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ORIGINAL RESEARCH

Real-World Outcomes of Switching to Faricimab in Treatment-Experienced and Resistant Neovascular Age-Related Macular Degeneration: A Single-Centre Retrospective Study

Christopher Stewart[1], Jaskaran Singh Bhangu[2], Parinita Keshav Swarnkar[2], Mohammed Rifat[2], Sarah Khalid[2], Ahmed Al-Janabi[2], Mahmoud H Awad[2], Gwyn Samuel Williams[2]

[1]Faculty of Medicine, Health, and Life Science, Swansea University, Swansea, Wales, UK; [2]Ophthalmology Department, Singleton Hospital, Swansea Bay University Health Board, Swansea, Wales, UK

Correspondence: Christopher Stewart, Faculty of Medicine, Health, and Life Science, Swansea University, Sketty, Swansea, Wales, SA2 8QA, UK, Email cdstewart@outlook.com

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Purpose: To evaluate anatomical, functional, and treatment burden outcomes of Faricimab in neovascular age-related macular degeneration (nAMD) patients with persistent disease activity despite prior anti-VEGF therapy.

Patients and Methods: Single-centre retrospective study of 67 eyes switched to Faricimab (November 2022–December 2024). This cohort was unable to be extended beyond 4–6-week intervals on existing anti-VEGF therapy. All patients received three monthly loading doses followed by treat-and-extend regimen. Primary outcomes: central macular thickness (CMT), best-corrected visual acuity (BCVA), macular dryness over eight injections, and treatment interval extension.

Results: The cohort had received mean 33 (range 10–78) prior anti-VEGF. Baseline mean BCVA was 0.42 logMAR (SD ± 0.28) and mean CMT was 244.5 µm (SD ± 62.2). Statistically significant CMT reduction occurred by injection 8 (−16.9 µm, p=0.0084). Complete macular dryness peaked by the time of third injection (43.3%) then declined to 32.8% at injection 8 (p=0.0089). Visual acuity remained unchanged (p=0.6043) with no correlation to CMT change (p=0.172). Treatment interval extension was achieved in 46.3% of patients (p=0.002). Dryness at injection 3 after switching to Faricimab did not predict treatment extension (p=0.217). Two patients (0.36% of total injections, 2/548) developed sterile intraocular inflammation requiring discontinuation.

Conclusion: Faricimab switching achieves statistically significant but modest anatomical improvement in heavily pretreated nAMD with meaningful treatment burden reduction in 46.3% of eyes. Our analysis revealed treatment burden did not indicate the potential for treatment interval extension.

Keywords: Faricimab, anti-VEGF switching, treatment-resistant nAMD, treat-and-extend

Introduction

Neovascular age-related macular degeneration (nAMD) is a leading cause of severe vision loss among older adults, imposing a significant clinical and socioeconomic burden.[1,2] While intravitreal anti-vascular endothelial growth factor (anti-VEGF) agents have substantially improved outcomes, their long-term effectiveness is limited by high treatment burden, variable durability, and persistent disease activity in a proportion of patients.[3,4] Faricimab, a dual-action antibody targeting both VEGF-A and angiopoietin-2, was initially developed to enhance efficacy with post-hoc analysis appeared to show evidence of maintaining vascular stability alongside durability seen in VEGF inhibition alone.[5] In the pivotal TENAYA and LUCERNE trials, Faricimab achieved non-inferior visual outcomes compared with aflibercept in treatment-naïve nAMD.[6] Approximately half of patients maintained 16-week intervals at year one, increasing to 59.0–66.9% by year two, indicating potential for meaningful treatment burden reduction.[6] Further two year data demonstrated sustained visual acuity gains with extended dosing, with 74.1–81.2% of the cohort achieving 12-week or longer

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intervals.[7] These landmark trials focussed on newly diagnosed AMD, neglecting those already on anti-VEGF therapy which represent the majority of patients in clinical practice. Chronic anti-VEGF exposure is associated with retinal pigment epithelium atrophy and photoreceptor degeneration, particularly affecting ellipsoid zone continuity and outer retinal architecture theorised to dampen outcomes compared with newly diagnosed nAMD eyes.[8,9]

More recent studies have explored these at-risk patients with chronic anti-VEGF exposure for nAMD.[10–16] Current literature demonstrates that switching partially responsive or refractory nAMD patients to faricimab consistently drives significant anatomical improvements, specifically in reducing central subfield thickness (CST) and drying the retina.[10–16] This anatomical change can reliably translate to a reduced treatment burden as seen in studies by Borchet al, Janmohamed et al and Hang et al from a significant proportion of patients successfully extending their injection intervals.[11–13,16] However, despite these structural gains, visual acuity typically remains stable rather than showing significant improvement.[10–16]

These positive functional outcomes tend to reflect temporary disease stabilisation, as the chronic progression of underlying macular atrophy and fibrosis ultimately limits long-term visual restoration.[17] Identifying predictors of response to Faricimab prior to switching remains a key gap in the literature and is essential for optimising patient selection.[18,19]

This study investigates short-term outcomes of switching to Faricimab in a UK single-centre, treatment-experienced nAMD population. The primary objective was to evaluate anatomical efficacy (CMT reduction and complete macular dryness) following Faricimab switching in treatment-experienced nAMD patients over eight injections. Secondary objectives included: (1) assessing functional outcomes (BCVA change and correlation with anatomical response), (2) determining treatment interval extension capacity, (3) identifying baseline predictors of anatomical response, (4) characterizing safety profile including intraocular inflammation incidence.

