Clinical Ophthalmology

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Real-World Efficacy of Intravitreal Faricimab for Macular Edema Secondary to Retinal Vein Occlusion: Short-Term Outcomes and Optical Coherence Tomography Biomarker Analysis

Soichiro Inokuchi[1,*], Yuki Mizuki[1,2,*], Akihiro Kamata[3], Junji Onishi[3], Takahiko Hayashi[4], Nobuhisa Mizuki[1]

[1]Department of Ophthalmology and Visual Science, Yokohama City University Graduate School of Medicine, Yokohama, Kanagawa, Japan; [2]Department of Ophthalmology, Yokohama Minami Kyosai Hospital, Yokohama, Kanagawa, Japan; [3]Department of Ophthalmology, International Goodwill Hospital, Yokohama, Kanagawa, Japan; [4]Department of Ophthalmology, Department of Visual Sciences, Nihon University School of Medicine, Itabashi, Tokyo, Japan

*These authors contributed equally to this work

Correspondence: Yuki Mizuki, Department of Ophthalmology and Visual Science, Yokohama City University Graduate School of Medicine, 3-9 Fukuura, Kanazawa-ku, Yokohama, 236-0004, Japan, Email mizuki.yuk.xj@yokohama-cu.ac.jp

Background: Retinal vein occlusion (RVO) is the second most common retinal vascular disease and a major cause of visual impairment due to macular edema (ME). Faricimab, a novel bispecific antibody targeting both VEGF-A and angiopoietin-2, has shown promise in clinical trials; however, real-world data on its efficacy and safety for ME secondary to RVO (RVO-ME) remain limited.

Objective: To evaluate the short-term efficacy and safety of intravitreal faricimab for RVO-ME in a real-world Japanese clinical setting, and to explore associations between baseline optical coherence tomography (OCT) biomarkers and treatment outcomes.

Methods: This retrospective observational study was conducted at the International Goodwill Hospital, Yokohama, Japan, and included 23 eyes with RVO-ME treated with intravitreal faricimab. Changes in best-corrected visual acuity (BCVA, logMAR) and central subfield thickness (CST) over 3 months were assessed. Baseline OCT biomarkers were analyzed for associations with visual and anatomical responses. Subgroup analyses compared treatment-naïve and previously treated eyes.

Results: The median number of injections was 1, and 52.2% of eyes achieved complete resolution of macular fluid. Median BCVA improved significantly from 0.40 to 0.22 logMAR ($p = 0.0025$), and median CST decreased from 352 μm to 194 μm ($p < 0.001$). Greater CST reduction was observed in treatment-naïve eyes ($p = 0.048$) and in eyes with chronic cyst ($p = 0.015$). No OCT biomarker was significantly associated with BCVA improvement. No ocular or systemic adverse events were observed.

Conclusion: Intravitreal faricimab was effective and well-tolerated for RVO-ME in this real-world study. Even a single injection frequently led to anatomical and functional improvement. These results support the clinical utility of faricimab and suggest a potential role for OCT biomarkers in predicting treatment response.

Keywords: faricimab, retinal vein occlusion, macular edema, optical coherence tomography, real-world study, visual acuity

Introduction

Retinal vein occlusion (RVO) is a common retinal vascular disorder caused by obstruction of the retinal venous system and is recognized as the second most common retinal vascular disease.[1] RVO is classified into central retinal vein occlusion (CRVO), which is thought to result from thrombus formation within the optic nerve and may lead to widespread ischemia and severe complications, particularly in ischemic subtypes, and branch retinal vein occlusion (BRVO), which is generally caused by arteriovenous compression at crossing sites and often presents with localized non-

Received: 26 June 2025
Accepted: 20 September 2025
Published: 4 October 2025

perfusion and macular edema (ME).[2] ME results from impaired capillary circulation and contributes to visual impairment and metamorphopsia.[3]

In 2015, the global prevalence of any RVO, BRVO, and CRVO in adults aged 30–89 years was 0.77%, 0.64%, and 0.13%, respectively, affecting an estimated 28.06, 23.38, and 4.67 million people.[4] Although some cases of BRVO show spontaneous improvement, the likelihood of achieving good visual acuity (≥20/40) without treatment is limited, underscoring the need for therapeutic intervention.[5] Currently, intravitreal injections of anti-vascular endothelial growth factor (VEGF) agents, such as ranibizumab and aflibercept, are widely used as standard treatment for macular edema secondary to retinal vein occlusion (RVO-ME), with established efficacy in improving vision and reducing macular thickness.[1] Although anti-VEGF therapy has dramatically improved visual outcomes in patients with RVO-associated macular edema, treatment burden and frequent recurrence remain key challenges in clinical practice. The RETAIN study showed that while half of BRVO patients achieved sustained edema resolution, many still required occasional injections. In contrast, most CRVO patients exhibited persistent edema and poorer visual outcomes despite ongoing treatment.[6]

Faricimab, a novel bispecific antibody targeting both VEGF-A and angiopoietin-2 (Ang-2), has emerged as a promising alternative. A recent meta-analysis demonstrated that faricimab provided comparable visual outcomes to conventional anti-VEGF agents in neovascular age-related macular degeneration (nAMD), diabetic macular edema (DME), and RVO, with superior reduction in central subfield thickness specifically in DME and RVO.[7] In the Phase 3 BALATON and COMINO trials for RVO, faricimab demonstrated non-inferiority to aflibercept in terms of visual and anatomical improvements, and a significantly higher proportion of eyes with absence of macular leakage on fluorescein angiography at week 24, compared with aflibercept.[8] Long-term follow-up showed that many patients achieved extended treatment intervals (≥12 weeks), suggesting the potential to reduce treatment burden.[9] Furthermore, exploratory analyses indicated potential advantages of faricimab in vascular stability, inflammation control, and fibrosis suppression.[10]

Beyond clinical trials, recent real-world studies have reported favorable outcomes with faricimab even in patients resistant to previous anti-VEGF therapy, including visual gains and resolution of ME after switching to faricimab.[11] In AMD and DME, structural optical coherence tomography (OCT) biomarkers have been investigated as predictors of treatment response.[12] However, to our knowledge, no such evaluation has yet been conducted in RVO.

