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One-Year Outcomes after Switching to Faricimab in Eyes with Pretreated Neovascular Age-Related Macular Degeneration

A Swiss Retina Research Network Report

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Purpose: To report the efficacy and safety of switching to faricimab in a real-world, Swiss cohort of patients with pretreated neovascular age-related macular degeneration (nAMD).

Design: Retrospective, multicenter, longitudinal observational study conducted at 11 centers of the Swiss Retina Research Network.

Subjects: We included 353 eyes of 325 patients who were switched to intravitreal faricimab after prior anti-VEGF therapy and followed for a minimum of 12 months between May 1, 2022, and October 30, 2024.

Methods: Demographic characteristics, baseline functional and OCT findings, treatment history, and outcomes at 12 months after switch to faricimab were extracted from the patients' electronic case report forms.

Main Outcome Measures: Change in best-corrected visual acuity (BCVA), central subfield thickness (CST), presence of retinal fluid (RF) and pigment epithelial detachment, treatment intervals, and safety signals.

Results: Twelve months after switch, mean BCVA remained unchanged, whereas mean CST decreased from 315.3 to 263.9 μm ($P < 0.01$). Fast drying (absence of RF) after 1 faricimab injection was observed in 134 eyes (38%) and correlated positively with the treatment interval at 12 months ($r(301) = 0.24$; $P < 0.01$). After 12 months, 169 (47.9%) eyes demonstrated the absence of RF compared with 10.2% at switch. Mean treatment interval increased from 5.8 ± 2.5 weeks at switch to 8.3 ± 4.2 weeks at 12 months, and extended treatment intervals (≥12 week) were achieved in 20% of patients. Mild intraocular inflammation was reported in 1.7% of cases.

Conclusions: Switching to faricimab in pretreated nAMD led to sustained anatomic improvements and stabilization of BCVA, with a substantial reduction in RF compared with baseline. Our results suggest the potential benefits of this switching strategy based on real-world data.

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Neovascular age-related macular degeneration (nAMD) is a leading cause of severe visual impairment in the aging population, its prevalence rapidly increasing as the global population ages.[1] Already today, nAMD affects millions worldwide, posing a significant public health challenge.[2] The standard of care for nAMD has since 2 decades been intravitreal injections of anti-VEGF agents, which have revolutionized the management of this condition.[3] However, the treatment burden associated with anti-VEGF therapy remains substantial, both for patients and health care providers.[4] Frequent injections, often required every 4 to 8 weeks, impose a heavy logistical burden, leading to challenges in patient adherence and straining clinic resources.[5]

Despite the efficacy of older anti-VEGF treatments, their durability is limited, and one third of patients do not reach a dry macula.[6] In the last few years, the field has entered an

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era of more durable therapeutic options. Faricimab (Vabysmo, F. Hoffmann-La Roche Ltd), a bispecific antibody targeting both angiopoietin-2 and VEGF-A, represents one of the advances in this regard. By simultaneously inhibiting 2 distinct pathways involved in the pathogenesis of nAMD, faricimab might offer more durable disease control compared with earlier therapies.[7] The pivotal phase III Tenaya and Lucerne trials were designed to assess the efficacy and safety of faricimab in treatment-naive patients with nAMD.[8] These trials demonstrated that faricimab 6 mg, when administered at intervals of up to 16 weeks, maintained visual acuity outcomes that were noninferior to aflibercept 2 mg, with nearly half of the patients being able to extend their treatment intervals beyond 12 weeks.[9] Furthermore, the safety profile of faricimab was comparable to that of aflibercept, with no new safety signals identified over the course of the trials.[9] Although these findings seem to suggest that faricimab reduces the treatment burden for both patients and health care systems, the generalizability of these findings to real-world practice is limited. Tenaya and Lucerne trials employed stringent inclusion criteria, focusing exclusively on treatment-naive patients and excluding those with either very low or very high baseline visual acuity, as well as those with certain comorbidities. Additionally, the trials utilized a capped treatment regimen, which may not fully reflect the flexibility required in routine clinical practice. As a result, although these trials provide critical evidence for faricimab's potential, there remains a need for real-world data to understand how these results translate into broader clinical settings.[10]

Given these limitations, real-world evidence is crucial to evaluate the efficacy, safety, and durability of faricimab in a representative clinical patient population. Several real-world studies have been published to date on faricimab use in patients with nAMD, providing valuable insights into its early performance outside of controlled trial settings.[11] The largest existing real-world case series on faricimab for nAMD predominantly originate from the United States.[12,13] The Truckee study reported positive outcomes in terms of visual acuity and treatment intervals, but it was limited by a short follow-up period of 6 months.[12] Other studies have been constrained by regional differences in health care systems, treatment protocols, and patient demographics, which can impact the generalizability of their findings to other settings.[11] European cohorts on faricimab have generally been more limited in scale,[11] characterized by relatively small sample sizes, single-center cohorts, and relatively short observation periods. This underscores the need for more extensive research in larger European populations with longer follow-up periods to fully assess the benefits and risks of faricimab and other novel compounds in routine clinical practice. To fill this gap, we established a national consortium of Swiss retina centers (Swiss Retina Research Network) from diverse settings, including hospital and private clinic networks.