Materials and Methods

Study Design

This retrospective, single-centre study was conducted at Swansea Bay University Health Board, Wales, UK. The study analysed data from November 2022 to December 2024; the first Faricimab injection at this site was November 2022. Patient records, OCT datasets, and notes were reviewed for the period November 2024–March 2025.

Study Population

Patients with active nAMD switched from prior anti-VEGF therapy to Faricimab and received at least eight injections were eligible. Switching was for inadequate response to previous anti-VEGF agents. Inadequate response was defined as an inability to extend intervals beyond 4–6 weeks due to persistent presence of fluid with or without significant drop in vision (greater than 5 letters on LogMAR).

Data Collection

Data included demographics, phacoemulsification history, date of diagnosis, method of diagnosis, prior injection history, and pre-switch treatment interval. OCT imaging used a Triton model. Macular volume scans (25° × 25°) centred on the fovea had been captured at each visit using automated settings. Assessment for the presence of intraretinal and subretinal fluid was done manually via trained ophthalmic clinicians; this was either specialty trainee ophthalmologists or hospital optometrists with a post-graduate qualification in AMD. To assess consistency, twenty randomly selected images were re-graded by a consultant ophthalmologist, yielding 95% agreement (19/20 cases), with the single discrepant case involving trace intraretinal fluid (IRF) resolved by consensus review.

Treatment Protocol: Faricimab

In accordance with local policy all patients were started on three monthly loading doses of Faricimab, then switched to a treat-and-extend regimen. Intervals were extended or reduced based on retinal activity: intervals followed a stepwise increase of four weeks if the retina was inactive or were reduced by two weeks if the retina was active. Patients were

defined as having active nAMD if they had IRF ± sub retinal fluid (SRF) ± new haemorrhages on their OCT images. Fluid or resolving haemorrhages that were present for three consecutive visits may have been considered inactive and were eligible for a trial of extension of treatment interval at the clinician's discretion. Detailed comparison of the loading and treat-extend protocol at this site with the existing Aflibercept standard 2 mg dose and the Faricimab 6 mg dose is demonstrated in Supplementary Figure 1. Patients with incomplete imaging or data, sight-altering interventions, or treatment interruptions >8 weeks were excluded.

Outcomes

Outcomes at baseline and after each of the eight injections included CMT, best-corrected visual acuity (VA), and fluid status (IRF, SRF, pigment epithelial detachment, haemorrhage) based on OCT images obtained prior to each injection. Complete macular dryness is defined by the absence of both intraretinal and subretinal fluid (SRF ± IRF). Active nAMD is defined by the presence of new or residual intraretinal and/or subretinal fluid and/or new haemorrhages; inactive nAMD is characterized by a dry macula, resolving old haemorrhage, and persistently unchanged fluid.

Statistical Analysis

All statistical analyses were performed using R version 4.3.x and Microsoft Excel. Statistical significance was set at $p<0.05$ for all tests. Cohen's d effect sizes are reported alongside statistical tests to aid clinical interpretation. Effect sizes are interpreted as follows: small ($|d|<0.2$), small-to-medium (0.2–0.5), medium (0.5–0.8), and large ($|d|>0.8$).

Safety

All adverse events, including intraocular inflammation, intraocular pressure rise, and endophthalmitis, were recorded. Each incident was reviewed by a consultant ophthalmologist in medical retina.

Ethics

Approved as a service evaluation by the Clinical Audit Department at Swansea Bay University Health Board. All procedures followed the Declaration of Helsinki and patient confidentially were strictly adhered too with data anonymisation.

Results

Study Cohort

A total of 892 eyes from 732 patients on Faricimab were initially identified. About 427 eyes were excluded as they were naïve with no previous anti-VEGF treatment. About 320 eyes were excluded as they were bilateral eyes. The reason for excluding bilateral eyes is due to the nature of treatment-and-extend regime at this centre which dictates you treat both eyes at the same interval as the worse performing eye. This would mean on analysis eyes that could be dry were not extended out due to the fellow eye remaining wet. Then a remaining 36 eyes did not have achieved 8 injections or data was missing across any of their visits. Discussed in further detail below, 2 eyes were excluded due inflammation secondary to Faricimab resulting in discontinuation of the drug. The final 67 eyes from 67 treatment-experienced patients with nAMD were included in the final analysis. All patients had received a three-dose loading course followed by a treat-and-extend regimen of Faricimab with eight injections in total. Baseline demographic and clinical characteristics are summarised in Table 1. "Baseline" was defined as the first Faricimab injection, and activity status at this point was recorded immediately prior to drug administration.

