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ORIGINAL RESEARCH

Efficacy and Safety of Switching from Ranibizumab to Brolucizumab in Age-Related Macular Degeneration: Multicenter Real-World Outcomes

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Video Abstract

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Purpose: To assess whether switching from ranibizumab (0.5 mg) to brolucizumab (6 mg) improves injection intervals, disease activity, and anatomical/functional outcomes in wet age-related macular degeneration (wAMD).

Methods: This multicenter retrospective study included patients aged ≥50 years with active wAMD, baseline visual acuity (VA) 35–70, lesion size ≤8 disc areas, and submacular hemorrhage ≤25%. All had prior ranibizumab and were switched to brolucizumab for suboptimal response. VA and central retinal thickness (CRT) were recorded at switch, 6, and 12 months. Injection counts before and after switching were analyzed. Safety was monitored for intraocular inflammation (IOI) and discontinuation.

Results: Seventy-nine eyes (75 patients) were enrolled; 66 eyes (60 patients, median age 75.0 years [IQR: 70.0–80.0]) completed 12 months. Patients received median 12.0 ranibizumab injections [IQR: 8.0–19.0] pre-switch and 5.0 brolucizumab injections [IQR: 4.0–6.0] post-switch. Median switch VA was 50.0 letters [IQR: 36.5–63.0]; CRT was 319.0 µm [IQR: 258.0–393.0]. At 6 months, VA improved to 51.0 [IQR: 38.0–66.5] ($p = 0.0001$) and CRT decreased to 255.0 µm [IQR: 216.0–298.0] ($p < 0.00000001$). At 12 months VA was 50.5 [IQR: 38.5–68.0] ($p = 0.0004$ vs baseline) and CRT 251.5 µm [IQR: 207.5–282.5] ($p < 0.0001$). Adverse events included 6 IOI cases, with discontinuation in 9 eyes overall.

Conclusion: Switching to brolucizumab reduced CRT, modestly improved or stabilized VA, and decreased injection frequency with acceptable safety. Limitations include retrospective design, modest sample size, and exclusion of poor visual outcomes, potentially introducing selection bias.

Keywords: wet age-related macular degeneration, anti-VEGF therapy, ranibizumab, brolucizumab, switch, real outcomes

Introduction

Wet age-related macular degeneration (wAMD) is a serious eye disease that may result in vision loss. This work presents data from real-world practice and evaluates the effect of switching. A large part of our aging population is at risk of serious vision loss (8.7% of the worldwide population has AMD, and the exposed number of people with the disease is around 196 million, increasing to 288 million in 2040).[1]

Early diagnosis and treatment are key aspects to stop or slow the disease progression. Modern therapeutic approaches are currently dominated by the repeated administration of anti–vascular endothelial growth factor (anti-VEGF) injections. Despite the most advanced treatment and its significant success, recurrent injections and monitoring visits still impose

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a heavy extension on patients and medical centers.[2] Even with the most frequent dosing schedules, therapy often does not achieve a complete response. In clinical practice, patients may be considered non-responders if, despite adequate dosing, they continue to show persistent or recurrent fluid on OCT, require very short treatment intervals to maintain disease control, or fail to achieve meaningful functional or anatomical improvement. However, the definition of a non-responder is not universally standardized and may vary slightly between institutions or treatment protocols.[3,4] Sometimes it is appropriate to change the treatment strategy, typically by changing the anti-VEGF agent (switching).[5–7] Long-term anti-VEGF therapy, for example with ranibizumab, requires multiple doses of intravitreal injections, and regular monitoring visits. This often causes difficulties, eg, reducing patients' adherence to therapy and increasing health care costs.[8–10]

In addition, potential complications such as endophthalmitis and retinal detachment associated with too frequent dosing underline the importance of finding alternative therapeutic options.[11,12] In recent years, brolucizumab, a novel anti-VEGF agent (approved by the Food and Drug Administration in October 2019) characterized by its smaller molecular size (26 kDa) and extended dosing interval, has gained recognition as a viable alternative for the treatment of wAMD.[13] The requirement for optimizing therapeutic strategies in wAMD has led to an examination of the safety, efficacy, and feasibility of transitioning from ranibizumab to brolucizumab. The advantages of brolucizumab are thought to arise from its unique structure as a single-chain antibody fragment, characterized by a lower molecular weight that potentially allows better tissue delivery and higher concentration in the intravitreal space.[14,15]