This first network report aims to provide comprehensive 1-year data from a large Swiss multicentric cohort of pretreated patients with nAMD switched to faricimab, with a view to offer insights into the efficacy and safety of intravitreal faricimab in a real-world setting.

Methods

This was a retrospective, noncomparative, multicenter case series including patients from 11 specialized eye centers in Switzerland (Berner Augenklinik, Bern [C.S., I.B.P., and J.G.G.]; Vista Augenklinik, Binningen [C.P. and K.H.]; Augenarzt-Praxisgemeinschaft Gutblick AG, Pfäffion [M.R.M. and R.S.]; Istituto Neuroscienze cliniche della Svizzera Italiana, Ospedale Regionale di Lugano, Lugano [A.P., G.G., and M.M.]; Kantonsspital St. Gallen [D.A. and A.E.]; Jules-Gonin Eye Hospital, University Hospital Lausanne, Lausanne [C.E., E.C.F.D.O., and J.C.]; University Hospital Basel, Basel [J.F. and N.F.]; Stadtspital Zürich [G.M.S. and T.S.]; University Hospital Zürich, Zürich [M.C. and S.Z.]; Pallas Kliniken, Olten [A.W.]; Swiss Visio Retina Research Center, Lausanne [A.A.]). The study was approved by all involved Ethics Committees, under the lead of the Ethics Committee of the Canton of Berne (registration number 2024-01026) based on the general consent of all included patients to use their coded data for this analysis, which was performed in accordance with the International Council for Harmonisation E6 Good Clinical Practice Guideline, the Declaration of Helsinki in its latest version, and federal laws.

All patients presented an active nAMD (defined as the presence or recurrence of retinal fluid (RF), exudates, or hemorrhage limiting treatment interval extension before switch) under continuous intravitreal anti-VEGF therapy (with ranibizumab, aflibercept 2 mg, bevacizumab, or brolucizumab) after a treat-and-extend protocol. A consecutive series of eyes that had been switched to faricimab since its approval by the Swiss authorities in May 2022 and had a follow-up of at least 12 $\pm$ 1 months by October 2024 were included. The inclusion of both eyes was accepted if they were eligible for this study. The following exclusion criteria were applied: pretreatment with photodynamic therapy or radiotherapy; preexisting structural damage to the macula from any reason without residual functional potential; any active systemic comorbidities possibly interfering with treatment outcomes, namely uncontrolled local or systemic rheumatoid diseases or vasculitis requiring anti-inflammatory or immunomodulatory treatment; any opacifications in the optic axis with relevance for visual function preventing ocular imaging and fundoscopy; any intraocular surgery within 3 months before inclusion except YAG laser capsulotomy; treatment with periocular or intraocular corticosteroids within 6 months before switch to faricimab.

Data were retrospectively collected from the electronic medical records, at the following time points: at the initial diagnosis and initiation of anti-VEGF therapy, after loading (after the first 3 monthly injections); 6 months before switching, at the time of switching to faricimab (baseline), and 3, 6, and 12, months thereafter. In patients switched away from faricimab to another anti-VEGF, data were censored after the last faricimab injection and the reasons for the switch were recorded.

The following data were retrieved: Snellen best-corrected visual acuity (BCVA), intraocular pressure, central subfield

thickness (CST), presence of intraretinal fluid (IRF), subretinal fluid (SRF), or both (RF) within the 6-mm radius of the ETDRS grid on OCT, presence of any pigment epithelium detachment (PED), and maximum PED height on OCT. Pigment epithelium detachment was defined as hyporeflective elevation of the retinal pigment epithelium (RPE) from the Bruch's membrane. Drusen and hyperreflective PED (reflectivity ≥50%) were not categorized as PED. For statistical analysis, BCVA was converted to ETDRS letter scores, where a Snellen BCVA of 1.0 was defined as 85 ETDRS letters.[14] To categorize hand motion and counting fingers, we used the guidelines given by Schulze-Bonsel et al.[15] Furthermore, the total number of injections per eye before switch, the last interval before switching, as well as the injection intervals after switch and number of injections in the first year after switching were recorded.