Best-Corrected Visual Acuity (BCVA)

No statistically significant improvement in BCVA occurred at any timepoint during the treatment course as shown in Table 2. Mean BCVA remained essentially unchanged from baseline (0.420 logMAR, SD 0.283) to the eighth injection (0.406 logMAR, SD 0.254; $p=0.6043$, paired *t*-test) visualized in Table 2.

Table 1 Baseline Characteristics of the Cohort

Characteristics	
Number of eyes	67
Number of patients	67
Age (years), mean ± SD	76.2 ± 8.1
Sex ratio (Male: Female)	25: 42
Disease duration* (weeks), mean (range)	37.1 (28.1–60.8)
Previous treatment	
Aflibercept	67 (100%)
Ranibizumab	19 (28%)
Previous injections, median (range)	30 (10–78)
Baseline visual and anatomical measures	
BCVA (logMAR), mean	0.42 ± 0.28 (0–1.22)
CMT (μm), mean (range)	244.5 ± 62.2 (120–561)
Baseline fluid status	
Any fluid present	52 (77.6%)
Intraretinal fluid (IRF)	29 (43.2%)
Subretinal fluid (SRF)	36 (53.7%)
Haemorrhage	2 (3.0%)

Note: *Time period from date of diagnosis of nAMD to most recent injection.

Table 2 Mean BCVA from Baseline Until Injection Eight

Injection	**Mean BCVA (logMAR)**	**SD**	**Δ from Baseline (logMAR)**	**p-value**
1 (Baseline)	0.42	±0.28	–	–
3	0.40	±0.27	−0.02	0.32
5	0.37	±0.26	−0.05	0.30
8	0.40	±0.25	−0.02	0.60

Note: The change in baseline is also shown with the p-value; No statistically significant differences were observed at any timepoint (All P>0.05).

Central Macular Thickness (CMT)

Central macular thickness results are shown in Table 3 and demonstrate rapid drying during the loading phases (injection 1–3) following a period of stabilization and steady reduction across the treatment course, with statistical significance achieved at the eighth injection. Mean CMT decreased from 244.5 μm (SD 62.2) to 227.6 μm (SD 38.5) at the eighth injection, representing a mean reduction of 16.9 μm (p=0.0084, Cohen's d=0.32, paired *t*-test). Intermediate measurements showed variable changes, with temporary increases observed at injection 5 (247.3 μm, SD 55.4), indicating a non-

Table 3 Central Macular Thickness (CMT) Changes Over Eight Faricimab Injections Showing the Mean, Standard Deviation, Change from Baseline, and p-value Indicating a Statistically Significant Difference

Injection	**Mean CMT (μm)**	**SD**	**Δ From Baseline (μm)**	**p-value**
1 (Baseline)	244.5	±62.2	–	–
2	237.5	±59.1	−7.0	–
3	233.1	±53.5	−11.4	–
5	247.3	±55.4	−10.5	–
8	227.6	±38.5	−17.0	0.0084

linear anatomical response pattern. Pearson correlation analysis revealed no significant association between CMT change and BCVA change (r=0.059, p=0.172). The rapid reduction in CMT and then stabilisation reflects the nature of the treat-and-extend regime which is protocol driven.

Treatment Interval

At baseline, 59 eyes (88.1%) were treated at 4-week intervals and 8 eyes (11.9%) at 6-week intervals, reflecting high treatment burden on prior anti-VEGF therapy. Following eight Faricimab injections, the distribution shifted: 36 eyes (53.7%) remained at 4-week intervals, 18 eyes (26.9%) extended to 6-week intervals, 8 eyes (11.9%) achieved 8-week intervals, and 5 eyes (7.5%) reached ≥12-week intervals. This change in distribution is shown in Figure 1A, (baseline intervals) compared to Figure 1B demonstrating the intervals at the end point of the study. Overall, 31 eyes (46.3%) achieved interval extension, 32 eyes (47.8%) maintained baseline intervals, and 4 eyes (6.0%) required interval shortening. To assess statistical significance, outcomes were separated into "extended" versus "not extended" intervals from baseline to injection 8. McNemar's test confirmed a statistically significant shift toward longer intervals (p=0.002), indicating that nearly half of heavily pretreated patients achieved meaningful treatment burden reduction. The median treatment interval at injection 8 was 4 weeks (IQR 4–6; range 4–16).