Registration studies (Phase III trial) have shown that brolucizumab is non-inferior to aflibercept in terms of visual function outcomes.[16] Extending the dosing interval can reduce treatment burdens, potentially improving patient adherence and leading to better treatment outcomes. However, brolucizumab's introduction has also been accompanied by well-recognized safety concerns. Post-marketing surveillance and clinical trial data have reported adverse events such as IOI and retinal vasculitis, sometimes with vascular occlusion, which may result in severe and irreversible vision loss.[17–22] These risks require careful patient selection and monitoring when considering therapy changes. Brolucizumab was selected as the switch agent in this study because of its demonstrated ability to achieve longer dosing intervals than ranibizumab in a proportion of patients, its high molar dose per injection, and evidence from registration trials suggesting robust anatomical drying.[23] Other available alternatives were considered but not chosen because the primary goal was to test an agent with potentially greater durability in patients already insufficiently controlled on ranibizumab. This retrospective real-world outcome analysis aims to assess the anatomical and functional results of switching from ranibizumab to brolucizumab in patients with non-response to previous therapy. As cases were selected retrospectively, the 12-month period varies between 48 and 52 weeks, depending on clinical inclusion criteria and power analysis. Although randomized clinical trials have demonstrated the efficacy of brolucizumab, real-world evidence on switching to brolucizumab in Treat-to-Extent regimen remains limited.[18]

Methods

This multicenter, retrospective, real-world study evaluated patients with wAMD who were switched from ranibizumab (0.5 mg) to brolucizumab (6 mg) due to non-responsiveness to prior treatment. Patients were followed for 12 months after the switch. The data were collected from February 2023 to December 2024.

Study Population

Eligible participants (with non-responsiveness conditions) were: (1) ≥50 years of age with active wAMD and baseline best-corrected visual acuity between 35 and 70 ETDRS letters, (2) lesion size ≤8 disc areas, and (3) submacular hemorrhage involving ≤25% of the lesion.

Non-responsiveness to ranibizumab[24] in our cohort was defined as follows: After completing the standard 3-dose monthly loading phase and during a treat-and-extend regimen (minimum observation ≥4 months; ≥4 visits/injections in total), patients met ≥1 of the following criteria, each confirmed at two consecutive visits: (a) persistent intraretinal or subretinal fluid (IRF/SRF) on OCT despite treatment[25] at ≤8-week intervals, or recurrence of fluid when attempting to extend beyond 8 weeks, (b) requirement to maintain treatment intervals ≤6 weeks to control exudation in the 3 months prior to switching, (c) <10% reduction in CRT from pre-switch baseline, (d) <5-letter gain or a loss ≥5 letters in ETDRS VA despite treatment.

All patients initially received intravitreal ranibizumab injections according to a treat-and-extend regimen, starting[26] with a three-dose loading phase (4-week intervals) as recommended by the Czech Vitreo-Retinal Society. Interval modifications followed the Society's guidelines and clinical findings at follow-up visits, with stepwise extension up to a maximum of 12 weeks in the absence of OCT-detected IRF/SRF, and shortening of intervals in case of recurrence.

Exclusion criteria were: (1) a ≥3-line loss of ETDRS score during follow-up, (2) final best corrected VA worse than 35 ETDRS letters, or (3) development of macular fibrosis or geographic atrophy during the study period. Patients who did not meet treatment criteria set by the EMA, the drug manufacturer, Czech public health insurance, or the Czech Vitreo-Retinal Society were excluded.