Primary outcomes included the change in visual acuity and CST and the change in injection intervals from switch to faricimab to the last appointment 1 year (±1 month) thereafter. Secondary outcomes included proportion of eyes with fluid at switch, which dried after 1 single faricimab injection, and proportion of eyes without RF at 12 months; proportion of eyes with persistent (intra- and/or sub-) RF; change in morphologic parameters (presence of IRF and SRF); proportion of eyes remaining under faricimab and being switched to another anti-VEGF drug; documented intraocular and systemic side effects, with special focus on intraocular inflammation. Fast drying was defined as the absence of any RF across the 6-mm ETDRS grid radius on macular OCT after the first intravitreal injection (IVT) of faricimab.

Descriptive statistics, subgroup comparisons, and correlation and regression analyses were applied. Results of regression analyses are presented as follows: r(degrees of freedom) = the r statistic, $P = P$ value. The Shapiro–Wilk test revealed that the data were not normally distributed. Data are presented as mean ± standard deviation, median, and interquartile ranges (IQR, 25%–75%). The Wilcoxon signed-rank test was applied to compare longitudinal data over time and the Friedman test for related samples to compare multiple time points. Safety was evaluated using descriptive summaries of both ocular and nonocular adverse events, including deaths, up to the conclusion of the study. A P value of ≤0.05 was considered statistically significant. All statistical analyses were performed using the SPSS software package V.27 (SPSS, Inc) and R (version 3.2.4; R: A language and environment for statistical computing, R Foundation for Statistical Computing, 2016).

Results

A total of 433 pretreated eyes with nAMD were identified, of which 80 were excluded (Fig 1). As a result, 353 eyes of 325 patients achieving 12 months of follow-up were included. Twenty-eight patients (7.9%) had both eyes treated with faricimab. At switch, the mean age was 79.9 ± 7.9 standard deviation years (range, 58–101 years). The mean number of anti-VEGF injections before switch to faricimab was 33 ± 25 standard deviation (range, 2–136). The mean treatment duration was 3.70 ± 3 years (range, 0.6–15.7 years). Demographics and baseline as well as switch data are summarized in Table 1.

Functional Outcomes

Mean BCVA in ETDRS letters remained stable from switch (mean, 70.6 ± 13.6; median, 75; IQR, 65.1–80.2) to 1 year after the first faricimab IVT (mean, 69.8 ± 15.8; median, 75; IQR, 65.1–80.2; $P = 0.10$). At switch, 92 eyes (26.1%) had a BCVA ≤0.4 (i.e., 65 ETDRS letters), whereas 200 eyes (56.7%) had a BCVA ≥0.5 (i.e., 70 EDRS letters). During the observation period, 59 eyes (16.7%) underwent cataract surgery. With the aim of minimizing an inherent bias, their BCVA data were censored. A longitudinal overview of changes in BCVA is displayed in Figure 2A. Best-

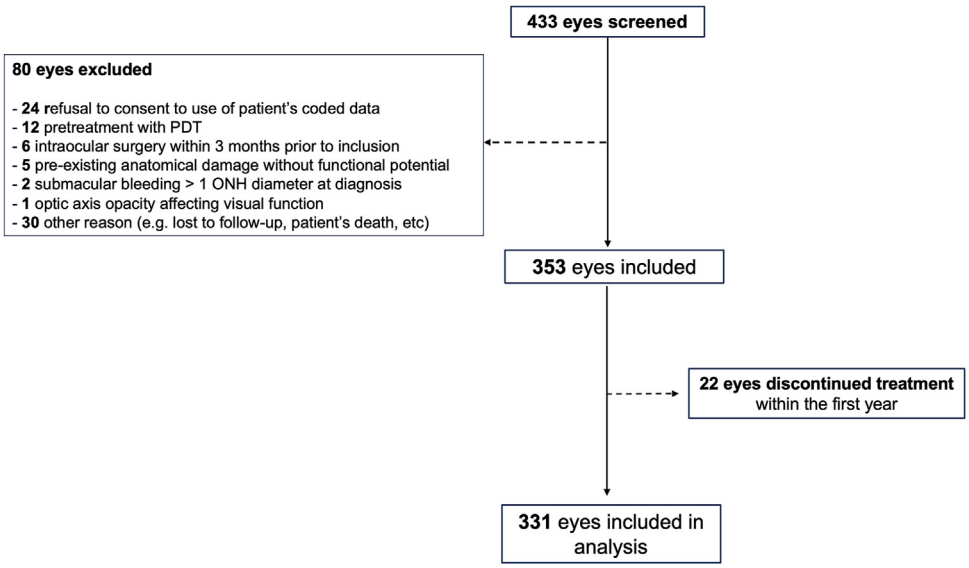

Figure 1. Inclusion and exclusion flow diagram. A detailed overview of exclusion reasons is provided. ONH = optic nerve head; PDT = photodynamic therapy.

corrected visual acuity at 12 months was significantly correlated to baseline BCVA ($r(275) = 0.82$; $P < 0.01$) and fast drying ($r(241) = 0.21$; $P = 0.001$) after 1 faricimab IVT. The persistence of IRF after 1 injection was negatively correlated with BCVA at 12 months ($r(109) = -0.24$; $P = 0.01$). No significant differences were observed in the change in BCVA from switch to 1-year follow-up between eyes treated with ranibizumab monotherapy, aflibercept 2 mg monotherapy, or ≥2 anti-VEGF agents before switching treatments ($P = 0.56$).