Fluid Status and Resolution Patterns

The proportion of eyes achieving complete macular dryness (absence of intraretinal and subretinal fluid) increased significantly across the treatment course. At baseline, 15 eyes (22.4%) were classified as dry, increasing to 29 eyes (43.3%) by the third injection, before declining and recovering to 22 eyes (32.8%) by the eighth injection. Cochran's Q test confirmed a statistically significant change in the proportion of dry eyes across the eight injections (Q=18.79, p=0.0089). Fluid phenotype distribution evolved substantially across the treatment course (Figure 2). At baseline, subretinal fluid (SRF) alone comprised 28.4% of cases, intraretinal fluid (IRF) alone 11.9%, combined IRF and SRF 37.3%, and dry eyes 22.4%. By the third injection, the dry proportion increased to 43.3%, with concurrent reduction in all fluid phenotypes. By injection 8, dry eyes represented 32.8% of the cohort, while combined IRF and SRF decreased from 37.3% to 17.9%, indicating preferential resolution of coexisting fluid types. Eyes with intraretinal fluid

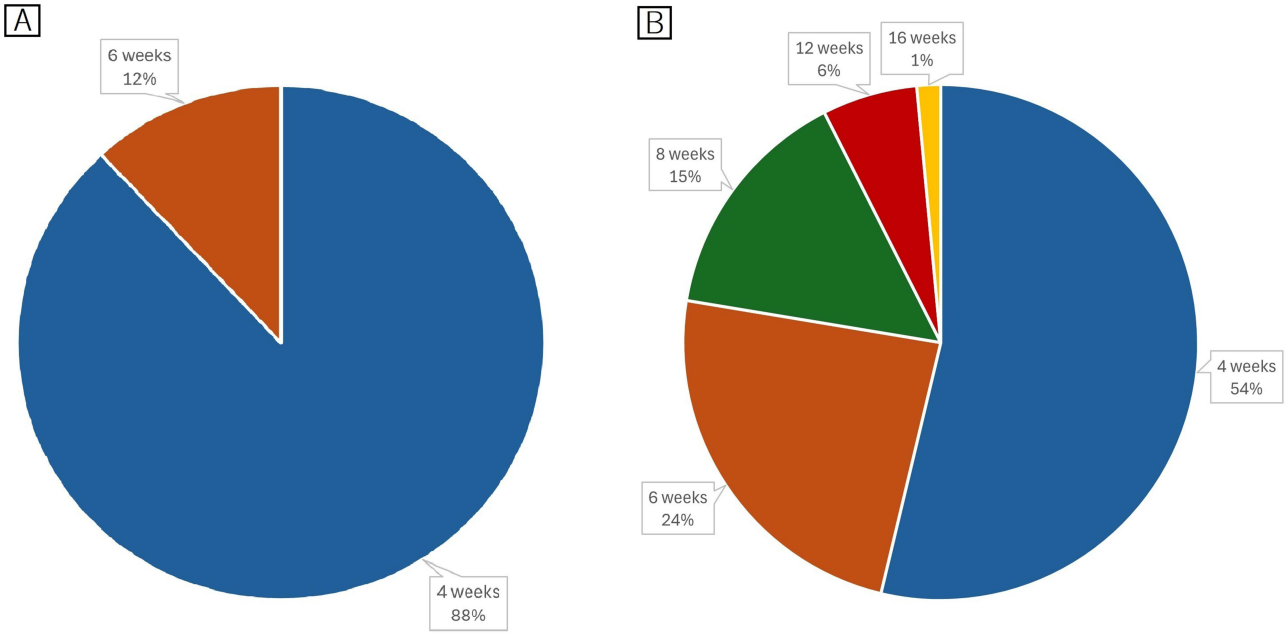

Figure 1 Distribution of Treatment Intervals at Baseline (**A**) [Left] and After Eight Faricimab Injections (**B**) [Right]. Baseline treatment was predominantly 4-weekly (88.1%), reflecting high burden on prior therapy.

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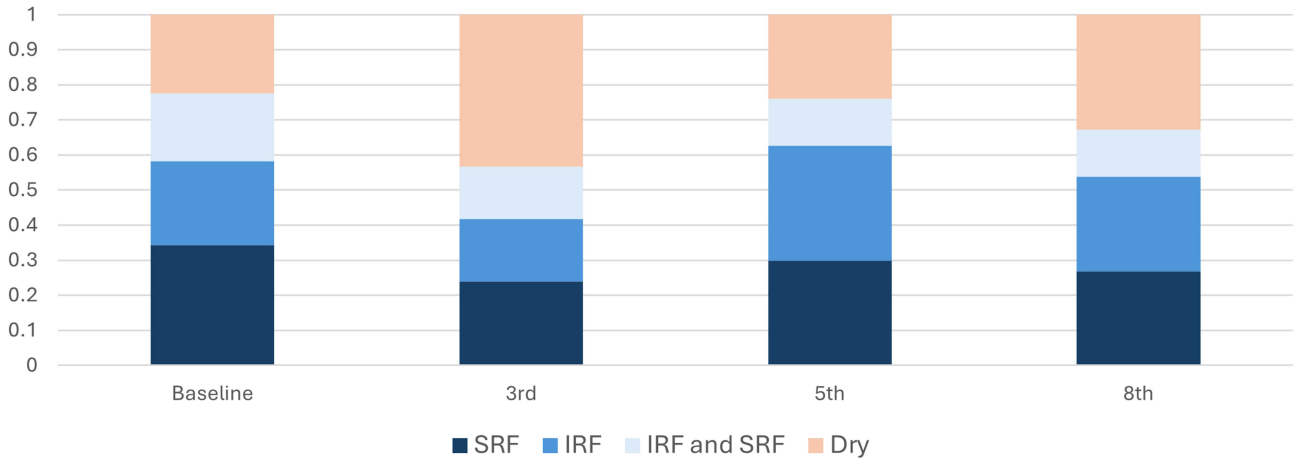