Although rare, serious ocular adverse events such as intraocular inflammation and retinal vascular occlusion have been occasionally reported following faricimab injections.[13] FAERS-based analyses have also suggested potential risks of adverse events not listed in the product labeling, including blindness, cerebral infarction, and retinal vasculitis.[14,15]

Given these considerations, faricimab represents a promising treatment option for RVO-ME based on its dual mechanism of action. While clinical trials have demonstrated its efficacy and safety, real-world evidence remains limited. This study aimed to assess the short-term efficacy and safety of intravitreal faricimab in patients with RVO-ME in a real-world Japanese clinical setting, and to explore potential associations between baseline OCT biomarkers and treatment outcomes.

Methods

Study Design

This retrospective observational study aimed to evaluate the real-world efficacy and safety of intravitreal faricimab injections for RVO-ME. We assessed changes in visual function and anatomical parameters over a 3-month period from treatment initiation and explored associations between baseline OCT biomarkers and treatment outcomes. Because the primary aim was to investigate short-term outcomes within a 3-month period, most patients received only a single injection during the observation window. This reflected the treating physicians' judgment in routine practice, as well as patient-related factors such as economic considerations and preference for fewer injections, rather than a predefined institutional protocol.

Participants

We included patients with RVO-ME who initiated faricimab therapy at the International Goodwill Hospital between December 2023 and November 2024 and had at least 3 months of follow-up data available. Eligible diagnoses included

CRVO and BRVO, confirmed by fluorescein angiography, OCT findings, or clinical diagnosis.Exclusion criteria included coexisting macular diseases such as diabetic retinopathy, age-related macular degeneration, or retinal detachment, as well as a history of ocular surgery within the prior 3 months.

Data Collection

Baseline patient characteristics included age, sex, laterality (right or left eye), RVO type (CRVO or BRVO), prior treatment history (number of previous intravitreal ranibizumab [IVR] or aflibercept [IVA] injections), lens status (phakic or pseudophakic), and prior vitrectomy.

Baseline OCT images were assessed for the presence of subretinal fluid (SRF), intraretinal fluid (IRF), chronic cyst, hyperreflective foci (HRF), disorganization of the retinal inner layers (DRILs), vitreomacular adhesion or traction (VMA/VMT), epiretinal membrane (ERM), and irregularities in the external limiting membrane (ELM) and ellipsoid zone (EZ). Chronic cyst was defined as an intraretinal cystoid space with thick hyperreflective walls and/or associated ELM/EZ disruption, suggestive of chronic degenerative change. All OCT findings were independently evaluated by two retinal specialists (S.I. and Y.M)., with any discrepancies resolved by consensus.

Outcome measures included changes in central subfield thickness (CST, μm) and best-corrected visual acuity (BCVA, logMAR) at baseline, 1 month, and 3 months. We also recorded the number of injections required to achieve complete resolution of macular fluid, time to resolution (weeks), and the rate of fluid resolution.

Primary and Secondary Outcomes

The primary outcomes were changes in CST and logMAR visual acuity over the 3-month period. Secondary outcomes included the rate of complete fluid resolution, the number of injections and time required to achieve fluid resolution, and associations between baseline OCT biomarkers and either fluid resolution or treatment response.

Statistical Analysis

Changes in CST and visual acuity were analyzed using the Wilcoxon signed-rank test, as appropriate. Associations with continuous outcomes, including changes in CST and BCVA, were analyzed using the Mann–Whitney *U*-test. Correlation between changes in BCVA and CST was assessed using Spearman's rank correlation coefficient.

Comparisons between treatment-naïve (eyes without prior anti-VEGF injections) and non-naïve eyes, between BRVO and CRVO groups, and between eyes with and without prior vitrectomy were performed using the Mann–Whitney *U*-test.

All statistical analyses were conducted using Python (version 3.11), SciPy (version 1.9.3), and pandas (version 1.5.3). A two-sided p-value <0.05 was considered statistically significant.

Ethical Considerations

This retrospective observational study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board of Yokohama City University Hospital (approval number: F250300004). The study was conducted under a single-center protocol at Yokohama City University, with the International Goodwill Hospital participating as a cooperating institution.

All patient data were anonymized before analysis, and the requirement for written informed consent was waived due to the retrospective nature of the study.The study has been registered with the University Hospital Medical Information Network (UMIN000057639).

Results

Patient Characteristics

This study included 23 eyes from 23 patients treated with intravitreal faricimab for macular edema secondary to RVO. The patients had a median age of 81 years (IQR: 75.5–86.0), with 13 females (56.5%) and 10 males (43.5%). The distribution of RVO types was 17 eyes with BRVO (73.9%) and 6 with CRVO (26.1%).

Table 1 Baseline Characteristics and Treatment Outcomes in Patients with RVO-Associated Macular Edema Treated with Faricimab

Characteristic	Summary
Age (years)	Median 81 [IQR: 75.5–86.0]; Mean: 79.6 (range 68–94)
Gender	Female: 13 eyes (56.5%), Male: 10 eyes (43.5%)
Disease subtype	BRVO: 17 eyes (73.9%), CRVO: 6 eyes (26.1%)
Prior anti-VEGF injections	Median: 9.0 [IQR: 1.5–14.0]; Mean: 8.5 (range 0–24)
Prior anti-VEGF injections, non-naïve eyes (n = 18)	Median: 10.5 (IQR 9–17); Mean: 11.2 (range 1–24)
Interval from last anti-VEGF injection to first faricimab, non-naïve eyes	Median: 31.5 months (IQR 18.0–46.5; range 3–72)
History of photocoagulation (PC)	Yes: 6 eyes (26.1%); 3 BRVO (PC for ischemia), 3 CRVO (PRP) No: 17 eyes (73.9%)
Lens status	Pseudophakic: 16 eyes (69.6%), phakic: 7 eyes (30.4%)
History of vitrectomy	Yes: 4 eyes (17.4%), No: 19 eyes (82.6%)
Number of faricimab injections at induction	Median: 1.0 [IQR: 1.0–1.0]; Mean: 1.4 (range: 1–3)
Macular drying at 3 months	Achieved: 12 eyes (52.2%), Not achieved: 11 eyes (47.8%)
Time to complete resolution of macular edema	Median: 4.0 weeks [IQR: 4.0–4.0]; Mean: 5.6 weeks (range 4–15) Naïve; Median: 4.0 weeks [IQR: 4.0–6.0]; Mean: 6.0weeks (range 4–12) Non-naïve; Median: 4.0 weeks [IQR: 4–4]; Mean: 5.4weeks (range 4–15)