Anatomic Outcomes

Mean CST significantly decreased from 344.3 ± 102 μm at switch (median, 320; IQR, 275–393) to 303 ± 85 μm at 12 months (median, 278; IQR, 244–340; mean change, −42 ± 72; median, −27; IQR, −71 to 0 μm; $P < 0.01$). Longitudinal changes in CST from the time of the first diagnosis to 12-months follow-up after switching to faricimab are presented in Figure 2B. At the time of switch, eyes previously treated with ranibizumab monotherapy displayed a median CST of 295 μm (IQR, 269, 356), whereas eyes previously treated with aflibercept 2 mg monotherapy and those treated with ≥ 2 or more anti-VEGF agents had a median CST of 318 μm (IQR, 273, 406) and 328 μm (IQR, 275, 387), respectively. At 12 months of follow-up, the ranibizumab subgroup had a median CST of 266 μm (IQR, 232, 286), which was significantly lower compared with eyes treated with aflibercept 2 mg only (289 μm; IQR, 246, 339) and with eyes treated with ≥2 or more anti-VEGF agents (278 μm; IQR, 246, 350) before switching

Table 1. Baseline and Demographic Data

Parameter	Patient Demographics	
	Number	%
Total eyes (patients)	353 (325)	
Female sex	185	57.9
Left eye	178	50.4
	Median (IQR)	
Age (yrs)	80 (75–85)	
Baseline Clinical Features		
Lens status		
Pseudophakic		201 (56.9%)
Phakic (until last visit)		81 (22.9%)
Phakic (cataract surgery during study time)		59 (16.7%)
Unknown		11 (3.1%)
Mean treatment duration in yrs (range)		3.70 ± 3 (0.6–15.7)
Median treatment duration in yrs		2.80 (1.2–5.4)
Mean IVT 1 yr before switch		8.7 ± 2.8 (9, 6–11)
Anti-VEGF before switch (total before switch period)		
Aflibercept 2 mg		128 (36.2%)
Ranibizumab		46 (13%)
Bevacizumab		1 (0.3%)
≥2		177 (50.1%)
Last anti-VEGF before switch		
Aflibercept 2 mg		258 (73.1%)
Ranibizumab		81 (22.9%)
Brolucizumab		10 (2.8%)
Bevacizumab		3 (0.8%)
Mean treatment interval before switch (mean ± standard deviation, median, IQR)		
Last 12 mos		5.9 ± 2.2 (5.1, 4.4–6.6)
Last 3 intervals		5.9 ± 2.3 (5, 4.3–6.7)
At the time of the switch		5.8 ± 2.5 (5.0, 4.0–7.0)
Reason for switch to faricimab		
Persistent activity on Q4W		200 (56.7%)
Fluid recurrence on extension		143 (40.5%)
Other (new-onset macular bleeding, switch to fellow eye, treatment reinitiation after ≥24 wks)		10 (2.8%)
BCVA (ETDRS)		70.6 ± 13.6 (75.0, 65.1–80.2)
Central subfield thickness (μm)		344.2 ± 101.8 (320.0, 275.0–393.0)
Presence of PED		174 (49.3%)
Maximal PED height in the central 3 mm (μm)		247.2 ± 160.4 (200.5, 127.8–329.3)
Presence of macular fluid		316 (89.7%)
Subretinal		168 (47.6%)
Intraretinal		93 (26.3%)
Both SRF/IRF		55 (15.6%)

BCVA = best-corrected visual acuity; IQR = interquartile range; IRF = intraretinal fluid; IVT = intravitreal injection; PED = pigment epithelium detachment; Q4W = every 4 weeks interval; SRF = subretinal fluid.