Figure 2 Stacked Bar Chart of Macular Fluid Phenotype Distribution Across Eight Faricimab Injections. Each Bar Represents the Proportion of Eyes in Each Fluid Category: SRF Alone (Dark Blue), IRF Alone (Light Blue), Combined IRF and SRF (Salmon), and Dry (Tan).

demonstrated slightly higher mean CMT (251.6 μm) compared with those without (239.1 μm; p=0.15, independent *t*-test), confirming the structural association between IRF presence and increased macular thickness.

Time to Macular Dryness

Kaplan–Meier survival analysis of all 67 eyes assessed time to first complete macular dryness. At baseline (injection 1), 22.4% (15/67) of eyes were classified as dry. The proportion achieving complete dryness increased to 43.3% (29/67) by the third injection, then declined to 32.8% (22/67) by the eighth injection. The median time to achieve complete dryness was 3 injections (95% CI: 2–5).

Baseline Characteristics and Treatment Response

To assess whether baseline characteristics predicted treatment response, patients were classified into three groups based on interval change from baseline to injection 8: good responders (n=31, 46.3%, interval extended), partial responders (n=32, 47.8%, interval maintained), and non-responders (n=4, 6.0%, interval reduced). The baseline and final characteristics by treatment response group are summarised below in Table 4.

Non-responders had significantly worse baseline BCVA (0.57 logMAR) compared to partial and good responders (0.38–0.39 logMAR; ANOVA p=0.042). However, this group difference was driven by only 4 non-responders, and correlation analysis across the full cohort revealed no significant linear relationship between baseline BCVA and final

Table 4 Baseline and Final Characteristics by Treatment Response Group**

Variable	Non-Responders (n=4)	Partial Responders (n=32)	Good Responders (n=31)	P-value*
Central Macular Thickness (μm)				
Baseline (Injection 1)	202 ± 52	240 ± 52	254 ± 72	0.255
Final (Injection 8)	214 ± 13	225 ± 40	232 ± 40	0.621
Change from baseline	−12 ± 57.0	15 ± 42.6	22 ± 57.9	0.425
Best-Corrected Visual Acuity (logMAR)				
Baseline (Injection 1)	0.57 ± 0.31	0.38 ± 0.27	0.39 ± 0.27	0.042*
Final (Injection 8)	0.65 ± 0.22	0.39 ± 0.24	0.39 ± 0.27	0.140
Change from baseline	0.08 ± 0.17	0.01 ± 0.24	−0.00 ± 0.19	0.599

Notes: *ANOVA used for all comparisons. p < 0.05. Positive CMT change indicates reduction in thickness (improvement). ** Good responders (interval extended), partial responders (interval maintained), and non-responders (interval reduced).

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treatment interval (Spearman's rho = −0.138, p=0.267). This suggests that while non-responders may have poorer baseline vision, baseline BCVA alone does not reliably predict treatment interval outcomes.

Baseline treatment burden was also analysed with patients being stratified by median prior anti-VEGF injection count (30 injections). High-burden patients (>30 injections, n=32, mean 47.7 ± 13.6 injections, range 31–78) were compared to low-burden patients (≤30 injections, n=35, mean 20.0 ± 5.4 injections, range 10–30) using Kaplan–Meier survival analysis depicted in Figure 3. Stratified analysis revealed no significant difference in time to first complete macular dryness between burden groups (log-rank p=0.9756).

Dryness and Interval Extension

To determine whether patients that were dry led to interval extension, analysis was performed at the 5th injection and 8th injection as visualized in Figure 4. Eyes that achieved macular dryness had significantly longer treatment intervals compared to those without dryness (median [IQR]: 6 [5.5–6] weeks vs. 4 [4–6] weeks; Mann–Whitney *U*-test, W = 285.5, p = 0.046). By the 8th injection, this difference was more pronounced (median [IQR]: 6 [6–8] weeks vs. 4 [4–5] weeks; W = 164.5, p < 0.001). Statistical analysis was performed at the 5th and 8th injections, representing the treat-and-extend phase of therapy. Injections 1–3 were excluded as they represent the standard loading phase with protocol-mandated 4-week intervals.

Early Anatomical Response and Sustained Dryness

Of the 67 patients analysed, 29 (43.3%) achieved dryness by injection 3, while 38 (56.7%) remained wet. Early responders demonstrated significantly higher rates of sustained dryness at subsequent timepoints. At injection 5, 41.4% of early responders were dry compared to 10.5% of non-responders (p = 0.008). By injection 8, these rates were 48.3% versus 21.1%, respectively (p = 0.037) (Figure 5).