Notes: "Naïve" refers to eyes without prior anti-VEGF treatment; "Non-naïve" refers to eyes previously treated with anti-VEGF agents.
Abbreviations: BRVO, branch retinal vein occlusion; CRVO, central retinal vein occlusion; VEGF, vascular endothelial growth factor; PC, photocoagulation; PRP, panretinal photocoagulation; IQR, interquartile range.

The median number of prior anti-VEGF injections was 9 (IQR: 1.5–14.0), and 5 eyes (21.7%) were treatment-naïve. Among non-naïve eyes (n = 18), the median number of prior anti-VEGF injections was 10.5 (IQR, 9–17; range, 1–24), and the median interval between the last anti-VEGF injection and the first faricimab injection was 31.5 months (IQR, 18.0–46.5; range, 3–72).

At baseline, intraretinal fluid (IRF) was observed in 20 eyes (87.0%) and subretinal fluid (SRF) in 4 eyes (17.4%). Retinal photocoagulation (PC) had been performed in 6 eyes (26.1%); 3 eyes with BRVO underwent focal PC for ischemic areas, and 3 eyes with CRVO underwent panretinal photocoagulation (PRP) for ischemic changes. Sixteen eyes (69.6%) were pseudophakic, seven were phakic (30.4%), and four (17.4%) had a history of vitrectomy, including 2 for vitreous hemorrhage, 1 for intraocular lens scleral fixation, and 1 for epiretinal membrane surgery (Table 1).

Initial Treatment and Fluid Resolution

The median number of faricimab injections over three months was 1 (IQR: 1–1), with 18 eyes (78.3%) receiving a single injection. Among the five eyes that received three injections, three had BRVO and two had CRVO; two were treatment-naïve. Complete resolution of retinal fluid was achieved in 12 eyes (52.2%), while 11 eyes (47.8%) did not. The median time to resolution was 4.0 weeks (IQR: 4.0–4.0) (Table 1). The resolution rate was 80% (4/5) in the treatment-naïve group and 44.4% (8/18) in the pretreated group. Median time to resolution was 4 weeks in both groups, with no significant difference ($p = 0.794$, Mann–Whitney U-test).

When stratified by vitrectomy status, all four vitrectomized eyes received only a single faricimab injection, and one eye (25%) achieved complete resolution at 3 months, whereas non-vitrectomized eyes (n=19) had a median of 1 injection (IQR: 1–2) and 11 eyes (57.9%) achieved complete resolution.

Changes in Visual Acuity (BCVA)

The median BCVA (logMAR) improved significantly from 0.40 (IQR: 0.22–0.52; mean: 0.43) at baseline to 0.22 (IQR: 0.05–0.40; mean: 0.29) at 3 months ($p = 0.0025$, Figure 1a). The median change in BCVA (ΔlogMAR) was 0.12 [IQR: 0.00–0.23]. When using a ≥0.1 logMAR threshold for improvement, 14 eyes (60.9%) improved, 8 (34.8%) remained stable, and 1 (4.3%) worsened. With a ≥0.2 threshold, 6 eyes (26.1%) improved, 16 (69.6%) were stable, and 1 (4.3%) worsened.