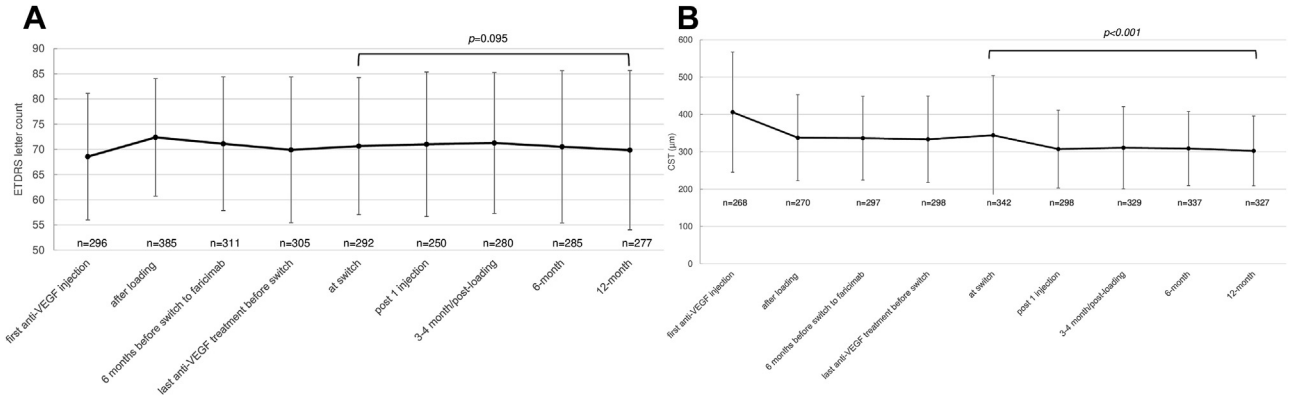

Figure 2. Changes in mean best-corrected visual acuity and central subfield thickness (CST) from the time of diagnosis to the 12-month follow-up after switching to faricimab. After treatment with faricimab, no significant change in best-corrected visual acuity is observed (**A**), whereas CST at 12 months is significantly decreased compared with baseline (**B**).

($P < 0.05$). No significant difference was found in terms of change in CST from switch to 12 months of follow-up between subgroups ($P = 0.34$).

At switch, 36 patients (10.2%) had no RF on macular OCT. Of the remaining eyes with fluid at switch, 134 eyes (38%) displayed completely dry macular OCT scans after a single faricimab IVT. Fast drying eyes had a lower BCVA and lower CST at baseline compared with eyes not drying completely after 1 injection ($P <$ 0.01 each). A multivariable regression analysis showed that PED at the time of switch was neither predictive for fast drying ($P = 0.93$) nor for final BCVA ($P = 0.96$), final treatment interval ($P = 0.84$), or presence of IRF at 12 months ($P = 0.74$), but it was predictive for the presence of SRF at 12 months ($P < 0.001$; adjusted R^2: 0.04; $F(5,229) = 3.0$; $P < 0.01$). Central subfield thickness at 12 months was positively correlated with CST at switch ($r(321) =$ 0.72; $P < 0.01$), whereas it was negatively correlated with fast drying ($r(323) = -0.25$; $P < 0.01$) and last faricimab interval ($r(323) = -0.25$; $P < 0.01$). A detailed overview of changes in macular fluid status over time is shown in Figure 3. At 12 months of follow-up, 169 eyes (47.9%) displayed a dry macula on OCT. Of the 161 eyes that had fluid on macular OCT, 84 (52.2%) had only SRF, 58 had only IRF (36%), and 19 (11.8%) had both SRF and IRF.

Treatment Density

At 12 months, the mean treatment interval was 8.3 ± 4.2 weeks, compared with the mean of the 3 last intervals before switch to faricimab of 5.9 ± 2.3 weeks ($P < 0.01$). In patients switched to faricimab due to persistent fluid at 4 weeks interval (n = 200, 56.7%), the last faricimab interval improved to a mean of 7.6 ± 3.8 weeks. The distribution of treatment intervals between switch and the 12-months follow-up is shown in Figure 4. Ten eyes (2.8%) at switch and 72 eyes at 12 months (20.4%) had a treatment interval ≥12 weeks. The total number of faricimab IVT in the first year after the switch was 8.7 ± 2.0 (range, 4−13). The last treatment interval correlated positively with fast drying ($r(301) = 0.24$; $P <$ 0.01), whereas it correlated negatively with SRF and with CST at baseline ($r(302) = -0.17$, $P = 0.003$ and $r(302) = -0.17$, $P = 0.004$, respectively). A negative correlation was also observed with the presence of RF ($r = -0.19$; $P <$ 0.01) and with CST ($r(323) = -0.25$; $P < 0.01$) at 12 months of follow-up. Single regression analysis revealed that fast drying predicted the injection interval after 1 year under faricimab. Adjusted R^2 was 6%. In eyes that were fast dryers (i.e., no IRF or SRF after 1 faricimab), this positively predicted the ability to extend the intervals one year later ($F(1,299) = 19.0$; $P < 0.0001$).