In this real-world cohort, some patients contributed data from both eyes. Excluding such patients would have reduced generalizability and introduced selection bias. Because all primary outcomes (CRT, VA, OCT fluid status) were objectively measured per eye and analyzed separately, the risk of bias from correlated subjective assessments between fellow eyes is minimal. A sensitivity analysis including only one randomly selected eye per patient produced results consistent with the primary analysis id displayed in Supplementary Table 1. Visual acuity and CRT outcomes were nearly identical, with differences <1 letter and <2 µm. Non-normally distributed variables are presented as median, and normally distributed change scores as mean ± SD, confirming the robustness of the primary findings.

Data Collection and Outcome Measures

At baseline (prior to switching therapy), patients underwent (1) comprehensive ophthalmic examination, including visual acuity assessment using ETDRS letter score, (2) fundus photography (Zeiss Clarus 500), and (3) optical coherence tomography (OCT; Carl Zeiss Angioplex) to measure central retinal thickness (CRT in statistics). These assessments were repeated at 6 and 12 months after initiating brolucizumab. n real-world practice, minor deviations from the nominal schedule occasionally occurred, most often due to patients rescheduling visits for health-related or logistical reasons. For this analysis, the 12-month follow-up was defined as the visit occurring within 48–52 weeks of the first brolucizumab injection; if this exact window was not met, the nearest available visit within the interval was used.

The indication for switching to brolucizumab included persistent or progressive exudative activity on OCT or clinical examination, and/or a clinical need to extend treatment intervals. Switching was performed using a loading phase followed by dosing per the approved label.

Patients were monitored at regular intervals with OCT imaging and visual acuity testing. Special attention was paid to signs of IOI in both the anterior and posterior segments. All OCT imaging data were analyzed using the Zeiss Forum platform, with a focus on fluid dynamics. Patients who completed 6 months of follow-up were included in the 6-month analysis, while only those completing 12 months were included in the 12-month analysis.

Statistical Analysis

Descriptive statistics were used to summarize patient demographics and clinical characteristics. Normality of continuous variables was assessed using the Shapiro–Wilk test. As all key outcome variables (VA, CRT) deviated significantly from a normal distribution ($p < 0.05$), only nonparametric statistical tests were applied. Changes in paired measurements were analyzed using the Wilcoxon signed-rank test, and associations between variables were assessed using Spearman's rank correlation coefficient (r_s). For the regression models, homoscedasticity was assessed using the Breusch–Pagan test, which indicated no violation of this assumption ($p > 0.05$). All outcomes are reported as medians and interquartile ranges (IQR). In cases where both eyes from the same patient were included, a sensitivity analysis using only one randomly selected eye per patient was performed, yielding results consistent with the primary analysis. Statistical analyses were performed using IBM SPSS Statistics (version 30.0.0) and GraphPad Prism 10 (GraphPad Software, San Diego, CA, USA). A p-value of < 0.05 was considered statistically significant.

Ethics

University Hospital Hradec Králové Ethics Committee approval was obtained for this study. Informed consent was obtained prior to treatment and data collection, in accordance with ethical standards and requirements and practices at the University Hospital as well. The research adhered to the tenets of the Declaration of Helsinki.

Results

Patient Characteristics

The study initially included 79 eyes (75 patients) meeting the non-responsiveness criteria. The median age at baseline was 75.0 years IQR:70.0–80). During the first 6 months after the switch, 3 eyes (3 patients) discontinued treatment due to vitreous occlusion and retinal pigment epithelium (RPE) atrophy, leaving 76 eyes (72 patients) in active follow-up. Between months 6 and 12, 6 additional eyes (6 patients) were withdrawn because of IOI, a switch from brolucizumab to another anti-VEGF agent, or vision deterioration below treatment criteria. At the 12-month follow-up, 70 eyes (66 patients) completed the study. Baseline demographic and clinical characteristics of the analyzed cohort, including details of excluded cases, are presented in Supplementary Table 2.

