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## Real-World Efficacy of Faricimab in Patients with Treatment-Resistant Neovascular Age-Related Macular Degeneration: Outcomes at Six Months

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**Purpose:** To evaluate the efficacy of switching to faricimab (VabysmoTM; Roche/Genentech) treatment for patients with neovascular age-related macular degeneration (nAMD) that was resistant to other anti-vascular endothelial growth factor (VEGF) therapies by assessing outcomes after 6 months.

**Methods:** We conducted a retrospective chart review of 102 nAMD patients who were switched to faricimab due to suboptimal responses to prior anti-VEGF treatments. Patients who showed persistent fluid on optical coherence tomography despite prior anti-VEGF injections every 4 to 8 weeks were treated with faricimab. We assessed changes in best-corrected visual acuity (BCVA), central subfield thickness (CST), subfoveal choroidal thickness, maximum pigment epithelial detachment (PED) height, and fluid status at baseline and 1, 3, and 6 months after switching to faricimab. Treatment intervals before and after switching were compared.

**Results:** Six months after switching to faricimab, the mean BCVA improved (0.50 ± 0.12 logMAR to 0.45 ± 0.10 logMAR, $p = 0.030$), while the mean CST decreased from 353.3 ± 40.5 μm at baseline to 311.4 ± 35.4 μm ($p = 0.012$). The mean choroidal thickness did not significantly decrease after switching. The mean PED height decreased from 309.1 ± 32.1 μm at baseline to 279.1 ± 30.8 μm at 6 months ($p = 0.040$). The mean treatment interval extended from 5.7 ± 1.4 to 10.4 ± 1.8 weeks after switching ($p = 0.001$). Additionally, dry macula was achieved in 43.1% of patients, while 76.5% were classified as good responders, 6.5% as partial responders, and 17% reverted to other anti-VEGF treatments due to non-response.

**Conclusions:** Switching nAMD patients to faricimab for 6 months produced substantial improvements in visual acuity and anatomical outcomes, together with extended treatment intervals, reducing the injection burden. Faricimab could be an effective treatment option for nAMD, particularly for patients with inadequate responses to previous therapies.

**Keywords:** Age-related macular degeneration; Anti-VEGF; Faricimab; Intravitreal Injections

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## Introduction

Neovascular age-related macular degeneration (nAMD) is one of the leading causes of severe vision loss among older adults [1]. As populations continue to age, the prevalence of nAMD is expected to rise, placing an increasing burden on healthcare systems and significantly impacting patients' quality of life. Standard treatments for nAMD involve intravitreal injections of anti-vascular endothelial growth factor (VEGF) agents, which have been shown to reduce disease progression and stabilize vision [2]. While most patients respond well to standard anti-VEGF treatments, some patients exhibit incomplete responses, with retention or reaccumulation of retinal fluid, highlighting the need for more effective therapeutic options.

Faricimab (Vabysmo$^{TM}$; Roche/Genentech), a recently developed bispecific antibody, offers a dual mechanism of action by targeting both VEGF-A and angiopoietin-2 (Ang-2), two key drivers of neovascularization and vascular instability in nAMD [3]. By binding VEGF-A and Ang-2 and inhibiting both downstream signaling pathways, faricimab enhances vascular stability and reduces inflammation in the retina, potentially improving fluid control and extending the treatment interval compared to other anti-VEGF agents used for nAMD. Recent clinical trials, such as the TENAYA and LUCERNE studies, have shown promising outcomes for faricimab in terms of efficacy, safety, and durability of response in patients with treatment-naive nAMD [4]. However, data are lacking regarding the clinical outcomes of patients previously treated with other anti-VEGF therapies who have been switched to faricimab due to suboptimal responses or treatment burden. The real-world efficacy and safety of switching treatment-resistant nAMD patients to faricimab must be verified to optimize treatment strategies and identify unmet needs in nAMD management. Therefore, this study aims to evaluate the visual and anatomical outcomes in nAMD patients who were switched from other anti-VEGF agents to faricimab in a real-world clinical setting.