While current dryness status at injection 8 strongly predicted treatment intervals (median 6 weeks [IQR 6–8] for dry patients vs 4 weeks [IQR 4–5] for wet patients, p < 0.001), historical dryness status at injection 3 did not independently

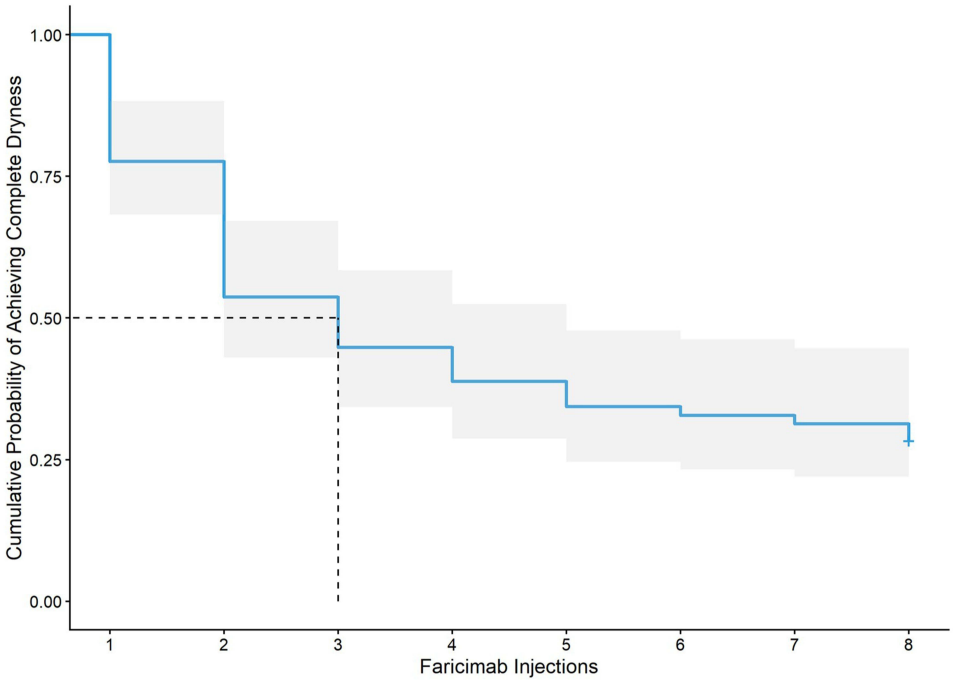

Figure 3 Kaplan–Meier Survival Curves from the total cohort looking at the time to complete macular dryness. Grey zone represents the 95% Confidence Interval. This demonstrates that by the 3rd injection 50% of the cohort were dry in a cohort of treatment resistant active nAMD.

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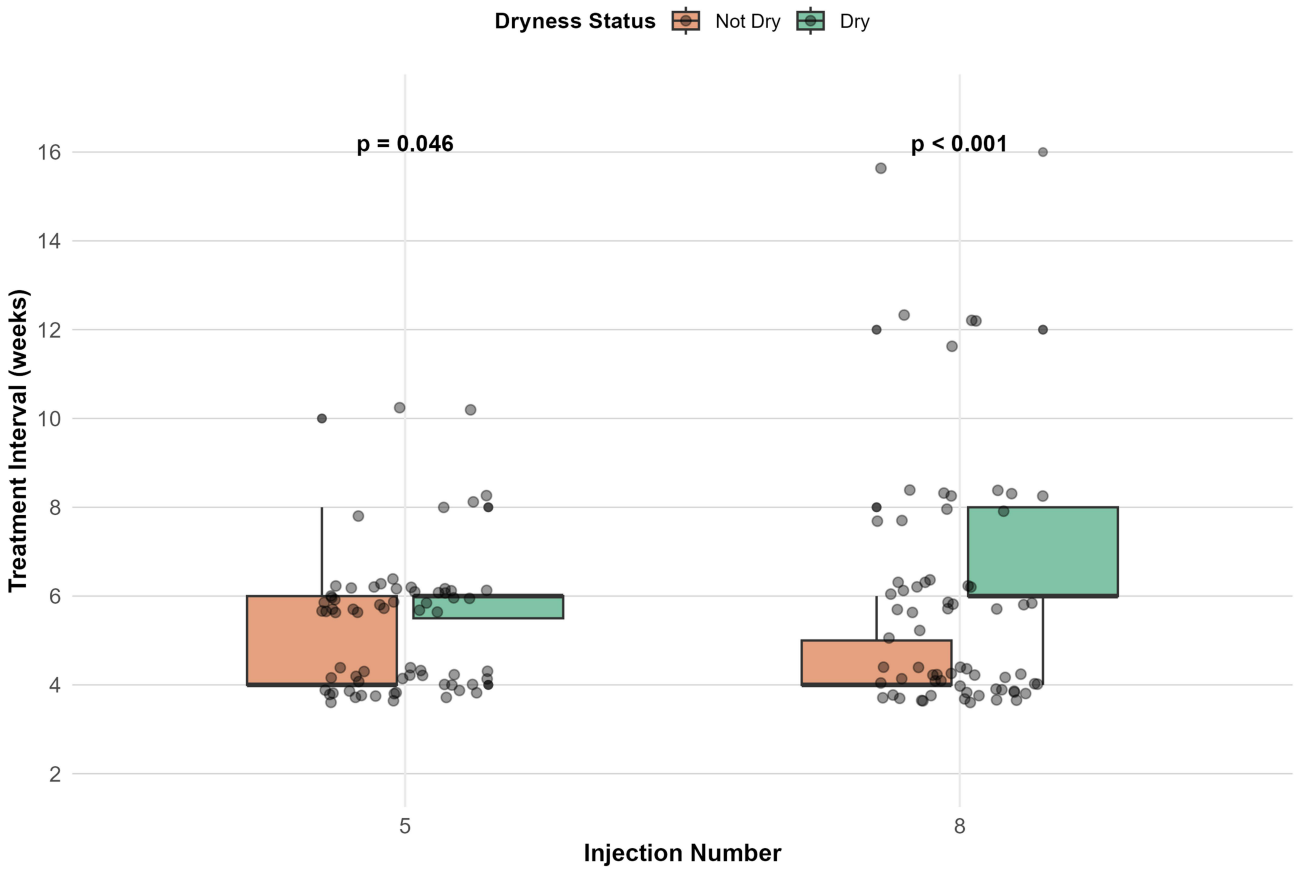