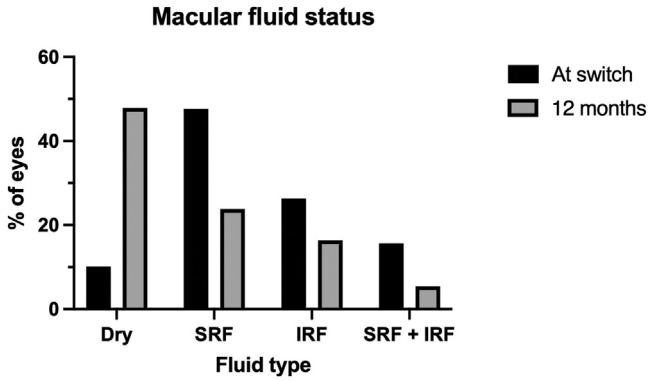

Figure 3. Macular fluid status at the time of switch and after 12 months. The proportion of eyes displaying a dry macular OCT scan markedly increases over time, changing from 10.2% at baseline to 47.9% at 12 months. The proportion of eyes with only SRF or only IRF decreased over follow-up, as did the proportion of eyes displaying both IRF and SRF. IRF = intraretinal fluid; SRF = subretinal fluid.

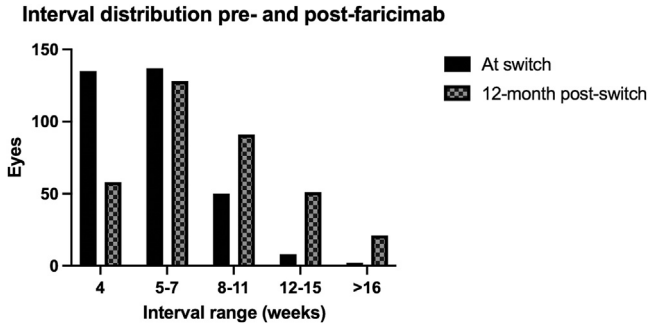

Figure 4. Distribution of treatment intervals at the time of switch and 12 months after faricimab treatment. The proportion of eyes on 4-week intervals markedly decreases at 12 months, whereas eyes on ≥12 weeks increase.

Safety and Discontinuation Rate

Safety signals were reported in 17 eyes (4.8%). A complete list of ocular and systemic safety findings is shown in Table 2. Intraocular inflammation was detected in 6 cases (1.7%), with 4 eyes developing anterior uveitis, 1 eye intermediate uveitis, and 1 eye both anterior and intermediate uveitis. No case of retinal vasculitis was observed. Retinal pigment epithelium tear and endophthalmitis occurred in 1 case each (0.3%).

In total, 22 eyes (6.2%) discontinued treatment with faricimab during the 12-months follow-up. Of these, 1 eye stopped intravitreal treatment definitely (4.5%), and 21 eyes (95.5%) were switched to another anti-VEGF drug, including aflibercept 8 mg (n = 9, 42.8%), aflibercept 2 mg (n = 8, 38%), brolucizumab (n = 3, 14.2%), and ranibizumab (n = 1, 5%). A complete list of reasons for discontinuation is shown in Table 3.

Discussion

In a large Swiss cohort, our study analyzed anatomic, functional, and durability outcomes in pretreated eyes with nAMD and switch to faricimab over a period of 12 months.

Since its first approval by the US Food and Drug Administration in January 2022,[11] increasing real-world evidence has been gathered worldwide on faricimab use in patients with nAMD. Collecting real-world evidence on faricimab is particularly relevant in pretreated patients with nAMD because data from pivotal clinical trials focused on the efficacy and safety of faricimab exclusively in treatment-naive patients.[8] By studying a broader population of pretreated patients, real-world studies can indeed provide more comprehensive information on the performance of faricimab in a variety of clinical scenarios, including those with recalcitrant nAMD and those who have previously received multiple anti-VEGF therapies.

Our study aimed to add information regarding the latter group of difficult-to-treat eyes with insufficiently controlled nAMD. The primary aim of switching in these eyes is to improve control of disease activity and reduce the treatment demand. Our findings confirm that switching to faricimab reduces disease activity and treatment demand to a relevant degree, although, as in other switching studies focusing on other drugs, our patients did not encounter a visual gain.[16]

