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First-year real-world outcomes of faricimab in clinically significant diabetic macular oedema: a Swiss retina research network report

Amr Saad,[1,2] Christina Plasencia,[3,4] Justus Garweg,[5,6,7] Isabel Barbara Pfister ,[7] Marion R Munk,[8,9,10] Chiara Maria Eandi,[11,12] Sandrine Anne Zweifel,[13] Gabriela Grimaldi,[14,15] Nicolò Bartolomeo,[16] Richard Stillenmunkes,[6,10] Christin Schild,[7] Jennifer Cattaneo,[11] Felix Gabathuler,[13] Moreno Menghini,[14,15] Aude Ambersin,[16] Jacqueline Froehlich,[17] Dmitri Artemiev,[18,19] Andreas Weinberger,[20,21] Hamza Mohamed,[1,2] Gabor Mark Somfai,[1,2] Katja Hatz [3,4]

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AS and CP are joint first authors.

GMS and KH are joint senior authors.

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For numbered affiliations see end of article.

Correspondence to
Dr Katja Hatz; katja.hatz@unibas.ch

ABSTRACT

Aims Evaluate the efficacy and safety of faricimab for treatment-naïve and pre-treated diabetic macular oedema (DME) in a real-world setting.

Methods This multicentre, retrospective cohort study examined consecutive DME patients treated with faricimab for ≥1 year. Data were collected at predefined time points. Primary outcomes were mean changes in corrected visual acuity (VA), centre-point retinal thickness (CRT) and central subfield thickness (CST) and treatment intervals and adverse events (AEs).

Results 184 eyes with DME were included: 61 (33.2%) were treatment-naïve, and 123 (66.8%) were pretreated. In treatment-naïve eyes, VA improved from 69.7±15 Early Treatment of Diabetic Retinopathy Study letters at baseline to 73.9±14.1 after 12 months (p=0.014), while it remained stable in pretreated eyes (71.2±14.2 vs 73.0±12.9; p=0.14). CST decreased significantly in both groups (treatment-naïve (366.1±108.3 µm to 316.4±113.5 µm, p<0.001); pretreated (339.1±93.1 µm to 298.3±65.8 µm, p<0.001)). Thirty-one percent of naïve eyes and 21.1% of pretreated eyes were completely dry after 12 months. In treatment-naïve eyes, the mean treatment interval was 12.7±6.4 weeks at 12 months. In pretreated eyes, the interval increased from 6.0±3.0 to 7.8±3.6 weeks (p<0.001). Over 12 months, 8.1±2.1 and 9.4±2.5 injections were administered to naïve and pretreated eyes, respectively (p<0.001). Of the five recorded AEs, two cases of non-infectious intraocular inflammation and one cerebrovascular event were reported.

Conclusion Over 12 months, faricimab demonstrated good efficacy and safety in both treatment-naïve and pretreated eyes with DME. There was a reduction in CST and improved VA in treatment-naïve eyes and stable VA in pretreated eyes. The low number of AEs supports a favourable risk-benefit profile of faricimab in a real-world setting.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Faricimab, a bispecific antibody targeting both vascular endothelial growth factor-A and angiopoietin-2, has demonstrated efficacy and durability in randomised clinical trials for diabetic macular oedema (DME).

WHAT THIS STUDY ADDS

⇒ This large Swiss multicentre study provides real-world data on the efficacy of faricimab, demonstrating significant anatomical improvements in both treatment-naïve and pretreated DME eyes over 12 months, with gains in visual acuity in treatment-naïve eyes and stabilisation in pretreated eyes. Treatment intervals could be extended, especially in treatment-naïve patients.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ These findings demonstrate that faricimab can effectively treat and control disease in everyday clinical practice.

INTRODUCTION

Diabetic macular oedema (DME) is a late microvascular complication of diabetes mellitus. It is characterised by increased vascular permeability driven by vascular endothelial growth factor (VEGF) and angiogenic factors that result in fluid accumulation in the macula.[1] DME is a leading cause of vision loss in working-age adults in industrialised countries and worldwide. Its prevalence is increasing in parallel with the global rise in diabetes.[2 3] Intravitreal anti-VEGF agents and corticosteroids have transformed the management of DME, helping to prevent visual loss and legal blindness over the past two decades.[4] However, despite the efficacy of anti-VEGF treatments, a significant proportion of patients do not respond completely.

These patients require frequent injections to maintain therapeutic benefits, underscoring the need for more effective, long-lasting treatment options.[5]

Faricimab, a novel therapeutic approach that inhibits both the VEGF-A and angiopoietin-2 (Ang-2) pathways, shows promise in this regard. Phase III clinical trials that have demonstrated their efficacy and safety.[6–8] However, to gain a more comprehensive understanding of its performance in routine clinical practice, it is crucial to evaluate its effectiveness in real-world treatment and adherence scenarios.

In this study, we evaluated the faricimab treatment outcomes in patients with DME across 11 centres in Switzerland using a treat-and-extend regimen. We assessed both functional and morphological responses, as well as treatment patterns and safety signals in the subgroups of treatment-naïve patients and those switched from other anti-VEGF treatments.

METHODS

This retrospective multicentre study analysed patient data from 11 major ophthalmology centres of the Swiss Retina Research Network. The data collection from May 2022 to December 2024 included a consecutive series of eyes treated with intravitreal faricimab injections for DME. The study was approved by all involved ethics committees (lead Ethics Committee Berne, registration number 2024–01026), based on the general or study-specific consent of all included patients to use their coded data and was conducted in accordance with the principles of the Declaration of Helsinki.