Administration of Treatment Pre- and Post-Switch

Prior to the switch, the eyes participating in our study received 4–39 injections of ranibizumab (median 12.0 [IQR: 8.0–19.0]). Then, during the 12-month follow-up, 3–8 injections of brolucizumab were administered (median 6.0 [IQR: 5.0–7.0]). Following the switch, brolucizumab was initiated with a loading phase of three consecutive monthly injections (4-week intervals, 3 applications in total) in accordance with the recommendations of the Czech Vitreo-Retinal Society and the manufacturer. Thereafter, a treat-and-extend regimen was applied, with interval modifications guided by the Society's recommendations and clinical findings at follow-up visits.[27] Extension was performed stepwise from 4 up to a maximum of 12 weeks, provided no intraretinal or subretinal fluid was present on OCT; intervals were shortened if disease activity recurred. This approach resulted in variation in the total number of injections administered during the observation period. Switching from ranibizumab to brolucizumab significantly lowered the need for injections ($p < 0.001$) (Figure 1, Supplementary Table 3). Patients eligible for brolucizumab treatment were fully briefed on its benefits, risks, and potential side effects, including possible agent substitution based on efficacy or tolerance. Upon switching, patients were clearly informed of the reasons and potential side effects. Intravitreal injections followed strict safety and hygiene protocols at each clinical site. Treatments were conducted in designated ambulatory settings, adhering to aseptic and procedural guidelines.

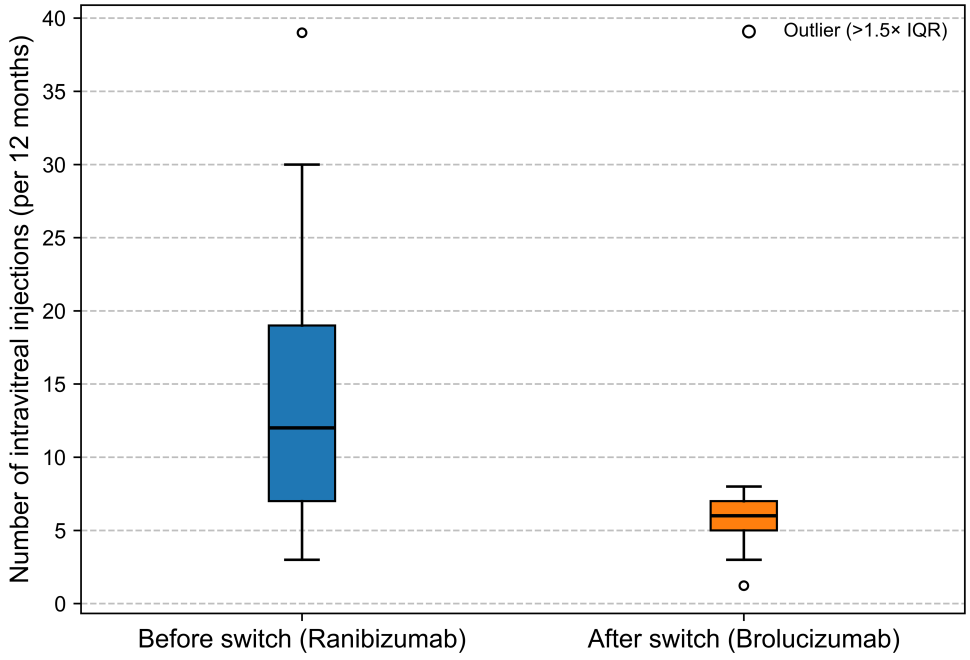

Figure 1 Reduction in injection frequency after switching from ranibizumab to brolucizumab. Boxplot showing the number of intravitreal injections before (RAN) and 12 months after switching therapy (BRO). Data are presented as medians with interquartile ranges. The reduction in injection frequency reflects the extended durability of brolucizumab and the associated decrease in treatment burden.

Abbreviations: RAN, ranibizumab; BRO, brolucizumab; AMD, age-related macular degeneration.

Visual Acuity Post-Switch

At the switch, the median ETDRS letter score (VA-S) was 50.0 [IQR: 36.5–63.0]. After 6 months of brolucizumab therapy, VA-6M improved, with a median ETDRS letter score of 51.0 [IQR: 38.0–66.5]. The difference in ETDRS letter score between VA-S and VA-6M was statistically significant (Wilcoxon p = 0.0001).