The recently published real-world studies remarkably vary in sample size, treatment regimen, and after switch follow-up time.[12,13,17–19] In a US cohort of 218 pretreated eyes switched to faricimab, Pandit et al[13] reported improved anatomic outcomes after switching and ≥4 intravitreal faricimab injections, with a significant reduction in the proportion of eyes with IRF, central subfoveal thickness, and maximum fibrovascular PED height, although no change in Snellen visual acuity was noted. Several Asian cohorts have been reported, mostly from Japan, offering insight into a patient population characterized by higher rates of polypoidal choroidal vasculopathy.[20–22] Takahashi et al[22] reported 1-year treatment outcomes in a Japanese cohort of 60 eyes previously treated with brolucizumab, demonstrating stable BCVA and CST, but significant reductions in subfoveal choroidal thickness and an increase in the treatment interval by 2–3 weeks among those previously requiring injections <12 weeks apart. In Europe, real-world studies have been predominantly conducted in the United Kingdom[23–25] and Switzerland,[26,27] because of a relatively early approval in May 2022 by the corresponding national regulatory agencies, allowing early adoption of faricimab in clinical practice. In a recently published study, Sim et al[25] analyzed 130 nAMD eyes switched to faricimab, followed across multiple sites at Moorfields Eye Hospital over a 12-month period. Specifically, they only included patients with a high treatment demand, requiring monthly treatment with their previous anti-VEGF in the last 3 visits before switch. The authors found that CST

Table 2. Ocular and Nonocular Side Effects Reported after Switch to Faricimab (n = 17)

Adverse Event	n (%)
Intraocular inflammation	6 (35.2)
Acute coronary syndrome	3 (17.6)
Anterior chamber cells (+0.5)	1 (5.8)
Endophthalmitis	1 (5.8)
Fibrosis	1 (5.8)
Nonarteritic ischemic optic neuropathy	1 (5.8)
Raised intraocular pressure	1 (5.8)
Retinal pigment epithelium tear	1 (5.8)
Subretinal hemorrhage	1 (5.8)
Vitreomacular traction	1 (5.8)

Table 3. Ocular and Nonocular Side Effects Reported after Switch to Faricimab (n = 17)

Adverse Event	Cases (N°)
Intraocular inflammation*	6
Acute coronary syndrome	3
Anterior chamber cells (+0.5)	1
Endophthalmitis	1
Fibrosis	1
Nonarteritic ischemic optic neuropathy	1
Raised intraocular pressure	1
Retinal pigment epithelium tear	1
Subretinal hemorrhage	1
Vitreomacular traction	1

*In 4 of these 6 cases, treatment was discontinued because of intraocular inflammation.

decreased over 12 months under faricimab treatment along with an extension in treatment intervals from 4.2 to 6.9 weeks, with 42.9% of patients on ≥8-week intervals and 11.4% on ≥12-week intervals. A similar trend was noted in our patients, where the mean treatment interval increased from 5.9 weeks in the year before switching to faricimab to 8.3 weeks at 12 months, with 46.2% of eyes on ≥8-week intervals at their final appointment and 20.4% on ≥12-week intervals.[25] Patients with a high treatment burden comparable to the Moorfields study accounted for 56.7% of our sample, explaining the favorable durability outcomes in our cohort. In the high treatment burden subgroup of our cohort, the treatment interval at 12 months was 7.6 weeks, indeed slightly shorter than the entire cohort. The fact that, in our study, nearly 80% of eyes could not be maintained on injection intervals ≥12 weeks contrasts to the registration trials, where between 77% and 79% of faricimab-treated patients received every 12 weeks or longer dosing at week 48.[9] This discrepancy is not surprising because pivotal trials exclusively enrolled treatment-naïve eyes, whereas in real-world settings, patients are only switched to other agents if disease control is not satisfying. This is typically the case in recalcitrant nAMD with a high treatment demand. Switcher eyes thus typically represent a selection of insufficiently treatment-responsive eyes, which do not meet the inclusion criteria of RCTs, highlighting the challenges of translating clinical trial results to real-world practice.

Recently, Ambati et al[28] reported the 12-month outcomes of intravitreal faricimab in a cohort of 263 previously treated eyes with chronic nAMD from the United States. The mean number of faricimab injections after the switch was 6.4, compared with 8.7 in our cohort. This relevant difference may be explained by differences in the portion of high demanders between the 2 cohorts, the majority of our patients needing treatment intervals of ≤6 weeks at switch. When comparing changes in treatment intervals by the end of the first year, nearly half (47.1%) of the study eyes had a maximal injection interval of ≤8 weeks in their study, whereas only 9.1% achieved an interval between 12 and 16 weeks.[28] Moreover, the average duration of nAMD was higher than in our cohort (5.8 vs. 3.7 years). Discontinuation rate was also higher in their study compared with our cohort, accounting for 11.8% of cases, which were mostly discontinued due to worsening fluid and/or visual acuity[28] compared with 6.2% in our series.

An interesting observation in our study is the large proportion of eyes with fluid at switch displaying complete drying after a single faricimab injection (38%). This subgroup of "fast dryers" showed a better visual acuity and a thinner macula at the time of switch and had a higher chance of achieving longer treatment intervals over follow-up, suggesting that anatomic response after the first injection might predict the later outcome. Notably, although the pivotal Tenaya and Lucerne trials relied on CST to assess disease activity, our study evaluated fluid control over a larger macular area, encompassing the entire 6-mm ETDRS macular grid. The fact that nearly half of eyes in our series achieved a dry macula at 12 months (Fig 3), compared with 10% at switch, demonstrates a better control of disease activity and the remarkable drying effect of faricimab in pretreated nAMD.