Eligible participants were adults (≥18 years) with treatment-naïve or pretreated DME receiving intravitreal faricimab injections and follow-up of at least 12 (±1) months. Allocation to faricimab treatment was at the discretion of the physician. Inclusion criteria comprised a Snellen visual acuity (VA) of ≥0.1 at initiation of faricimab therapy. Prior treatment with other anti-VEGF drugs was permitted. Pretreated eyes were categorised as treatment-naïve if they had not received any injections within 6 months prior to baseline, in order to exclude a potential bias on the effect of switching from one to another anti-VEGF drug. This pragmatic classification reflects real-world clinical conditions, including therapy pauses due to disease stability and minimises carryover bias based on the pharmacodynamic effects of anti-VEGF agents, which rarely persist beyond 6 months.[9] Patients with the following conditions were excluded: no consent to use coded data, less than 12 (±1) months of follow-up, significant structural macular damage, pretreatment with intravitreal corticosteroids and intraocular surgery (except for YAG laser capsulotomy) within 6 months prior to baseline and significant opacifications in the optical axis. Pretreated eyes did not routinely follow a formal loading but were scheduled at least at the same interval as the last prior to switch. Significant structural macular damage was defined as extensive disorganisation of retinal inner layers of the foveal ellipsoidal zone or external limiting membrane disruption, macular atrophy or fibrosis on OCT.[10 11] OCT imaging used standard macular volume scan protocols in all centres.

Data from electronic medical records were retrospectively collected at five predefined time points: prior (baseline) to and 1, 3–4, 6 and 12 month(s) following the initiation of faricimab therapy. In pretreated eyes, data at the following time points were additionally collected: (1) start of first anti-VEGF treatment, (2) 3–4 months after the first anti-VEGF, (3) 6 months before switching and (4) at the last injection prior to switching. At each time point, corrected Snellen VA, intraocular pressure and adverse events (AEs), as well as optical coherence tomography (OCT) imaging data including centre point retinal thickness (CRT), central subfield thickness (CST), the central presence of subretinal fluid (SRF) and/or intraretinal fluid (IRF), were recorded. All sites used Heidelberg Spectralis OCT devices (Heidelberg Engineering, Heidelberg, Germany), and CRT and CST measurements were performed according to a standard operating procedure, after the segmentation had been corrected manually, if necessary. In pretreated eyes, no routine fluorescein angiography or OCT angiography was performed at switch. Best-refracted VA was evaluated at baseline and key follow-up visits. For statistical purposes, Snellen VA was converted to the Early Treatment of Diabetic Retinopathy Study (ETDRS) letter scores.[12]

The primary outcome measures were change in ETDRS letters, change in CST and CRT, and treatment intervals. Secondary outcomes included the number of eyes with absence of retinal fluid in the central subfield after a single injection with faricimab (fast dryers) and after 3–4, 6 and 12 months; the proportion of eyes with IRF and/or SRF at these timepoints; the number of injections administered; the proportion of eyes switching to another drug; and the incidence of clinically relevant side effects. Data of patients switching to another drug were henceforth censored after switch.

Descriptive statistics, subgroup comparisons and correlation analyses were performed. Data distribution was tested using the Shapiro-Wilk test and was not normally distributed. Therefore, the data are presented as mean±SD as well as median and IQRs. Non-parametric tests were used for comparisons. The longitudinal changes in functional and morphological parameters from baseline to 12 months were analysed using the Wilcoxon rank test. The Friedman test for dependent samples was used to compare multiple time points in longitudinal analyses. For comparison of functional and morphological outcomes of naïve and switcher subgroups, Mann-Whitney U test was applied. The level of significance was set at $p<0.05$. All statistical analyses were performed using the SPSS software package V.27 (SPSS, Inc., Chicago, Illinois, USA) and R (V.4.4.2, R Foundation for Statistical Computing, Vienna, Austria, 2016).

RESULTS

During the study period, 350 eyes (327 patients) were started with faricimab treatment. Of these, 184 eyes (161 patients) met the inclusion criteria and were included in the final data set. Of these, 123 (66.8%) were pretreated with other anti-VEGF agents (switchers), and 61 (33.2%) were treatment naïve (38) or untreated (23) for at least 6 months. Detailed patient demographics are presented in table 1A, baseline ocular characteristics of treatment-naïve and pretreated treatment groups in table 1B and pretreatment characteristics of switchers in table 1C. The eyes untreated for at least 6 months before the start of faricimab were not included in table 1C and were considered treatment-naïve for the analyses. The baseline characteristics of these eyes did not differ from those of eyes that had never received any intravitreal therapy (online supplemental table 1). Bilateral treatment with faricimab was applied to 23 patients from the whole cohort (14.3%).

Visual outcomes

Treatment-naïve eyes experienced a significant VA improvement of +2.8±7.7 letters (p=0.014, n=53) from 69.7±15.0 (n=59) ETDRS letters at baseline to 73.9±14.1 (n=53) letters at 12 months. VA remained stable in pretreated eyes (baseline 71.2±14.2 letters (n=106), at 12 months 73.0±12.9 letters (n=100); p=0.14; figure 1A). VA data from 15 eyes (12.2%) undergoing cataract surgery during the observation period were censored at baseline to exclude a bias in response to cataract surgery. Nine naïve eyes (14.8%) and five pretreated eyes (4.1%) gained 10 to 14 letters, and five naïve eyes (8.2%) as well as six pretreated eyes (4.9%) gained 15 or more letters in response to faricimab treatment.