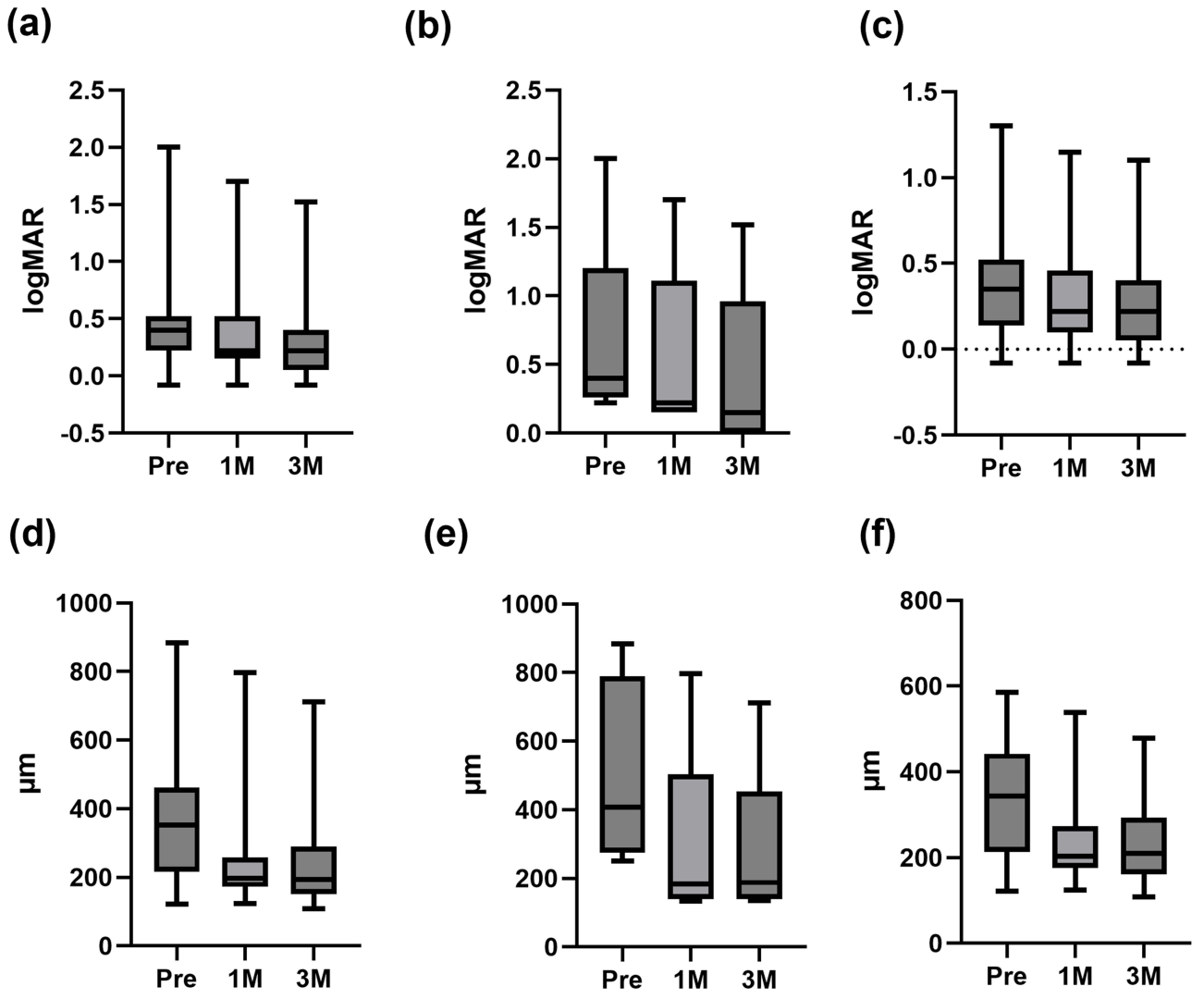

Figure 1 Changes in best-corrected visual acuity (BCVA) and central subfield thickness (CST) following intravitreal faricimab injection. (**a**) BCVA (logMAR) significantly improved at 3 months compared to baseline ($p = 0.0025$). (**b**) In treatment-naïve eyes (n = 5), BCVA showed a trend toward improvement ($p = 0.068$). (**c**) In previously treated eyes (non-naïve, n = 18), BCVA improved significantly ($p = 0.0143$). (**d**) CST significantly decreased from baseline at 3 months ($p < 0.001$). (**e**) CST reduction in treatment-naïve eyes showed a non-significant trend ($p = 0.0625$). (**f**) CST reduction in non-naïve eyes was significant ($p = 0.0016$). Box plots show median, interquartile range (IQR), and individual data points. Statistical comparisons were performed using the Wilcoxon signed-rank test.

There was no significant difference in BCVA improvement between BRVO and CRVO (median ΔlogMAR: 0.13 vs 0.09, $p = 0.673$) (Table 2). In treatment-naïve eyes (n = 5), the median logMAR improved from 0.40 (IQR: 0.30–0.40) to 0.15 (IQR: 0.00–0.40), showing a trend toward improvement but without statistical significance ($p = 0.068$, Figure 1b). In non-naïve eyes (n = 18), the median improved from 0.35 (IQR: 0.17–0.52) to 0.22 (IQR: 0.08–0.38), with significant improvement ($p = 0.0143$, Figure 1c). No significant difference in BCVA change was observed between the two groups ($p = 0.261$) (Table 2).

We additionally stratified outcomes by vitrectomy status. At 3 months, the median improvement in BCVA (ΔlogMAR) was 0.12 [0.00–0.28] in non-vitrectomized eyes (n = 19) and 0.11 [0.06–0.16] in vitrectomized eyes (n = 4) ($p = 0.838$) (Table 2).

Changes in Central Subfield Thickness (CST)

The median CST decreased significantly from 352.0 μm (IQR: 230.0–449.0; mean: 367.5 μm) at baseline to 194.0 μm (IQR: 157.5–289.0; mean: 244.5 μm) at 3 months ($p < 0.001$, Figure 1d). The median CST reduction (ΔCST) was

https://doi.org/10.2147/OPTH.S549896

Table 2 Comparisons of BCVA and CST Changes by RVO Subtype and Treatment Status

	BRVO (n = 17)	**CRVO (n = 6)**	**p-value**
ΔlogMAR, Median [IQR]	0.13 [0.00–0.25]	0.09 [0.02–0.18]	0.673
-ΔCST (μm), Median [IQR]	86.0 [26.0–210.0]	58.0 [17.3–150.5]	0.599
	Naïve (n = 5)	**Non-naïve (n = 18)**	**p-value**
ΔlogMAR, Median [IQR]	0.30 [0.07–0.40]	0.11 [0.00–0.18]	0.261
-ΔCST (μm), Median [IQR]	172.0 [113.0–272.0]	43.5 [15.3–156.5]	0.048
	Non-vitrectomized (n=19)	**Vitrectomized (n=4)**	**p-value**
ΔlogMAR, Median [IQR]	0.12 [0.00–0.28]	0.11 [0.06–0.16]	0.838
-ΔCST (μm), Median [IQR]	86.0 [28.0–195.0]	37.5 [11.2–128.2]	0.598

Notes: ΔlogMAR indicates the improvement in visual acuity over 3 months (baseline minus month 3). A higher value reflects greater visual improvement. –ΔCST indicates the amount of CST reduction over 3 months (baseline minus month 3). A higher value reflects greater anatomical improvement. p-values were calculated using the Mann–Whitney *U*-test.

Abbreviations: BRVO, branch retinal vein occlusion; CRVO, central retinal vein occlusion; CST, central subfield thickness; logMAR, logarithm of the minimum angle of resolution; IQR, interquartile range.

86.0 μm (IQR: 25.0–196.0; mean: 123.0 μm). When categorized by a ±50 μm threshold, 14 eyes (60.9%) improved, 8 (34.8%) were stable, and 1 (4.3%) worsened. Using a ±100 μm threshold, 10 eyes (43.5%) improved and 13 (56.5%) were stable.