## Materials and Methods

This study was conducted in accordance with the Declaration of Helsinki and received approval from the Institutional Review Board of Yeungnam University Hospital (IRB no. 2024-10-001), which waived the requirement for informed consent. We performed a retrospective chart review of consecutive patients older than 50 years who were diagnosed with nAMD and were switched to faricimab after showing incomplete responses to prior anti-VEGF treatments. The study was conducted at a single center and covered a follow-up period of 6 months, during which clinical and anatomical outcomes were assessed. Faricimab was administered to patients who showed persistent fluid on optical coherence tomography (OCT) despite receiving prior anti-VEGF injections at 4−8 week intervals. All patients had undergone at least 6 months of prior treatment before switching. The exclusion criteria included a history of other significant retinal diseases, such as diabetic retinopathy, uveitis, epiretinal membrane, retinal detachment, or refractive error exceeding ± 6 diopters, and a history of vitreoretinal surgery. Additionally, patients with poor imaging quality on OCT scans, which could interfere with accurate assessment of retinal parameters, were excluded.

We evaluated changes in BCVA, CST, SFCT, and maximum PED height. Retinal fluid status was also evaluated. We defined PED as retinal pigment epithelium (RPE) elevation of greater than 350 μm, while the maximum PED height was defined as the greatest distance between the inner surface of Bruch's membrane and the outer surface of the RPE. All patients underwent OCT (Spectralis OCT; Heidelberg Engineering) imaging at baseline and 1, 3, and 6 months after switching to faricimab treatment to assess these parameters. The patients were catergorized as either good responders (complete resolution of retinal fluid or a reduction of >75% in CST), partial responders (0%-75% reduction of CST) or non-responders (increased CST) [5].

To assess the significance of differences in the recorded values before and after switching treatments, a paired t-test and Wilcoxon signed-rank test were employed. The paired t-test was applied to data that followed a normal distribution, while the Wilcoxon signed-rank test was used for non-normally distributed data. Changes in BCVA, CST, SFCT, and maximum PED height at various time points were analyzed using repeated-measures analysis of variance. All statistical analyses were performed using SPSS$^®$ V23 (IBM Corp.), with a $p$-value less than 0.05 considered a statistically significant difference.

## Results

### Demographics and clinical characteristics

A total of 102 eyes of 102 patients were included in this study, with a mean age of 72.4 ± 8.5 years. The cohort comprised 55 males and 47 females. Of these, 37 (36.3%) were classified as typical nAMD, 59 (57.8%) as polypoidal choroidal vasculopathy, and 6 (5.9%) as retinal angiomatous proliferation. Regarding prior anti-VEGF treatments, 60 patients (58%) had received aflibercept, 17 patients (17%) had received bevacizumab and aflibercept alternatively, 21 patients (21%) had been treated with ranibizumab, and 4 patients (4%) had been treated with a ranibizumab biosimilar. The average time from diagnosis to the first faricimab injection was 42.7 ± 11.6 months, with patients having received an average of 16.3 ± 4.2 injections prior to switching to faricimab. The mean injection interval before switching was 5.7 ± 1.4 weeks. At baseline, the mean best-corrected visual acuity (BCVA) was 0.50 ± 0.12 logMAR, and the mean CST was 353.3 ± 40.5 μm. The SFCT was measured at 178.7 ± 20.3 μm, and the maximum PED height was 309.1 ± 32.1 μm (Table 1).

**Table 1.** Demographics and clinical characteristics when switching to faricimab

| Characteristic | Value (n = 102) |
|---|---|
| Age (years) | 72.4 ± 8.5 |
| Gender (male/female) | 55/47 |
| Type of age-related macular degeneration | |
|   Typical neovascular age-related macular degeneration | 37 (36) |
|   Polypoidal choroidal vasculopathy | 59 (58) |
|   Retinal angiomatous proliferation | 6 (6) |
| Prior anti-VEGF treatment | |
|   Aflibercept | 60 (58) |
|   Bevacizumab/aflibercept alternative | 17 (17) |
|   Ranibizumab | 21 (21) |
|   Ranibizumab biosimilar | 4 (4) |
| Time from diagnosis to first faricimab (months) | 42.7 ± 11.6 |
| Injection number before switching | 16.3 ± 4.2 |
| Injection interval before switching (weeks) | 5.7 ± 1.4 |
| Best-corrected visual acuity (logMAR) | 0.50 ± 0.12 |
| Central subfield thickness (μm) | 353.3 ± 40.5 |
| Subfoveal choroidal thickness (μm) | 178.7 ± 20.3 |
| Maximum pigment epithelial detachment height (μm) | 309.1 ± 32.1 |

Values are presented as mean ± standard deviation, number only, or number (%).
VEGF = vascular endothelial growth factor.