VA at 12 months was positively correlated with VA at baseline (naïve $r(53)=0.85$, p<0.001, switcher $r(98)=0.83$, p<0.001), but not to CST or CRT at baseline. No correlations were found between VA change from baseline to 12 months and baseline CST, CRT or macular fluid in pretreated eyes.

Morphological outcomes

Both treatment groups showed a significant decrease in CRT and CST from baseline to 12 months after switch to faricimab (table 2; figure 1B).

Macular fluid had completely resolved after a single faricimab injection in six treatment-naïve (9.8%) and five pretreated eyes (4.1%) and after 12 months in 19 naïve (31.1%) and 26 pretreated (21.1%) eyes (McNemar test, p<0.001). Forty naïve eyes (65.6%) displayed persistent macular fluid 12 months after switch, of which 35 eyes (57.4%) showed only IRF, and five eyes (8.2%) showed both IRF and SRF. Of 89 pretreated eyes (72.4%) with persisting macular fluid at 12 months, after switching to faricimab, 85 eyes (69.1%) showed IRF and four eyes (3.3%) had both IRF and SRF (figure 2).

Treatment intervals

The mean last treatment interval for naïve eyes reached 12.7±6.4 weeks; in pretreated eyes, it changed from 6.0±3.0 weeks at baseline to 7.8±3.6 weeks at 12 months (p<0.001). The mean number of injections in the first year was 8.9±2.4 (median, 9.0; IQR, 8.0–11.0), with 8.1±2.1 injections (median, 8.0; IQR, 7.0–9.0) in treatment-naïve and 9.4±2.5 injections in pretreated eyes (median, 10.0; IQR, 8.5–11.5). The portion of subjects at a q4 dosing was reduced from 38% to 18%, whereas the portion of eyes on q12-q15 increased from 2.4% to 15.4%.

The mean treatment interval of all eyes between the first and the second faricimab injection was 5.7±6.1 weeks (median, 4.1; IQR, 4.0–5.2), between the second and the third faricimab injection 5.9±5.2 weeks (median, 4.4; IQR, 4.0–5.9) and between the third and fourth faricimab injection 5.8±3.3 weeks (median, 4.1; IQR, 4.0–6.0). No differences were found between the treatment subgroups (p>0.05). The distribution of treatment intervals is displayed on figure 3.

Treatment with faricimab was interrupted or switched to a PRN scheme in a total of 12 naïve eyes (19.7%) within the first year of treatment due to complete resolution of retinal fluid. Two naïve eyes (3.3%) were switched to aflibercept 8 mg due to persistence of macular fluid. Treatment was stopped in nine pretreated eyes (7.3%) due to success (absence of retinal fluid), whereas 13 eyes (10.6%) were switched to another anti-VEGF agent due to persistent fluid (nine eyes (7.3%) to aflibercept 8 mg, 3 eyes (2.4%) to aflibercept 2 mg and one eye (0.8%) to intravitreal dexamethasone).

Safety outcomes

Safety findings were registered in five pre-treated eyes: two eyes suffered from procedure-related ocular surface problems, two cases of drug-related severe intraocular inflammation (IOI) with a rise in intraocular pressure were reported (one with panuveitis, and one with granulomatous anterior and intermediate uveitis). One was a granulomatous anterior/intermediate uveitis with IOP elevation after the fifth injection, managed by topical corticosteroids, followed by a switch to aflibercept 2 mg. The second case was an anterior uveitis following the third injection, managed with topical corticosteroids and switched to aflibercept 8 mg. Additionally, one case of cerebrovascular insult was reported; this patient had been treated bilaterally.

DISCUSSION

This study represents a large real-world cohort of DME patients from the Swiss Retina Research Network, treated with faricimab with a follow-up period of 12 months. So far, real-world evidence regarding faricimab outcomes in DME treatment was limited to short-term and smaller analyses.[13 14] In Switzerland, faricimab has been approved for the treatment of DME in May 2022 and received insurance coverage in August 2022. After completion of the first year of real-world treatment with faricimab, our

Table 1 Demographics and baseline characteristics of naïve and pretreated eyes. Data are shown as mean±SD deviation and (median (IQR)). (A) Baseline patient demographics. (B) Baseline ocular characteristics. (C) Pretreatment features (switchers only).