The improvement in visual acuity appeared to stabilize during the follow-up period of up to 12 months post-switch. The median ETDRS letter score at VA-12M was 50.5 [IQR: 38.5–68.0]. The difference in ETDRS letter score between VA-6M and VA-12M was not statistically significant (p = 0.691).Although the median VA slightly declined between 6 and 12 months, the change was minimal and within the interquartile range, indicating overall stability. This suggests a sustained treatment effect rather than a true functional loss. Conversely, the comparison between baseline VA-S and VA-12M showed a statistically significant improvement (Wilcoxon p = 0.0004), supporting a sustained functional benefit. Strong positive correlations were noted between VA-S and VA-6M (Spearman's r_s = 0.9426, p < 0.0001) and between VA-6M and VA-12M (Spearman's r_s = 0.9434, p < 0.0001). These findings suggest that the observed improvement in visual acuity is not random but follows a consistent and statistically significant trend over time. The strong positive correlation between VA-S and VA-12M (Spearman's r_s = 0.9142, p < 0.0001) further supports the effective brolucizumab treatment outcomes after the switch. The p-value also indicates a statistically highly significant result, suggesting that it is extremely unlikely that this correlation occurred by chance (Figures 2 and 3). Visual acuity data at each time point and paired changes are available in Supplementary Table 4.

Central Retinal Thickness Post-Switch

At baseline, the median central retinal thickness (CRT-S) was 319.0 µm [IQR: 258.0–393.0]. After six months of brolucizumab therapy, CRT-6M decreased to 255.0 µm [IQR: 216.0–298.0]. At twelve months, CRT-12M further decreased to 251.5 µm [IQR: 207.5–282.5]. A statistically significant reduction was observed between CRT-S and CRT-6M (Wilcoxon p < 0.0001) and between CRT-S and CRT-12M (p < 0.0001). The difference between CRT-6M and CRT-12M was smaller but remained statistically significant (p = 0.014). A strong positive correlation was observed between CRT-S and CRT-6M (Spearman's r_s = 0.4269, p < 0.0001), and a moderate correlation between CRT-6M and

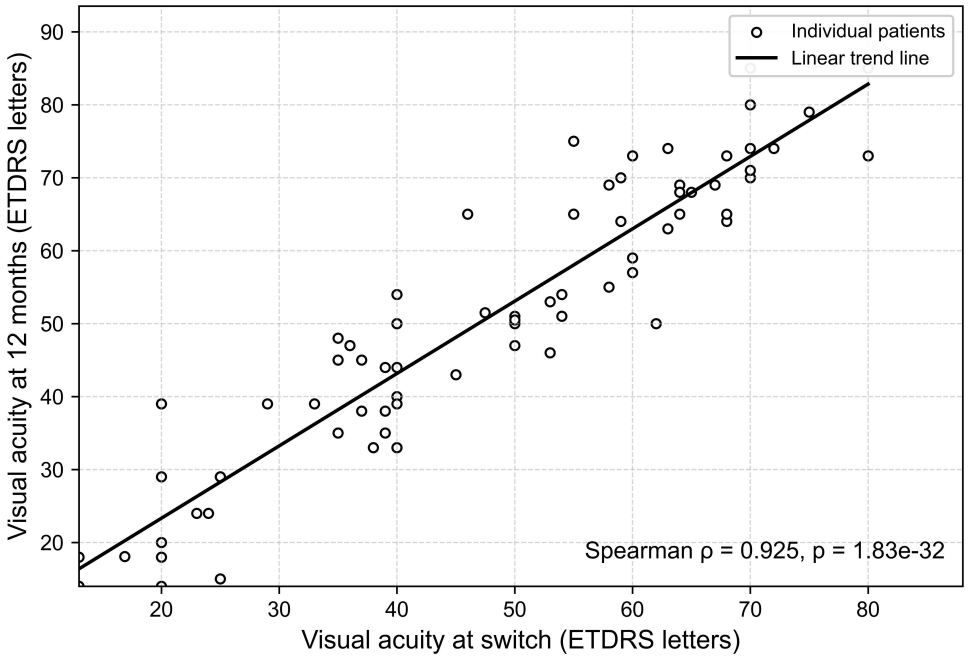

Figure 2 Correlation between visual acuity at switch and at 12 months post-switch. Scatter plot showing a strong positive correlation (Spearman) between baseline and 12-month visual acuity, indicating that patients with better initial vision were more likely to maintain or improve their outcomes following the switch.
Abbreviations: VA-S, visual acuity at switch; VA-12M, visual acuity at 12 months; ETDRS, Early Treatment Diabetic Retinopathy Study.