Figure 4 Treatment Interval Extension by Macular Dryness Status Boxplots showing median treatment intervals (horizontal line within box), interquartile range (box), and individual patient values (dots) at the 5th and 8th Faricimab injections, stratified by macular dryness status. Patients achieving macular dryness are shown in green compared to those without dryness Orange.

predict intervals at injection 8 (median 6 weeks [IQR 4–6] for early responders vs 4 weeks [IQR 4–6] for non-responders, p = 0.217). Early dryness alone was not significantly associated with long term interval extension.

Safety Profile

Two cases of sterile intraocular inflammation (IOI) were observed, representing a rate of 0.36% (2/548; 548 represents the total number injections this cohort of 69 patients received). Both cases resolved following Faricimab discontinuation. A detailed analysis of the patients' characteristics is shown in Supplementary Table 1.

Discussion

Anatomical Outcomes

While the CMT reduction here was less than in switching cohorts reported by Janmohamed et al (−27.5 µm), Bantounou et al (−27.1 µm), and Borchert et al (−38 µm).[10–12] Our results align with other real-world series that found substantial variability associated with greater prior treatment exposure, however dryness at the endpoint (injection 8, 32.8%) was lower than comparator studies.[10–16] Fluid re-accumulation after initial dryness (43.3% at injection 3, declining to 32.8% at injection 8) mirrors prior real-world evidence and contrasts with sustained dryness in treatment-naïve populations of the pivotal TENAYA and LUCERNE trials (61–67% at 2 years).[6,7,10–16,20] This reduced durability in switching cohorts may reflect incomplete therapeutic response in chronic disease, or persistent vascular instability—even with dual VEGF-A/Ang2 blockade.[21–23] Fluid volatility has been mechanistically linked to subretinal hyperreflective material and photoreceptor disruption, limiting efficacy of new higher dose therapies.[22,23] Consistent with biomarker-based studies, eyes with IRF at injection 8 had higher mean CMT correlating IRF with greater macular thickening than SRF alone.[24–26]