There were no significant differences in CST reduction between BRVO and CRVO (median: 74.0 μm vs 86.0 μm, p = 0.599) (Table 2). In the naïve group, CST decreased from a median of 407.0 μm (IQR: 301.0–695.0) to 188.0 μm (IQR: 144.0–194.0), showing a trend but not reaching significance (p = 0.0625) (Figure 1e). In the non-naïve group, CST decreased from 343.0 μm (IQR: 214.8–426.5) to 210.0 μm (IQR: 165.8–289.5), with significant improvement (p = 0.0016) (Figure 1f). The CST reduction was significantly greater in the naïve group (median 172.0 μm vs 43.5 μm, p = 0.048) (Table 2). There was a weak, non-significant positive correlation between BCVA and CST improvement (Spearman ρ = 0.24, p = 0.277).

When stratified by vitrectomy status, the median CST reduction (–ΔCST) was 86.0 [28.0–195.0] μm in non-vitrectomized eyes and 37.5 [11.2–128.2] μm in vitrectomized eyes (p = 0.598). Given the small number of vitrectomized eyes (n=4), these subgroup results should be interpreted with caution (Table 2).

Associations Between Baseline OCT Biomarkers and Treatment Outcomes

Representative OCT images illustrating key biomarkers, including chronic cyst and hyperreflective foci, are shown in Figure 2. No significant associations were found between baseline OCT biomarkers and visual improvement (all p > 0.05, Table 3). However, CST reduction was significantly greater in eyes with chronic cyst than those without (median: 172 μm vs 17.5 μm, p = 0.015). A trend toward greater improvement was observed in eyes with SRF, but not statistically significant (p = 0.081). No other biomarkers were significantly associated with CST changes (all p > 0.05) (Table 4).

Adverse Events and Safety Profile

No adverse events related to faricimab treatment were observed during the study period. There were no reports of serious ocular adverse events, such as intraocular inflammation, elevated intraocular pressure, vitreous opacity, retinal detachment, or vascular occlusion. In addition, no systemic adverse events were observed.

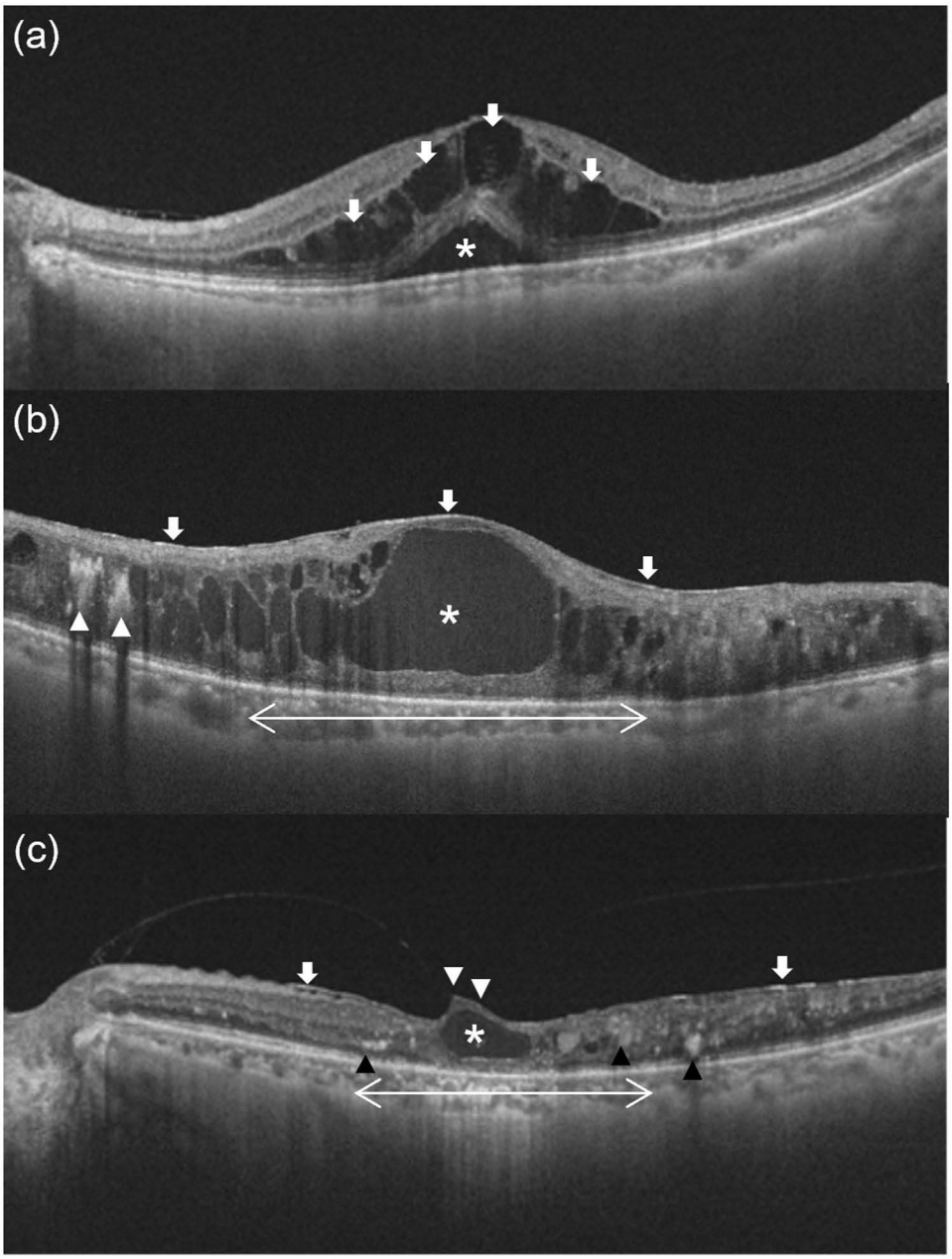

Figure 2 Representative baseline OCT images showing key biomarkers. (**a**) Intraretinal fluid (IRF, arrows) with accompanying subretinal fluid (SRF, asterisk). (**b**) Epiretinal membrane (ERM, arrows), a large chronic cyst (asterisk), hyperreflective foci (HRF, arrowheads), and irregularities in the external limiting membrane (ELM) and ellipsoid zone (EZ, double-headed arrow). (**c**) ERM (white arrows), vitreomacular adhesion/traction (VMA/VMT, white arrowheads), a chronic cyst (asterisk), HRF (black arrows), and irregularities in the ELM and EZ (double-headed arrow).