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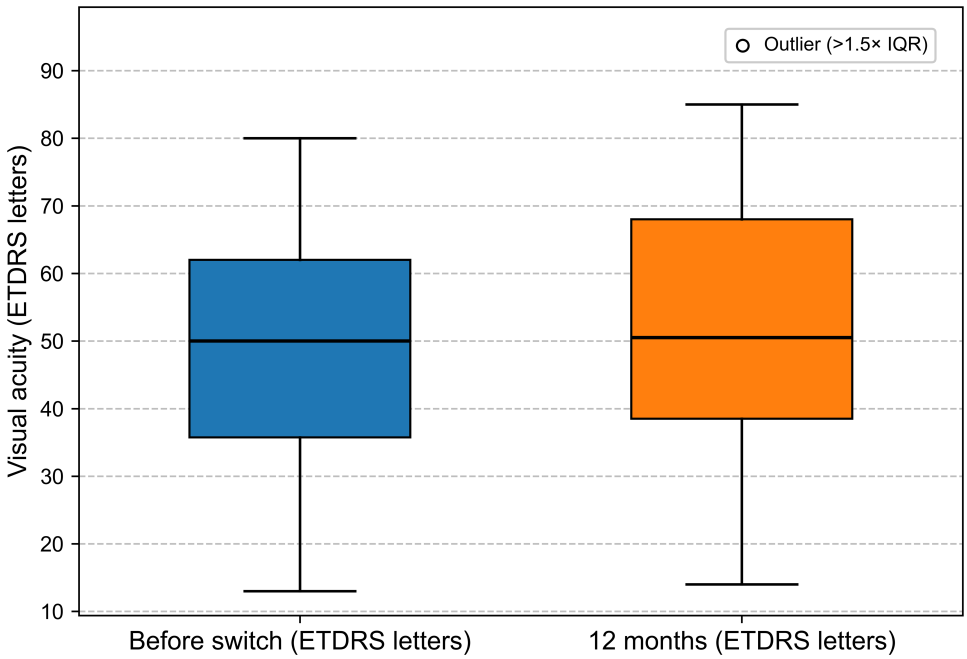

Figure 3 Visual acuity before and after 12 months of brolucizumab treatment. Boxplot showing median and interquartile range values at switch (VA-S) and after 12 months (VA-12M). Stable values over time suggest a maintained functional benefit in patients who were previously suboptimal responders to ranibizumab.
Abbreviations: VA-S, visual acuity at switch; VA-12M, visual acuity at 12 months; ETDRS, Early Treatment Diabetic Retinopathy Study.

CRT-12M (r_s = 0.5916, p < 0.0001), despite the relatively small numerical change. Additionally, CRT-S and CRT-12M were moderately correlated (rs = 0.4211, p < 0.0001), reflecting a sustained anatomical response (Figures 4 and 5).

Representative OCT scans from five patients illustrate the range of anatomical and functional responses observed after switching from ranibizumab to brolucizumab Figure 6 illustrates representative OCT scans from five patients,

