4 doses, followed by optical coherence tomography and visual acuity evaluations 8 and 12 weeks later to inform whether to give a 6 mg dose via intravitreal injection on one of the following three regimens: 1) Weeks 28 and 44; 2) Weeks 24, 36 and 48; or 3) Weeks 20, 28, 36 and 44. Although additional efficacy was not demonstrated in most patients when faricimab was dosed every 4 weeks compared to every 8 weeks, some patients may need every 4 week (monthly) dosing after the first 4 doses. Real-world evidence suggests that extended dosing intervals are achievable without compromising efficacy. This might be advantageous for reducing treatment burden and improving patient compliance. However, the balance between extending dosing intervals and preserving optimal visual outcomes remains a subject of ongoing investigation. [19]

Patient-specific factors, including age, baseline disease severity, and comorbidities, can influence treatment outcomes. Some studies in our review indicate that older age may be associated with less robust visual acuity gains, highlighting the need for individualized treatment approaches. Furthermore, baseline disease characteristics, such as lesion type and size, influence the response to treatment. Clinicians should consider these factors when making treatment decisions, and additional research is required to delineate the optimal strategies for specific patient subgroups.

In terms of cost efficiency, research conducted by Meer et al., Utilizing information from drug labels and pivotal studies, The total expenses over the initial three years of treatment amount to $32,491 for faricimab, $70,200 for ranibizumab 0.5 mg, and $38,850 for aflibercept (Table 10). Notably, faricimab proves to be more economical, being $37,709 and $6,359 less expensive than ranibizumab and aflibercept, respectively. The study demonstrated that travel distance and time expenses can substantially affect the overall cost of treatments. This influence goes beyond the initial therapy acquisition cost and injection frequency. To elaborate, the study indicates that when accounting for travel time and distance expenses, faricimab emerges as a more cost-effective option in comparison to ranibizumab and aflibercept. It leads to savings of $37,709 and $6,359, respectively, during the initial three years of therapy. [20]

Table 10. The total expenses over the initial three years of Anti-VEGF treatment

Pricing	Year 1	Year 2	Year 3	Total
Ranibizumab 0.5 mg ($)	23,400	23,400	23,400	70,200
Aflibercept ($)	14,800	12,025	12,025	38,850
Faricimab ($)	14,862	8,814	8,814	32,491

Several limitations within the reviewed studies should be acknowledged. Heterogeneity in study designs, endpoints, and follow-up durations made direct comparisons challenging. The lack of randomized controlled trials in the real-world evidence available underscores the need for more rigorous prospective studies. Additionally, many of the included studies were conducted over relatively short timeframes, highlighting the need for longer-term investigations to comprehensively assess the safety and efficacy of faricimab in the real world.

In conclusion, this systematic review provides a valuable synthesis of real-world evidence on the efficacy and safety of intravitreal faricimab in the management of neovascular age-related macular degeneration. Faricimab appears to be an effective and safe option, with the potential for extended dosing intervals, although ongoing research is necessary to refine treatment strategies and better understand its comparative effectiveness. As clinical practice evolves, ongoing surveillance and investigation will be crucial to ensure that patients with nAMD receive the most appropriate and effective treatments tailored to their unique characteristics and needs.

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