### Clinical outcomes of faricimab treatment

Following the first faricimab injection, the mean follow-up period was 27.8 ± 2.1 weeks. During this period, an average of 2.7 faricimab injections were administered at 10.4 ± 1.8 week intervals. By month 6, a dry macula was observed in 44 of 102 eyes (43.1%). Of the 102 total patients, 76.5% were categorized as good responders, 6.5% as partial responders, and 17% were switched to other anti-VEGF therapies due to a lack of response. Six months after switching to faricimab, the mean BCVA had improved significantly (0.50 ± 0.12 logMAR to 0.45 ± 0.10 logMAR; $p = 0.030$), and the mean CST (353.3 ± 40.5 μm to 311.4 ± 35.4 μm; $p = 0.012$) and mean maximum PED height (309.1 ± 32.1 μm to 279.1 ± 30.8 μm; $p = 0.040$) were both significantly reduced (Table 2). The changes in visual and anatomical outcomes at 1, 3, and 6 months are shown in Fig. 1. The improvement in BCVA was maintained for at least 6 months, with values of 0.47 ± 0.11 ($p < 0.05$) recorded at 3 months and 0.45 ± 0.10 ($p < 0.05$) at 6 months. The CST decreased significantly from 353.3 ± 40.5 μm before the initial treatment to 330.5 ± 37.0 μm at 1 month ($p < 0.01$) and was maintained at 320.0 ± 35.6 μm ($p < 0.01$) at 3 months and 311.4 ± 35.4 μm ($p < 0.05$) at 6 months. The SFCT did not significantly decrease over the 6 months of faricimab treatment. The maximum PED height decreased sig-

**Table 2.** Clinical outcomes before and 6 months after switching to faricimab

| Variables | Baseline | 1 Month | 3 Months | 6 Months | p-value |
|---|---|---|---|---|---|
| Best-corrected visual acuity (logMAR) | 0.50 ± 0.12 | 0.48 ± 0.11 | 0.47 ± 0.11 | 0.45 ± 0.10 | 0.030 |
| Central subfield thickness (μm) | 353.3 ± 40.5 | 330.5 ± 37.0 | 320.0 ± 35.6 | 311.4 ± 35.4 | 0.012 |
| Subfoveal choroidal thickness (μm) | 178.7 ± 20.3 | 176.5 ± 19.8 | 175.0 ± 19.5 | 172.8 ± 19.4 | 0.064 |
| Maximum pigment epithelial detachment height (μm) | 309.1 ± 32.1 | 295.0 ± 31.0 | 285.2 ± 29.5 | 279.1 ± 30.8 | 0.040 |

Values are presented as mean ± standard deviation.

nificantly from 309.1 ± 32.1 μm before the initial treatment to 295.4 ± 31.0 μm at 1 month ($p < 0.05$) and was maintained at 285.2 ± 29.5 μm ($p < 0.05$) at 3 months and 279.1 ± 30.8 μm ($p < 0.05$) at 6 months.

The proportions of SRF and IRF after 6 months were 40.2% (41 eyes) and 24.6% (25 eyes), respectively, while the
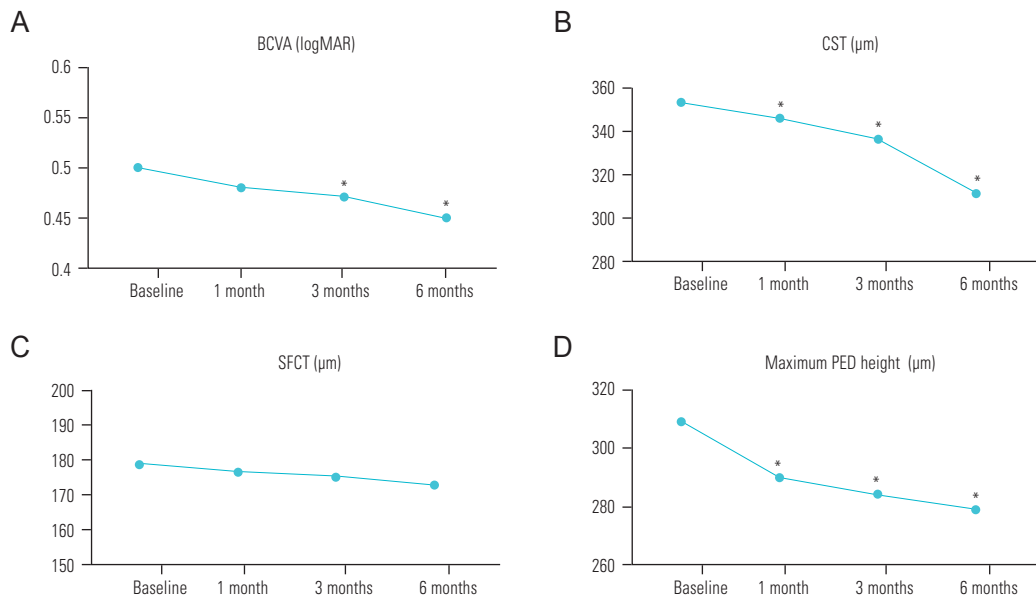