Demographics	Naïve (n=61, 33.2%)	Switchers (n=123, 66.8%)	Total (n=184)
Age (years)	64.2±11.5 (67 (57, 70))	67.0±10.2 (68 (60, 75))	66.1±10.7 (68 (59, 73))
Sex (% female)	45.1%	39.1%	41.0%
Diabetes type			
Type 1	6 (11.8%)	15 (13.7%)	21 (13.0%)
Type 2	45 (88.2%)	93 (84.5%)	138 (85.8%)
Other		2 (1.8%)	2 (1.2%)
Insulin usage			
No	14 (11.8%)	35 (28.5%)	49 (26.6%)
Yes	42 (88.2%)	86 (69.9%)	128 (69.6%)
Missing	5 (8.2%)	2 (1.6%)	7 (3.8%)
HbA1c (n=131)	8.4±2.2 (7.8 (6.9, 9.0))	7.4±1.2 (7.1 (6.5, 7.9))	7.7±1.7 (7.2 (6.7, 8.2))
B. Baseline ocular characteristics			
Lens status			
Pseudophakic	22 (36.1%)	63 (51.2%)	85 (46.3%)
Phakic (until last visit)	33 (54.1%)	43 (35%)	76 (41.3%)
Phakic (cataract surgery during observation)	6 (9.8%)	15 (12.2%)	21 (11.4%)
Unknown		2 (1.6%)	2 (1%)
VA (ETDRS letter scores)	69.7±15.0 (75 (65.1, 80.2))	71.2±14.2 (75 (65.1, 80.2))	70.7±14.4 (75 (65.1, 80.2))
Central retinal thickness (µm)	335.4±140.1 (318 (238, 416))	313.5±110.1 (279.5 (238, 387.5))	320.7±120.9 (289 (238, 397))
Central subfield thickness (µm)	366.1±108.3 (347 (290, 420))	339.1±93.1 (321.5 (280, 366))	347.9±98.8 (330 (282, 386.5))
Macular fluid			
No fluid	0	3 (2.4%)	3 (1.6%)
IRF	51 (83.6%)	113 (91.9%)	164 (89.1%)
Both IRF and SRF	10 (16.4%)	6 (4.9%)	16 (8.7%)
Missing	0	1 (0.8%)	1 (0.5%)
Diabetic retinopathy severity			
No apparent DR	0	2 (1.6%)	2 (1.1%)
Mild NPDR	9 (14.8%)	18 (14.6%)	27 (14.7%)
Moderate NPDR	16 (26.2%)	40 (32.5%)	56 (30.4%)
Severe NPDR	27 (44.3%)	45 (36.6%)	72 (39.1%)
PDR	2 (3.3%)	14 (11.4%)	16 (8.7%)
High-risk PDR	3 (4.9%)	2 (1.6%)	5 (2.7%)
Missing	4 (6.6%)	2 (1.6%)	6 (3.3%)
Prior laser treatment			
No	39 (63.9%)	60 (48.8%)	99 (53.8%)
Focal macular	5 (8.2%)	5 (4.1%)	10 (5.4%)
Incomplete PRP	6 (9.8%)	14 (11.4%)	20 (10.9%)
Complete PRP	5 (8.2%)	30 (24.4%)	35 (19.0%)
Combined (1+2 or 1+3)	2 (3.3%)	11 (8.9%)	13 (7.1%)
Missing	4 (6.6%)	3 (2.4%)	7 (3.8%)
C. Pretreatment features (switchers only)			

Continued

Table 1 Continued

Demographics	Naïve (n=61, 33.2%)	Switchers (n=123, 66.8%)	Total (n=184)
Duration of previous treatments (years)		3.8±3.7 (2.2 (0.9, 5.9))	
Number of intravitreal injections prior to switch		31±30 (20 (10, 44))	
Number of intravitreal injections during the 6 months prior to switch		4.1±1.6 (4 (3, 5))	
Eyes pre-treated with intravitreal dexamethasone (n (%))		14 (11.4%)	
Last intravitreal treatment: aflibercept		102 (82.9%)	
Last intravitreal treatment: ranibizumab		15 (12.2%)	
Last intravitreal treatment: unknown		6 (4.9%)	
Reasons for switch: persistent macular fluid on Q4W		84 (68.3%)	
Reasons for switch: fluid recurrence under extension		29 (23.6%)	
Reasons for switch: switch for potentially extended treatment intervals		9 (7.3%)	

DR, diabetic retinopathy; ETDRS, Early Treatment of Diabetic Retinopathy Study; HbA1c, glycosylated hemoglobin; IRF, intraretinal fluid; NPDR, non-proilferative diabetic retinopathy; PDR, proliferative diabetic retinopathy; PRP, panretinal photocoagulation; Q4W, every 4 weeks interval; SRF, subretinal fluid; VA, visual acuity.

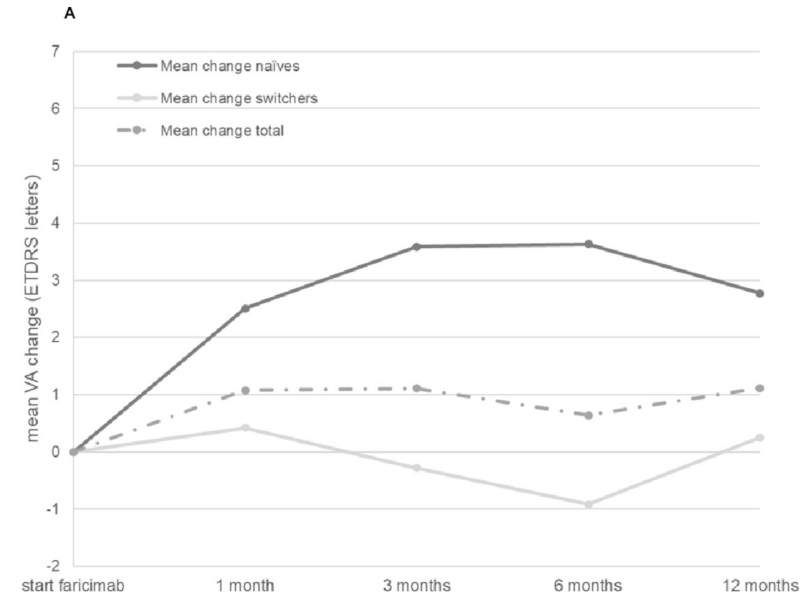
findings indicate significant improvements in anatomical outcomes, which show a robust control of disease activity.