Discussion

This retrospective study investigated 23 eyes with RVO-ME treated with faricimab in real-world clinical practice, evaluating changes in visual and anatomical outcomes at three months and their associations with baseline OCT biomarkers. Both BCVA and CST significantly improved, with complete resolution of macular edema achieved in 52.2% of eyes overall. Resolution was observed in 80% of treatment-naïve eyes and 44.4% of non-naïve eyes. CST reduction was significantly greater in the naïve group. The presence of chronic cyst was significantly associated with CST improvement.

Table 3 Associations Between Baseline OCT Biomarkers and Visual Improvement

Biomarker	n (Absent)	n (Present)	ΔlogMAR, Median [IQR] (Absent)	ΔlogMAR, Median [IQR] (Present)	p-value
SRF	19	4	0.10 [0.00–0.23]	0.14 [0.12–0.19]	0.625
IRF	3	20	0.12 [0.06–0.16]	0.12 [0.00–0.26]	0.89
Chronic cyst	8	15	0.09 [0.00–0.21]	0.13 [0.04–0.24]	0.795
DRILs	6	17	0.09 [0.02–0.16]	0.13 [0.00–0.25]	0.573
HRF	15	8	0.13 [0.00–0.23]	0.11 [0.05–0.26]	0.746
VMA/VMT	21	2	0.12 [0.00–0.20]	0.2 [0.15–0.25]	0.546
ERM	15	8	0.17 [0.08–0.28]	0.05 [0.00–0.11]	0.127
ELM Abnormal	17	6	0.13 [0.07–0.25]	0.05 [0.00–0.16]	0.46
EZ Abnormal	15	8	0.12 [0.04–0.23]	0.14 [0.00–0.21]	0.922

Notes: ΔlogMAR indicates the amount of improvement in best-corrected visual acuity (BCVA) over 3 months, calculated as baseline logMAR minus final logMAR; positive values indicate improvement. p-values were calculated using the Mann–Whitney *U*-test.
Abbreviations: SRF, subretinal fluid; IRF, intraretinal fluid; DRILs, disorganization of the retinal inner layers; HRF, hyperreflective foci; VMA, vitreomacular adhesion; VMT, vitreomacular traction; ERM, epiretinal membrane; ELM, external limiting membrane; EZ, ellipsoid zone.

Table 4 Associations Between Baseline OCT Biomarkers and Changes in Central Subfield Thickness

Biomarker	n (Absent)	n (Present)	-ΔCST(μm), Median [IQR] (Absent)	-ΔCST(μm), Median [IQR] (Present)	p-value
SRF	19	4	57.0 [17.5–176.0]	217.5 [95.0–372.0]	0.081
IRF	3	20	113.0 [63.0–146.5]	74.0 [25.0–225.5]	0.964
Chronic cyst	8	15	17.5 [5.5–69.3]	172.0 [46.0–282.0]	0.015
DRILs	6	17	28.0 [23.0–87.0]	86.0 [30.0–272.0]	0.234
HRF	15	8	62.0 [26.0–282.0]	96.0 [20.5–174.0]	0.651
VMA/VMT	21	2	62.0 [22.0–180.0]	293.5 [189.8–397.3]	0.23
ERM	15	8	62.0 [9.5–176.0]	99.5 [50.3–225.5]	0.272
ELM Abnormal	17	6	62.0 [22.0–272.0]	86.0 [41.0–106.3]	0.7
EZ Abnormal	15	8	57.0 [17.5–226.0]	99.5 [71.0–181.5]	0.722

Notes: -ΔCST indicates the amount of reduction in central subfield thickness (CST) from baseline to 3 months; positive values indicate a decrease in CST. p-values were calculated using the Mann–Whitney *U*-test.
Abbreviations: SRF, subretinal fluid; IRF, intraretinal fluid; DRILs, disorganization of the retinal inner layers; HRF, hyperreflective foci; VMA, vitreomacular adhesion; VMT, vitreomacular traction; ERM, epiretinal membrane; ELM, external limiting membrane; EZ, ellipsoid zone.

This study demonstrated three key findings. First, a single intravitreal injection of faricimab led to improvements in both visual acuity and macular thickness at three months. Next, eyes with chronic cyst showed greater anatomical improvement. Finally, no serious adverse events were observed, supporting the short-term safety of faricimab in real-world clinical settings.

The median BCVA improved from 0.40 to 0.22 ($p = 0.0025$), indicating a clinically meaningful change. Although this is smaller than the mean improvement reported in the BALATON/COMINO trials (approximately −0.34 logMAR),[8] those trials included six loading doses in treatment-naïve patients, whereas most cases in this study were previously treated and received a single injection. Among naïve cases in this study, the mean improvement reached −0.25 logMAR, showing a treatment response reasonably comparable to that in clinical trials. CST also significantly decreased, from a median of 352 μm to 194 μm ($p < 0.001$). Although the magnitude of reduction was smaller than that in the BALATON/COMINO trials (311.4/461.6 μm),[8] this may be due to milder baseline CST, prior treatments in many cases, and the predominance of single-injection regimens. In the naïve group, the mean reduction was 232.8 μm (from 507.2 μm to 274.4 μm), indicating a treatment response reasonably comparable to that in clinical trials. It should be noted that our study was designed as a short-term observational analysis, and therefore direct comparison with large randomized protocols such as BALATON and COMINO, which included loading regimens and extended follow-up, is limited. Nevertheless, our findings provide exploratory real-world evidence suggesting that even a single injection may

yield meaningful short-term anatomical and functional benefits, suggesting the need for larger, longer-term studies to validate these observations.