In nonrandomized, retrospective switching studies, interpreting outcomes can be challenging due to potential biases such as regression to the mean.[29] Switch is typically considered when the treatment response does not meet expectations. Some of these eyes would, however, also improve over time under continued treatment, independent of the switch. This can create the impression that a new therapy is responsible for the improvement when, in some cases, patients might have responded similarly had they remained on their previous regimen. However, in our study, the extended follow-up period before switching renders a relevant impact of regression to the mean unlikely, particularly in relation to retinal drying, strengthening the validity of our findings and their relevance to real-world clinical practice.

As expected, treatment with intravitreal faricimab did not lead to changes in BCVA, with stable BCVA values at 12 months of follow-up. The observed trends in visual acuity can be attributed to the pretreated status of our patient population and the extended treatment duration before the switch. In patients with nAMD, it is well known that secondary complications, such as macular atrophy and fibrosis, can significantly influence visual prognosis.[30] This result reinforces the findings of previous real-world series, characterized by a discrepancy between anatomic and functional outcomes upon switching to faricimab.[11] A subgroup analysis revealed no variations in efficacy based on prior anti-VEGF treatment. Changes in BCVA and CST from switch to 12 months of follow-up were not statistically different between eyes previously treated with ranibizumab monotherapy, aflibercept 2 mg monotherapy, or ≥2 anti-VEGF agents before switching.

Finally, we conducted correlation and regression analyses to identify potential prognostic factors of improved response and longer treatment intervals over the follow-up. Of note, BCVA 1 year after the switch was positively correlated with fast drying and a better BCVA at baseline. And vice versa, the presence of IRF after the first IVT and a thicker macula at baseline correlated negatively with final

BCVA, as expected from poorly responsive patients starting with more advanced disease at baseline. As for anatomic trends, having a thinner macula at baseline correlated with a better CST over follow-up, with thinner maculae expected in fast dryers and eyes on longer intervals at 12 months.

In terms of safety, the rate of intraocular inflammation in our series (1.7%) aligns with that reported in the published series, which ranges from 0.3% to 3%, and resolved under topical therapy.[11] Reassuringly, no cases of severe intraocular inflammation or vasculitis were observed. The rate of RPE tears in our cohort was low, with 0.3%, compared with 0.3% to 9% reported in other real-world cohorts of pretreated patients with nAMD.[11] Shorter treatment duration and higher PED height (>400 μm) at baseline are risk factors for RPE tears,[31] which would predict a lower risk in switchers. In our study, the median treatment duration before the switch was high (2.8 years), whereas the mean PED height at switch was relatively low (290 μm), contributing to the low rate of RPE tears in our cohort. On the other hand, the risk seems almost 10-fold higher in patients with vascularized PED than in those without,[31] which was not registered in our series.

This study has inherent limitations based on its retrospective, observational design. One limitation was the inclusion criterion requiring 12 months of treatment. Consequently, patients who were switched and did not complete 12 months of faricimab treatment were excluded from the observational data set. Variability in treatment protocols adopted across different centers, including loading dose and criteria for interval extension or reduction, may have influenced the results to some but not likely to a relevant extent. The absence of information on neovascular lesion type may limit the analysis of factors influencing treatment response and durability. We did a manual, qualitative rather than quantitative, analysis of fluid presence that could nowadays be surpassed by artificial intelligence-based tools, reducing the bias in fluid detection and monitoring.[32] However, at the moment of the study conception, we did not have access to such tools, nor did we plan to conduct quantitative analyses because this would have extended the scope of our study.

In conclusion, this study demonstrates the satisfying efficacy and safety of faricimab in a large cohort of pretreated patients with nAMD in a Swiss real-world setting. The improvement in anatomic and durability outcomes over one year, with a reduction in RF and extension of treatment intervals upon switch, highlights the potential of faricimab to offer a durable and convenient treatment option for pretreated patients with nAMD. Future prospective studies with standardized protocols might further substantiate the long-term benefit of faricimab in this diverse patient population.

Footnotes and Disclosures

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No animal subjects were used in this study.

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Abbreviations and Acronyms:
BCVA = best-corrected visual acuity; **CST** = central subfield thickness; **IQR** = interquartile range; **IRF** = intraretinal fluid; **IVT** = intravitreal injection; **nAMD** = neovascular age-related macular degeneration; **PED** = pigment epithelium detachment; **RF** = retinal fluid; **RPE** = retinal pigment epithelium; **SRF** = subretinal fluid.

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