We observed only a moderate VA improvement of 2.8 ETDRS letters in treatment-naïve patients that falls short of the outcomes reported in the YOSEMITE and RHINE phase III trials,[8] while stabilisation of VA was as expected in pretreated eyes. Although statistically significant (p=0.014), the VA gain in this cohort lacks clinical relevance.[15] The discrepancy in VA gains in naïve patients may partially be attributed to less rigid inclusion criteria in a real-world setting compared with YOSEMITE/RHINE, where 41.8% of screened patients were excluded from randomisation due to not meeting the study's narrow inclusion criteria.[7 8] Early diagnosis and access to treatment may have accounted for the high baseline VA of 75 letters in our treatment-naïve patients, along with a real-world variability that may cause a ceiling effect and limit improvement potential.[8]

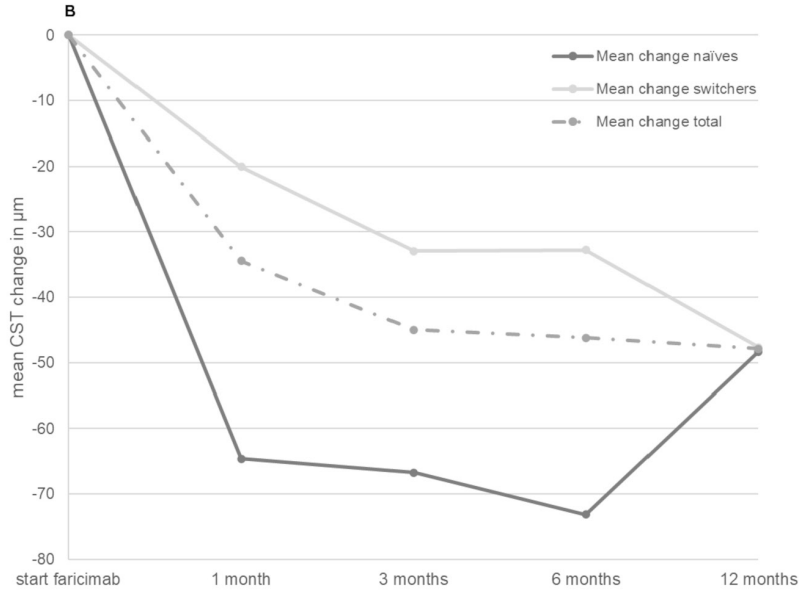
Notably, our study included a larger portion of pretreated patients than YOSEMITE/RHINE (66.8% vs 25%) with extensive prior anti-VEGF therapy (mean 31±30 injections). The stability of VA, along with an improved control of disease activity with reduction in CST and a significant extension of treatment intervals observed in this demanding pretreated group over a 12-month period, is particularly encouraging. The magnitude of CST/CRT improvement was comparable between treatment-naïve and pretreated patients, suggesting that the therapeutic benefits of faricimab may extend beyond the previous anti-VEGF therapy. Possibly, Ang-2 upregulation adds to persistent DME despite VEGF suppression,[16] given that Ang-2 has been implicated in destabilising the blood-retinal barrier independently of VEGF-A.[17 18]

An early drying effect was observed in 9.8% of naïve and 4.1% of pretreated eyes after a single intravitreal injection of faricimab. This is particularly relevant in the context of DME management, as persistent retinal fluid is associated with worse visual outcomes and long-term photoreceptor damage.[19 20] The proportion of eyes without central SRF and IRF in our study is, however, not comparable to the absence of DME defined by CST <325 µm as reported in the YOSEMITE and RHINE trials.[8]

Absence of IRF in only 31.1% of naïve and 21.1% of pretreated eyes at 12 months this real-world study differs from YOSEMITE/RHINE, which reported absence of IRF in 44–63% of patients (pooled YOSEMITE/RHINE population) at weeks 92–100.[8] Part of this difference may be explained by longer intervals between the first injections in our patients compared with the 4-weekly injections during the first months in the randomised



n naïves	38	54	52	53
Mean change	+2.5	+3.6	+3.6	+2.8
n switchers	82	96	100	101
Mean change	+0.4	-0.3	-0.9	+0.2
n total	120	150	152	154
Mean change	+1.1	+1.1	+0.6	+1.1



n naïves	45	59	56	57
Mean change	-64.6	-66.7	-73.1	-48.3
n switchers	94	107	112	112
Mean change	-20.0	-32.9	-32.7	-47.6
n total	139	166	168	169
Mean change	-34.5	-45.0	-46.2	-47.9

Figure 1 Changes in (A) Snellen visual acuity (VA) and (B) mean central subfield thickness (CST) in optical coherence tomography scans of naïve and pretreated eyes from baseline to 12 months after switch to faricimab. CST was in both treatment groups significantly decreased at 12 months compared with baseline. While VA significantly improved in naïve eyes during the first year of faricimab treatment, it remained stable in pretreated eyes. Change in VA in pretreated eyes was not significant at any point of time. Data pertaining to the 17 eyes (13.3%) undergoing cataract surgery during the 1 year observation period were censored after cataract surgery to exclude a bias in response to cataract surgery.