In non-naïve cases, the improvements in BCVA and CST were consistent with findings reported previously.[11] They showed improvements from 0.20 to 0.00 in logMAR and from 325 μm to 280 μm in CST after four loading injections. In contrast, our study observed significant improvements from 0.35 to 0.22 ($p = 0.0143$) in logMAR and from 343 μm to 210 μm ($p = 0.0016$) in CST after only a single injection, suggesting that even limited dosing may provide short-term benefit in real-world settings. The relatively high rate of edema resolution after approximately a single injection (52.2%) also has potential clinical and economic implications. In real-world practice, reducing the number of injections may lower treatment burden for both patients and physicians, decrease the risk of procedure-related complications, and alleviate financial constraints associated with repeated anti-VEGF therapy. These aspects suggest that faricimab may provide meaningful advantages in terms of cost-effectiveness and patient quality of life if such outcomes are sustained in larger, longer-term studies.

Previous studies have shown that ranibizumab administered using a 1+PRN (pro re nata) regimen is effective for RVO,[16–18] and that the number of injections during the induction phase may have a limited impact on outcomes. Consistently, the present study also found that a single faricimab injection often led to functional and anatomical improvements at three months, supporting the potential usefulness of a 1+PRN regimen with faricimab.

Although visual and CST changes appeared similar between non-vitrectomized and vitrectomized eyes, only 25% of vitrectomized eyes achieved complete drying at 3 months, and all vitrectomized eyes in our cohort had received only a single injection. Considering the accelerated intravitreal clearance after vitrectomy,[19] these eyes may benefit from an induction phase or shorter dosing intervals.

No significant association was observed between baseline OCT biomarkers and visual improvement, consistent with findings from a post hoc analysis of the multicenter prospective SHORE trial for ranibizumab.[20] HRF have been reported as poor prognostic indicators for anti-VEGF treatment in RVO, particularly those in the outer plexiform layer.[21] Johari et al reported that HRF, DRILs, and ELM disruption were associated with poor response to bevacizumab in RVO-ME.[22] However, in the present study, the presence of HRF, DRILs, or ELM disruption was not significantly associated with changes in BCVA or CST, suggesting that faricimab may exert therapeutic effects even in cases with biomarkers linked to bevacizumab resistance.

The association between chronic cyst and CST improvement was also noteworthy. However, their presence did not correlate with BCVA improvement, suggesting a potential dissociation between anatomical and functional responses. This discrepancy has been noted in the SCORE study, which reported only a moderate correlation between central retinal thickness (CRT) and visual acuity.[23] Previous reports on bevacizumab for RVO-ME have also demonstrated inconsistent associations between intraretinal cystoid space (ICS) and visual prognosis.[24] In addition, Yiu et al reported that the presence of ICS ≥50 μm at baseline was not significantly associated with BCVA improvement.[20] Although our study did not assess cyst size, our finding that cystoid presence did not correlate with visual improvement aligns partially with these previous reports. Notably, eyes with chronic cyst showed significant CST reduction, suggesting that the cysts may represent reversible pathology rather than chronic damage, or that faricimab may have effectively resolved these changes. Further studies are warranted to clarify the morphological characteristics and drug responsiveness of cystoid changes.

Although CST reduction was significant, the improvement in BCVA did not fully align with the anatomical changes. This dissociation may be explained by unmeasured macular ischemia or chronic structural damage, as well as photoreceptor integrity. In our analysis, disruptions of the ELM and EZ were not significantly associated with BCVA outcomes, but such factors may still have attenuated the structure–function correlation in this short-term study.

There have been reports of serious adverse events associated with faricimab, including intraocular inflammation and vascular occlusion. Analyses using the FAERS database have suggested new safety signals such as blindness, retinal hemorrhage, retinal vasculitis, and cerebral infarction.[14,15] However, no serious adverse events were observed during the follow-up period in the present study, confirming the short-term safety of faricimab in this clinical setting.

Limitations

This was a single-center, retrospective observational study with a small sample size (n = 23), limiting the generalizability of the findings. In particular, subgroup analyses may lack statistical power due to the limited number of cases in each category (naïve vs non-naïve, BRVO vs CRVO, with vs without prior vitrectomy). Although multiple OCT biomarkers were evaluated, the small sample size may have prevented detection of clinically meaningful associations between biomarkers and treatment outcomes. Moreover, the classification of chronic cyst may involve some degree of subjectivity, particularly in borderline cases. In addition, the number of variables relative to the limited sample size makes these analyses exploratory, and the results should be interpreted with caution. Furthermore, most patients received only a single injection during the 3-month observation period, reflecting the short-term design of the study, and therefore long-term efficacy and durability of repeated dosing could not be assessed. Future multicenter, prospective studies with larger sample sizes and longer follow-up periods will be necessary to validate and expand upon our findings.

Conclusion

This study suggests that intravitreal faricimab is an effective and safe option for RVO-associated macular edema in real-world practice. In many cases, edema resolved after a single initial injection, potentially reducing treatment burden. Significant CST reduction was observed, particularly in eyes with chronic cyst. No serious adverse events were detected over 3 months, supporting short-term safety. However, these findings are based on a short-term, single-center cohort; larger, multicenter prospective studies with longer follow-up are warranted to validate these results and assess durability.

Acknowledgments

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author Contributions

Soichiro Inokuchi and Yuki Mizuki contributed equally and are co-first authors. 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, or in all these areas; 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.

Disclosure

The authors declare that they have no conflicts of interest related to this work.