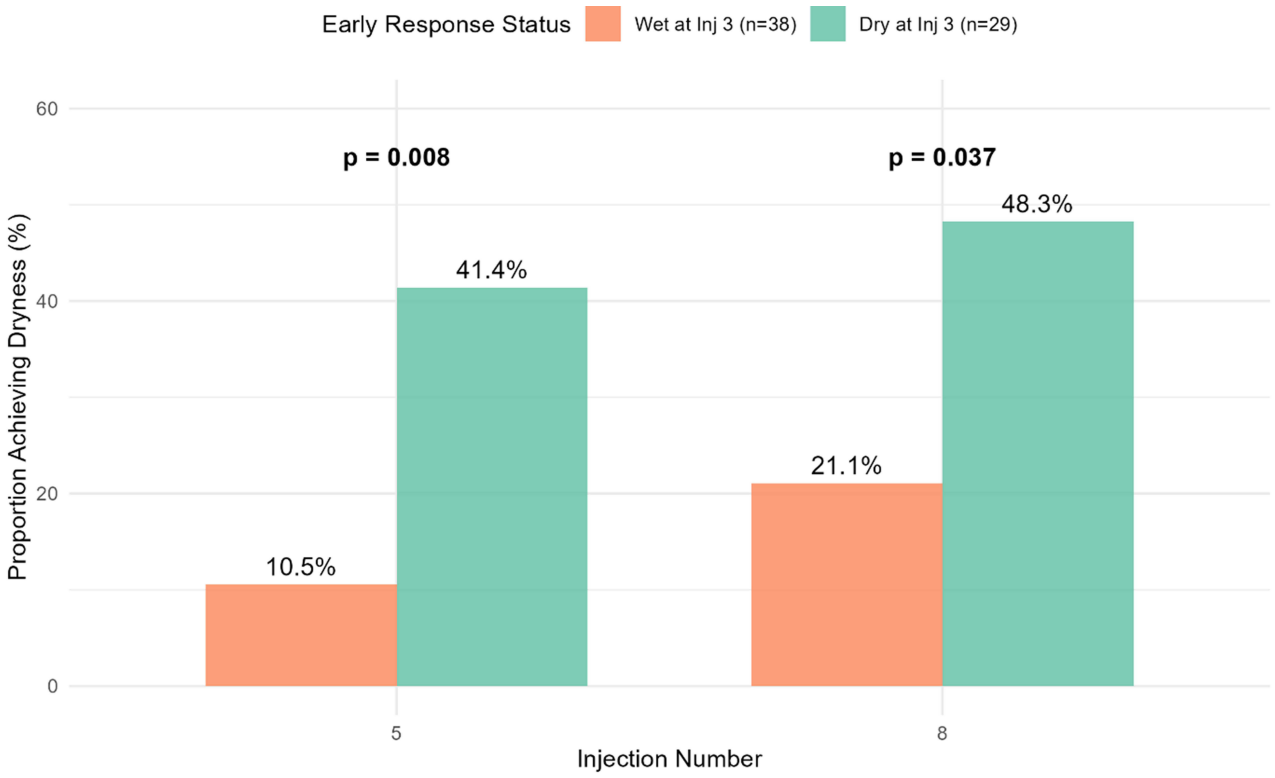

Figure 5 Dryness Trajectory by Early Response Status. Early responders (dry at injection 3) had significantly higher dryness rates at injections 5 (41.4% vs 10.5%, p = 0.008) and 8 (48.3% vs 21.1%, p = 0.037) compared to non-responders.

Structure–Function Dissociation and Predictors of Response

Visual stability despite anatomic improvement reiterates the well-characterized structure–function dissociation seen in chronic nAMD; Ehlers et al linked fluid volatility to photoreceptor and ellipsoid zone loss, with functional ceiling effects in treatment-experienced eyes.[22,23] Chronic disease and higher cumulative anti-VEGF exposure are associated with greater risk of irreversible photoreceptor atrophy and attenuated treatment response.[6,24,27] No significant relationship was detected between baseline BCVA or BCVA change and final treatment interval, consistent with the paradigm that individualised intervals should be based on retinal anatomy, not vision.[3,26] Our findings reinforce a recent systematic review by Patel et al and expert consensus by Zur et al that visual function should not guide interval extension once chronic atrophic changes have developed.[28,29]

Treatment Burden and Interval Extension

The absence of association between prior anti-VEGF injection burden and time to dryness, as well as similar extension rates between high- and low-burden groups, dispels the notion that heavy pretreatment precludes Faricimab responsiveness.[14] The mechanistic rationale lies in Faricimab's dual-targeted pathway; laboratory and clinical studies confirm its added benefit relative to anti-VEGF monotherapy by targeting angiopoietin-2.[6] This new mechanism may address VEGF-independent drivers of exudation, supporting the observed interval extension and reproducible treatment burden reduction in nearly half of real-world switchers.[10–15] Early dryness during loading did not predict the capacity for interval prolongation seen in both this cohort and existing studies.[11,13]

Safety Profile

The rate of sterile intraocular inflammation (IOI) (0.36%) in this cohort is significantly less than the TENAYA/LUCERNE trial rates (2.0%) but similar to the frequency seen in recent European reports.[6,7,30,31] The literature attributes Faricimab associated IOI to immunological responses unique to its bispecific antibody structure, with no definitive

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mechanism established.[31,32] All IOI cases in our cohort resulted in incomplete visual recovery, reiterating the importance of vigilance.[30,31]

Clinical Implications

Faricimab offers meaningful burden reduction and statistically significant anatomical improvement in heavily pretreated, refractory nAMD.[11,12,14] Visual gains remain elusive once irreversible atrophy has set in, supporting an approach where real-time OCT activity, not functional measures or historic response, guides extension.[13,22] There is no evidence that high prior injection count should deter appropriate therapy switching, and adverse event vigilance is paramount in real-world settings.[30,31]

Limitations

The small sample size, particularly the non-responder group (n=4), limited statistical power for stratified analyses. The single-centre retrospective design and relatively short follow-up duration (8 injections, approximately 8–18 months) limit generalizability and assessment of long-term durability. The absence of imaging biomarkers beyond central macular thickness (such as ellipsoid zone integrity or subretinal hyperreflective material quantification) limited assessment of mechanisms underlying structure-function dissociation.[22,23]

Conclusion

Faricimab switching achieves modest anatomical improvement with meaningful treatment burden reduction in a refractory nAMD population, albeit without vision recovery, a direct function of advanced and atrophic disease.[24,27] Treat-and-extend protocols based on current OCT activity best serve such patients, and interval extension using Faricimab is feasible even after extensive prior treatment. Continued monitoring for IOI is warranted, with patient selection and education a critical part of ongoing care.

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