Table 2 Morphological outcomes from baseline to 12 months after switch

	Naïve (n=61)		Switchers (n=123)	
	Mean±SD (µm)	Median (IQR) (µm)	Mean±SD (µm)	Median (IQR) (µm)
Central retinal thickness				
At baseline	335.4±140.1	318 (238, 416)	313.5±110.1	280 (238, 388)
after 12 months	284.9±139.3	242 (214, 295)	265.8±84.2	247 (207, 296)
mean change (p<0.001)	−48.3±145.4	−41 (−109 to −6)	−47.6±108.7	−30(−90 to −1)
Central subfield thickness				
at baseline	366.1±108.3	347 (290, 420)	339.1±93.1	322 (280, 366)
after 12 months	316.4±113.5	280 (264, 330)	298.3±65.8	284 (250, 333)
mean change (p<0.001)	−47.4±110.2	−45 (−94 to −11)	−39.7±92.9	−23 (−71 to −1)

clinical trials. This discrepancy also reflects the difference in the study populations with a higher proportion of hard-to-treat switchers in our cohort. Additionally, the limited VA gain in switcher eyes may reflect subtle baseline structural changes, as previously reported in chronic DME.[11 21] Although a PRN protocol was applied to few stable and naïve eyes, proactive treat-and-extend therapy was the treatment of choice for most patients to mitigate the risk of relapse, according to the YOSEMITE/RHINE data.[7]

The safety profile of faricimab in this study aligns with the findings from YOSEMITE/ RHINE, with a low number of serious AEs. However, the observed cases of IOI require careful consideration. Patients deserve to be informed about the symptoms of IOI so that they report early in case of any irregularities.[22] The simultaneous

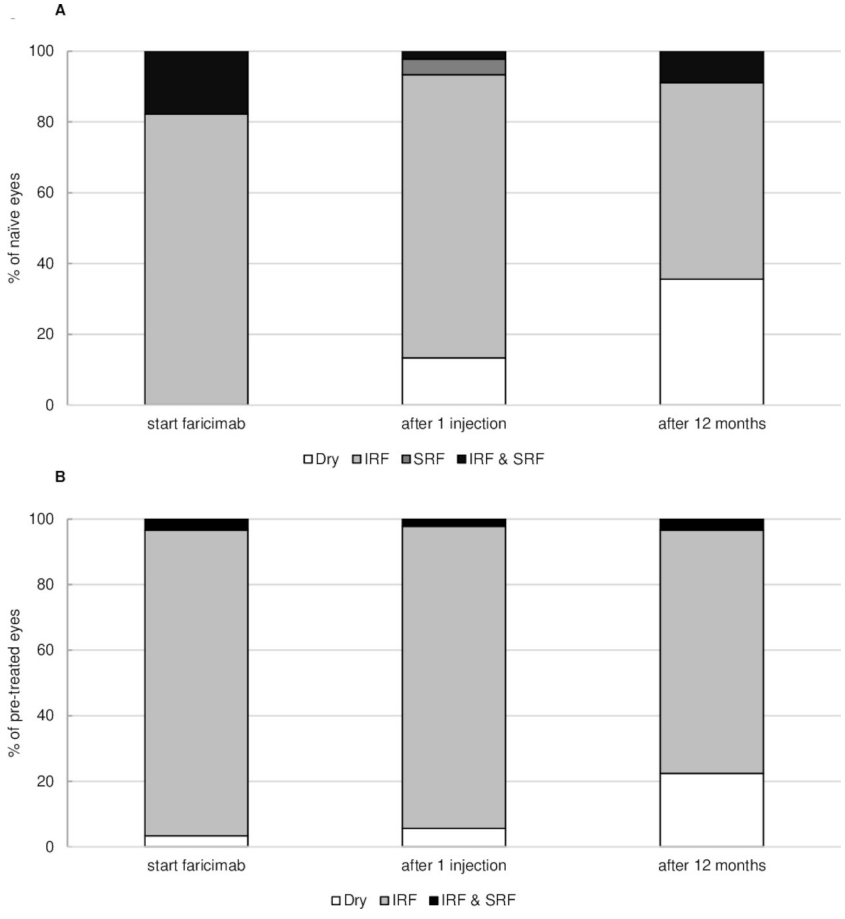


Figure 2 Macular fluid status after initiation of intravitreal faricimab in (A) treatment-naïve eyes and (B) eyes switched from any other anti-VEGF drug to faricimab. Distribution of macular fluid and absence of fluid in optical coherence tomography scans of naïve and pretreated eyes at baseline, after the first injection of faricimab and after 12 months. The proportion of eyes without macular fluid remarkably increased during the first year of faricimab treatment in both treatment groups. IRF, intraretinal fluid; SRF, subretinal fluid; VEGF, vascular endothelial growth factor.