References

1. Romano F, Lamanna F, Gabrielle PH, et al. Update on retinal vein occlusion. *Asia Pac J Ophthalmol*. 2023;12(2):196–210. doi:10.1097/APO.0000000000000598
2. Scott IU, Campochiaro PA, Newman NJ, Biousse V. Retinal vascular occlusions. *Lancet*. 2020;396(10266):1927–1940. doi:10.1016/S0140-6736(20)31559-2
3. Ip M, Hendrick A. Retinal vein occlusion review. *Asia Pac J Ophthalmol*. 2018;7(1):40–45. doi:10.22608/APO.2017442
4. Song P, Xu Y, Zha M, Zhang Y, Rudan I. Global epidemiology of retinal vein occlusion: a systematic review and meta-analysis of prevalence, incidence, and risk factors. *J Glob Health*. 2019;9(1):010427. doi:10.7189/jogh.09.010427
5. Rogers SL, McIntosh RL, Lim L, et al. Natural history of branch retinal vein occlusion: an evidence-based systematic review. *Ophthalmology*. 2010;117(6):1094–101.e5.
6. Campochiaro PA, Sophie R, Pearlman J, et al. Long-term outcomes in patients with retinal vein occlusion treated with ranibizumab: the RETAIN study. *Ophthalmology*. 2014;121(1):209–219. doi:10.1016/j.ophtha.2013.08.038
7. Nichani PAH, Popovic MM, Mihalache A, et al. Efficacy and safety of intravitreal faricimab in neovascular age-related macular degeneration, diabetic macular edema, and retinal vein occlusion: a meta-analysis. *Ophthalmologica*. 2024;247(5–6):355–372. doi:10.1159/000541662
8. Tadayoni R, Paris LP, Danzig CJ, et al. Efficacy and safety of faricimab for macular edema due to retinal vein occlusion: 24-week results from the BALATON and COMINO Trials. *Ophthalmology*. 2024;131(8):950–960. doi:10.1016/j.ophtha.2024.01.029
9. Danzig CJ, Dinah C, Ghanchi F, et al. Faricimab treat-and-extend dosing for macular edema due to retinal vein occlusion: 72-week results from the BALATON and COMINO Trials. *Ophthalmol Retina*. 2025;9:848–859. doi:10.1016/j.oret.2025.03.005
10. Chaudhary V, Mar F, Amador MJ, et al. Emerging clinical evidence of a dual role for Ang-2 and VEGF-A blockade with faricimab in retinal diseases. *Graefes Arch Clin Exp Ophthalmol*. 2024;263:1239–1247. doi:10.1007/s00417-024-06695-4

11. Hafner M, Herold TR, Kufner A, et al. Switching to faricimab in therapy-resistant macular edema due to retinal vein occlusion: initial real-world efficacy outcomes. *J Clin Med*. 2025;14(7):2454. doi:10.3390/jcm14072454
12. Giancipoli E, Guglielmi A, Bux AV, et al. Real-world outcomes of a loading phase with intravitreal faricimab in neovascular age-related macular degeneration (n-AMD) and Diabetic Macular Edema (DME). *Ophthalmol Ther*. 2024;13(8):2163–2184. doi:10.1007/s40123-024-00980-5
13. Chen X, Wang X, Li X. Intra-ocular inflammation and occlusive retinal vasculitis following intravitreal injections of faricimab: a case report. *Ocul Immunol Inflamm*. 2024;32(10):2544–2547. doi:10.1080/09273948.2024.2361834
14. Han F, Li X, Tao T, Wang J. A pharmacovigilance study on the safety of faricimab in real-world scenario using FDA adverse event reporting system database. *Expert Opin Drug Saf*. 2025;1–8.
15. He CZ, Qiu Q, Lu SJ, Xue FL, Liu JQ, He Y. Adverse event reporting of faricimab: a disproportionality analysis of FDA adverse event reporting system (FAERS) database. *Front Pharmacol*. 2025;16:1521358. doi:10.3389/fphar.2025.1521358
16. Sakanishi Y, Lee A, Usui-Ouchi A, Ito R, Ebihara N. Twelve-month outcomes in patients with retinal vein occlusion treated with low-frequency intravitreal ranibizumab. *Clin Ophthalmol*. 2016;10:1161–1165. doi:10.2147/OPTH.S107594
17. Miwa Y, Muraoka Y, Osaka R, et al. Ranibizumab for macular edema after branch retinal vein occlusion: one initial injection versus three monthly injections. *Retina*. 2017;37(4):702–709. doi:10.1097/IAE.0000000000001224
18. Bayat AH, Çakır A, Ş g Ö, Bölükbaşı S, Erden B, Elçioğlu MN. Comparison of one and three initial monthly intravitreal ranibizumab injection in patients with macular edema secondary to branch retinal vein occlusion. *Int J Ophthalmol*. 2018;11(9):1534–1538. doi:10.18240/ijo.2018.09.17
19. Kakinoki M, Sawada O, Sawada T, Saishin Y, Kawamura H, Ohji M. Effect of vitrectomy on aqueous VEGF concentration and pharmacokinetics of bevacizumab in macaque monkeys. *Invest Ophthalmol Vis Sci*. 2012;53(9):5877–5880. doi:10.1167/iovs.12-10164
20. Yiu G, Welch RJ, Wang Y, Wang Z, Wang PW, Haskova Z. Spectral-domain OCT predictors of visual outcomes after ranibizumab treatment for macular edema resulting from retinal vein occlusion. *Ophthalmol Retina*. 2020;4(1):67–76. doi:10.1016/j.oret.2019.08.009
21. Mo B, Zhou HY, Jiao X, Zhang F. Evaluation of hyperreflective foci as a prognostic factor of visual outcome in retinal vein occlusion. *Int J Ophthalmol*. 2017;10(4):605–612. doi:10.18240/ijo.2017.04.17
22. Johari M, Attar A, Eghtedari D, Razavizadegan SA. Characteristics of macular edema associated with retinal vein occlusion showing poor anatomic response to three loading anti-vascular endothelial growth factor injections: an optical coherence tomography analysis. *BMC Ophthalmol*. 2024;24(1):30. doi:10.1186/s12886-024-03298-9
23. Scott IU, VanVeldhuisen PC, Oden NL, et al. SCORE Study report 1: baseline associations between central retinal thickness and visual acuity in patients with retinal vein occlusion. *Ophthalmology*. 2009;116(3):504–512. doi:10.1016/j.ophtha.2008.10.017
24. Hoeh AE, Ruppenstein M, Ach T, Dithmar S. OCT patterns of macular edema and response to bevacizumab therapy in retinal vein occlusion. *Graefes Arch Clin Exp Ophthalmol*. 2010;248(11):1567–1572. doi:10.1007/s00417-010-1419-5