**Figure 1.** Visual and anatomic outcomes in treatment-resistant nAMD patients before and 6 months after switching to faricimab. (A) There was significant improvement in the best-corrected visual acuity (BCVA) over 6 months of faricimab treatment. (B) The mean central subfield thickness (CST) was significantly reduced 1, 3, and 6 months after switching to faricimab. Subfoveal choroidal thickness (SFCT) (C) was not significantly reduced after switching to faricimab over the 6 months of treatment. (D) There was significant change in the maximum pigment epithelial detachment (PED) height at 1, 3, and 6 months after switching to faricimab. Asterisks indicate significant difference ($p < 0.05$). nAMD = neovascular age-related macular degeneration.
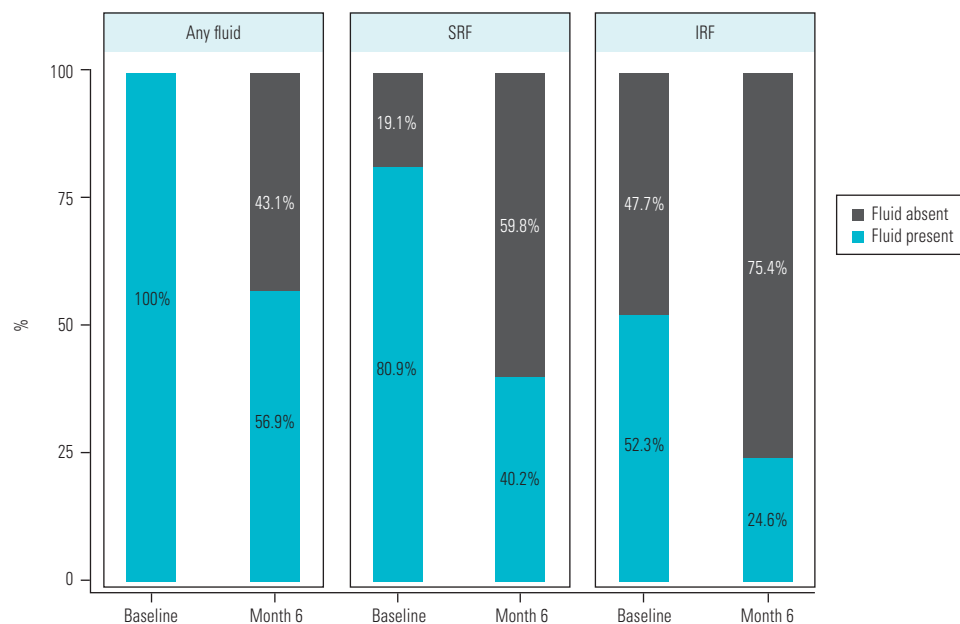


**Figure 2.** Distribution of retinal fluid status in treatment-resistant nAMD patients at baseline and 6 months after switching to faricimab. nAMD = neovascular age-related macular degeneration; SRF = subretinal fluid; IRF = intraretinal fluid.

proportion of eyes with concurrent SRF and IRF was 8.8% (9 eyes; Fig. 2). There were no occurrences of RPE tears, endophthalmitis, or intraocular inflammation.