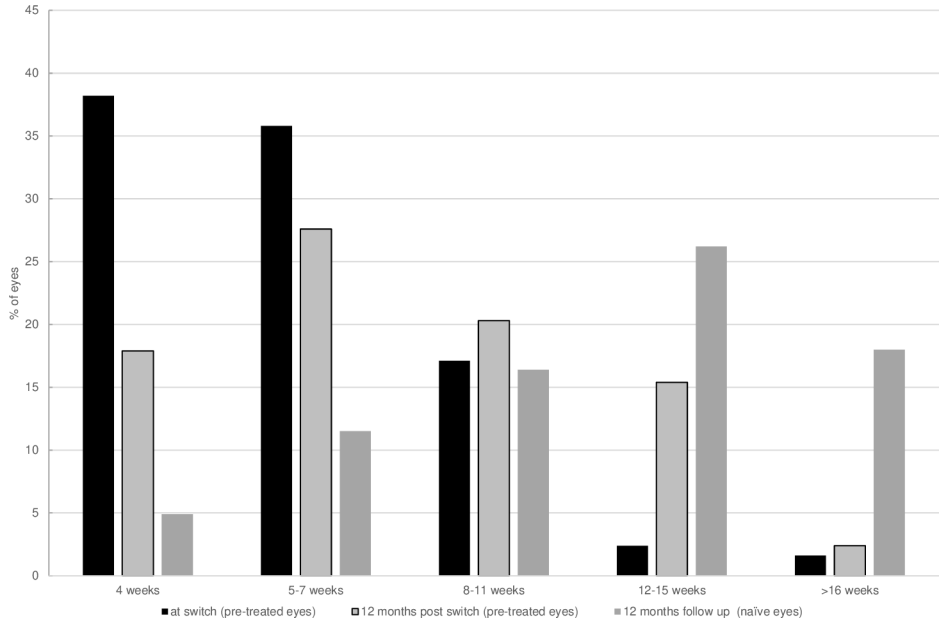


Figure 3 Distribution of treatment intervals of pretreated eyes at start with faricimab and of pretreated and naïve eyes after first year of faricimab treatment. In pretreated eyes, the proportion of eyes with intervals of ≥12 weeks increased, while those with intervals of 4 weeks decreased.

inhibition of the VEGF-A and Ang-2 pathways introduces unique considerations for the long-term safety monitoring, as Ang-2 has a multifaceted role in vascular homeostasis and inflammatory processes. The occurrence of inflammatory events exclusively in pretreated patients also raises considerations about the cumulative effects of long-term intravitreal therapy and possible immune responses.[23 24]

A significant strength of the present study is the evaluation of faricimab therapy in a larger well-controlled real-world population over 1 year. This study was conducted independently, without involvement from pharmaceutical companies. Despite its potential strengths, our study has inherent limitations such as its retrospective nature, the large, but still limited number of cases and the possible slight treatment inconsistencies across the different sites. Switzerland's healthcare context, namely, the wide access to anti-VEGF drugs and intravitreal steroids, the relatively good control of diabetes and flexible anti-VEGF labels, combined with broad cost coverage by compulsory basic insurance, may also limit the generalisability of the findings to other populations. On the other hand, unrestricted choice of the anti-VEGF drug allows less biased analysis of the data compared with countries where access is limited or dictated by reimbursement policies. While the 12-month follow-up period offered valuable insights, it might not fully capture the long-term efficacy and safety profile, particularly when considering the chronic nature of DME. Finally, the exclusion of patients with significant structural macular damage or systemic comorbidities and other real-world factors, such as higher baseline VA, may limit the generalisability of the results to the broader DME population.

In conclusion, this real-world analysis of faricimab in DME patients contributes to the growing body of evidence and provides further insights supporting clinical decision-making. Its efficacy, particularly regarding anatomical outcomes and treatment durability, along with a favourable safety profile, positions faricimab as a valuable addition to the DME treatment armamentarium. The potential for improved outcomes with early intervention and the possibility of extended treatment intervals address current unmet needs in DME management. However, the low portion of eyes with complete retinal fluid resolution after 12 months of treatment stresses the risk of over-extension of individual treatment intervals and supports the multifactorial nature of DME.

Author affiliations
[1]Department of Ophthalmology, Stadtspital Zurich Triemli, Zürich, Switzerland
[2]Spross Research Institute, Zurich, Switzerland
[3]Medical Retina & Clinical Research Department, Vista Klinik, Binningen, Switzerland
[4]University of Basel Faculty of Medicine, Basel, Switzerland
[5]Berner Augenklinik am Lindenhofspital, Bern, Switzerland
[6]Department of Ophthalmology, Inselspital University Hospital Bern, Bern, Switzerland
[7]Swiss Eye Institute, Bern, Switzerland
[8]Ophthalmology, Inselspital, University Hospital Bern, Bern, Switzerland
[9]Northwestern University, Feinberg School of Medicine, Chicago, Illinois, USA
[10]Augenärztepraxisgemeinschaft Gutblick AG, Pfäffikon, Switzerland
[11]Department of Ophthalmology, Jules Gonin Eye Hospital, Lausanne, Switzerland
[12]Department of Surgical Sciences, University of Torino, Torino, Italy
[13]Universitatsspital Zurich Augenklinik und Poliklinik, Zurich, Switzerland
[14]Ophthalmology, Institute of Clinical Neurosciences of Southern Switzerland, Lugano, Switzerland
[15]Faculty of Biomedical Sciences, University of Southern Switzerland, Lugano, Switzerland
[16]Research Center, Swiss Visio Montchoisi, Lausanne, Switzerland
[17]Department of Ophthalmology, University of Basel, Basel, Switzerland

[18]Department of Ophthalmology, Kantonsspital St Gallen, St. Gallen, Switzerland
[19]University of Bern, Bern, Switzerland
[20]Pallas Kliniken AG, Olten, Switzerland
[21]Department of Ophthalmology, RWTH Aachen University, Aachen, Germany

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ORCID iDs
Isabel Barbara Pfister https://orcid.org/0000-0001-8752-8390
Katja Hatz https://orcid.org/0000-0003-2807-0310

REFERENCES

1 Romero-Aroca P, Baget-Bernaldiz M, Pareja-Rios A, *et al*. Diabetic Macular Edema Pathophysiology: Vasogenic versus Inflammatory. *J Diabetes Res* 2016;2016:2156273.
2 Lee R, Wong TY, Sabanayagam C. Epidemiology of diabetic retinopathy, diabetic macular edema and related vision loss. *Eye Vis (Lond)* 2015;2:17:17:.
3 Ong KL, Stafford LK, McLaughlin SA, *et al*. Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: a systematic analysis for the Global Burden of Disease Study 2021. *The Lancet* 2023;402:203–34.
4 National Institute for Health and Care Excellence. Diabetic retinopathy: management and monitoring. 2023.
5 Rennie C, Lotery A, Payne J, *et al*. Suboptimal outcomes and treatment burden of anti-vascular endothelial growth factor treatment for diabetic macular oedema in phakic patients. *Eye (Lond)* 2024;38:215–23.
6 Regula JT, Lundh von Leithner P, Foxton R, *et al*. Targeting key angiogenic pathways with a bispecific CrossMAb optimized for neovascular eye diseases. *EMBO Mol Med* 2019;11:e10666.
7 Wykoff CC, Abreu F, Adamis AP, *et al*. Efficacy, durability, and safety of intravitreal faricimab with extended dosing up to every 16 weeks in patients with diabetic macular oedema (YOSEMITE and RHINE): two randomised, double-masked, phase 3 trials. *The Lancet* 2022;399:741–55.
8 Wong TY, Haskova Z, Asik K, *et al*. Faricimab Treat-and-Extend for Diabetic Macular Edema: Two-Year Results from the Randomized Phase 3 YOSEMITE and RHINE Trials. *Ophthalmology* 2024;131:708–23.
9 Veritti D, Sarao V, Di Bin F, *et al*. Pharmacokinetic and Pharmacodynamic Rationale for Extending VEGF Inhibition Increasing Intravitreal Aflibercept Dose. *Pharmaceutics* 2023;15:1416.
10 Panozzo G, Cicinelli MV, Dalla Mura G, *et al*. Enhancing Diabetic Macular Edema Treatment Outcomes: Exploring the ESASO Classification and Structural OCT Biomarkers. *Ophthalmol Ther* 2024;13:1383–98.
11 Sun JK, Lin MM, Lammer J, *et al*. Disorganization of the retinal inner layers as a predictor of visual acuity in eyes with center-involved diabetic macular edema. *JAMA Ophthalmol* 2014;132:1309–16.
12 Gregori NZ, Feuer W, Rosenfeld PJ. Novel method for analyzing snellen visual acuity measurements. *Retina* 2010;30:1046–50.
13 Nasimi N, Nasimi S, Grauslund J, *et al*. Real-world efficacy of intravitreal faricimab for neovascular age-related macular degeneration: a systematic review. *Int J Retina Vitreous* 2024;10:48.
14 Huber KL, Stino H, Steiner I, *et al*. Real-World Outcomes After Switch From Aflibercept to Faricimab in Eyes With Diabetic Macular Edema. *Invest Ophthalmol Vis Sci* 2024;65:46.
15 Beck RW, Maguire MG, Bressler NM, *et al*. Visual acuity as an outcome measure in clinical trials of retinal diseases. *Ophthalmology* 2007;114:1804–9.
16 Chen-Li G, Martinez-Archer R, Coghi A, *et al*. Beyond VEGF: Angiopoietin-Tie Signaling Pathway in Diabetic Retinopathy. *J Clin Med* 2024;13:2778:1–23:.
17 Nicolò M, Ferro Desideri L, Vagge A, *et al*. Faricimab: an investigational agent targeting the Tie-2/angiopoietin pathway and VEGF-A for the treatment of retinal diseases. *Expert Opin Investig Drugs* 2021;30:193–200.
18 Rush RB. One Year Results of Faricimab for Aflibercept-Resistant Diabetic Macular Edema. *Clin Ophthalmol* 2023;17:2397–403.
19 Maheshwary AS, Oster SF, Yuson RMS, *et al*. The association between percent disruption of the photoreceptor inner segment-outer segment junction and visual acuity in diabetic macular edema. *Am J Ophthalmol* 2010;150:63–7.
20 Panos GD, Lakshmanan A, Dadoukis P, *et al*. Faricimab: Transforming the Future of Macular Diseases Treatment - A Comprehensive Review of Clinical Studies. *Drug Des Devel Ther* 2023;17:2861–73.
21 Bressler NM, Beaulieu WT, Glassman AR, *et al*. Persistent Macular Thickening Following Intravitreous Aflibercept, Bevacizumab, or Ranibizumab for Central-Involved Diabetic Macular Edema With Vision Impairment: A Secondary Analysis of a Randomized Clinical Trial. *JAMA Ophthalmol* 2018;136:257–69.
22 Garweg JG, Blum CA, Copt RP, *et al*. Brolucizumab in Neovascular Age-Related Macular Degeneration and Diabetic Macular Edema. *Ophthalmology and Diabetology Treatment Aspects Ophthalmology and Therapy* 2023;12:639–55.
23 Cox JT, Eliott D, Sobrin L. Inflammatory Complications of Intravitreal Anti-VEGF Injections. *J Clin Med* 2021;10:1–16.
24 Canonica J, Foxton R, Garrido MG, *et al*. Delineating effects of angiopoietin-2 inhibition on vascular permeability and inflammation in models of retinal neovascularization and ischemia/reperfusion. *Front Cell Neurosci* 2023;17:1192464.