## Discussion

This study evaluated the efficacy of switching nAMD patients with incomplete responses to prior anti-VEGF therapies to firicimab. The results demonstrated significant improvement in BCVA and reductions in CST and maximum PED height over 6 months of faricimab treatment in real-world practice.

The significant extension of treatment intervals following the switch to faricimab, with some patients achieving intervals of 12 weeks, is one of the key findings of this study. The ability to maintain disease control with fewer injections is particularly beneficial for patients with nAMD, as it reduces the burden of frequent clinic visits and intravitreal injections, improving overall quality of life. This finding is consistent with the results of another real-world study of refractory AMD patients, in which 40% of patients experienced prolonged fluid-free intervals after switching to faricimab in a treat and extend regimen comprising 4 monthly injections [6].

In this study, improvements in both BCVA and CST were measured 6 months after switching to faricimab. Several previous studies addressing switching to faricimab in patients with AMD reported favorable anatomical outcomes, though visual improvements may vary across the enrolled patients [7-9]. Cancian et al. reported that faricimab improved anatomical outcomes, such as CST and macular volume, compared to previous anti-VEGF therapies [6]. However, while anatomical outcomes, including reductions in retinal fluid and CST, were consistently favorable, visual acuity was unfavorable in some studies [10-12]. For example, one study showed that, although 89.1% of eyes exhibited anatomical improvement, visual gains were limited [10]. These findings suggest that, while faricimab may control disease progression effectively, functional improvements in vision may be influenced by other patient-specific factors, such as disease chronicity or prior treatment history.

Despite the availability of multiple anti-VEGF agents, achieving satisfactory treatment outcomes for PED remains challenging [13-15]. The reduction in measured PED in our nAMD patients after switching to faricimab is an interesting outcome, as PED is often associated with persistent disease activity and can be resistant to standard anti-VEGF treatments [15-17]. Previous studies have indicated that factors such as PED type, baseline PED height, and the specific anti-VEGF agent used can influence the likelihood of PED resolution, suggesting that variations in resolution rates may be attributed to the underlying pathogenesis of PED and the binding affinity of different anti-VEGF agents [18]. The binding affinity of faricimab for VEGF is reportedly comparable to that of ranibizumab, while its molar concentration is approximately four times greater than that of ranibizumab [19]. In the current study, the maximum PED height decreased significantly over the 6-month treatment period, indicating that faricimab is effective in reducing PED size. Although reductions in PED are not always associated with corresponding improvements in nvisual acuity, this anatomical improvement is an important indicator of disease control, and future studies are needed to explore the long-term visual benefits associated with sustained PED reduction [18,20].

A dry macula is a key goal in the management of refractory nAMD, as it is associated with better visual outcomes and reduced disease activity. At 6 months, a dry macula was present in 43.1% of eyes in our study, indicating that faricimab effectively resolved retinal fluid in a significant portion of patients. The ability of the bispecific faricimab monoclonal antibody to bind both VEGF-A and Ang-2 may contribute to resolution of retinal fluid by both enhancing vascular stability and reducing leakage.

This study has several limitations, the most important of which was the retrospective design. Additionally, the relatively small sample size limits the generalizability of the findings. A larger cohort with longer follow-up would provide more robust data on the long-term efficacy and safety of switching to faricimab. Another limitation of this study is the lack of analyses based on nAMD subtypes or type of previous anti-VEGF treatment, the assessment of which should also be considered in future studies to identify any sub-group-specific effects.

In conclusion, switching to faricimab can result in significant visual and anatomical improvements in nAMD patients who are refractory to other anti-VEGF treatments. Faricimab also provides effective retinal fluid control and extends the treatment interval, making it a promising option for managing nAMD in the long term.

## Conflicts of Interest

Min Sagong reported being a consultant for and receiving grant support from Samsung Bioepis, Novartis, Bayer, Roche, Allergan/Abbvie, Celltrion, Alteogen, Alcon and Curacle, and receiving lecture fee from Novartis, Bayer, Roche, and Allergan/Abbvie. Seung Chul Baek and Areum Jeong declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Author Contribution

Conception (M.S.); Design (M.S); Data acquisition (S.C.B.); Analysis (S.C.B., A.J.); Interpretation (M.S., A.J.); Writing (S.C.B., A.J.); Review (M.S., A.J.); Final approval of the article (All authors)

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