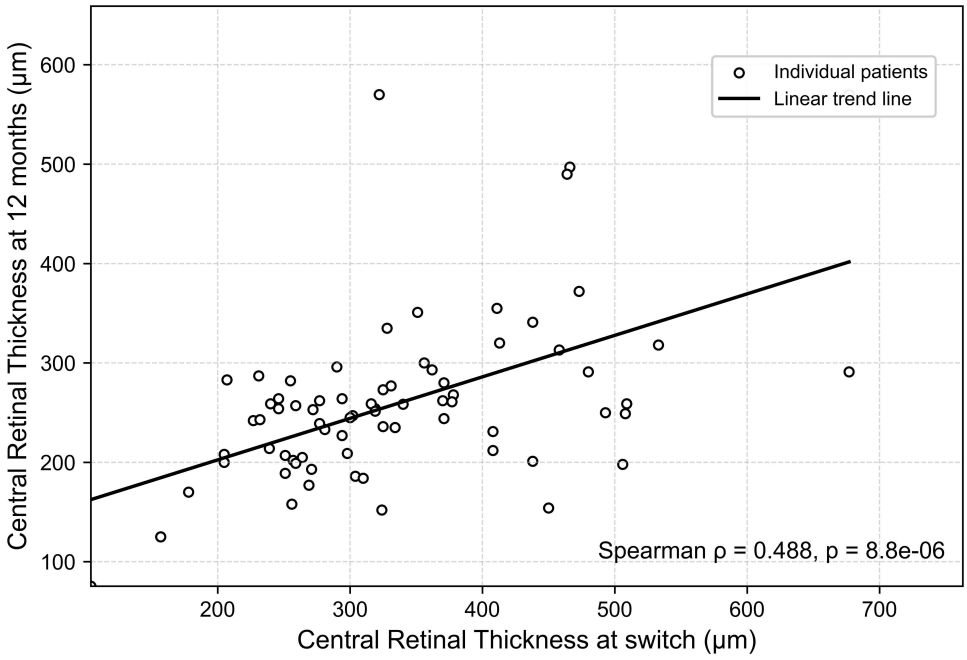

Figure 4 Correlation between central retinal thickness at switch and at 12 months. Scatter plot showing a positive correlation (Spearman) between CRT-S and CRT-12M, suggesting that patients with higher baseline CRT tended to maintain proportionally higher values after 12 months, despite overall anatomical improvement.
Abbreviations: CRT-S, CRT at switch; CRT-12M, CRT at 12 months.

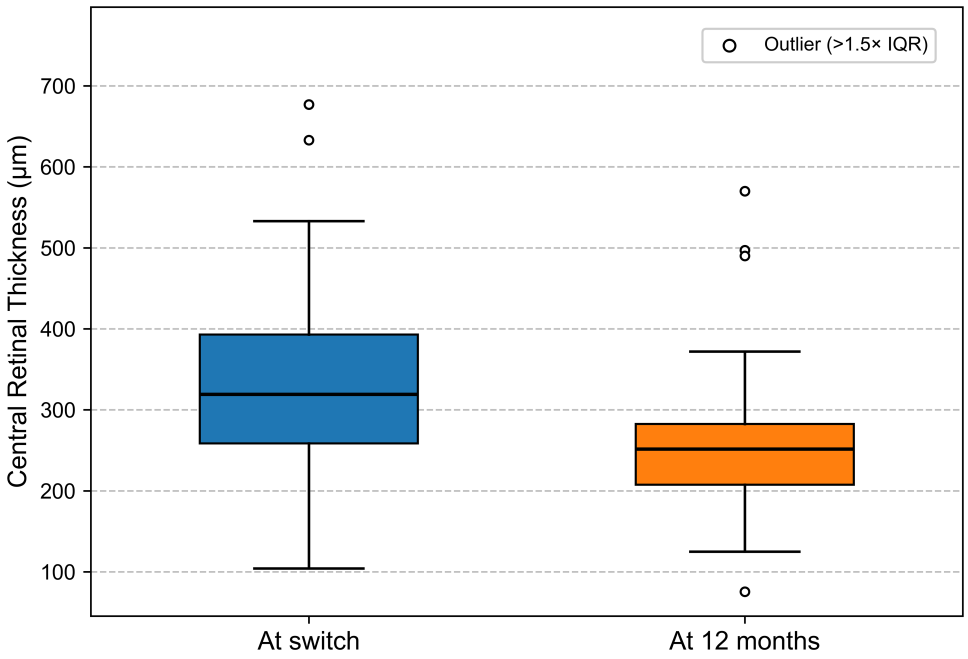

Figure 5 Central retinal thickness before and after 12 months of brolucizumab treatment. Boxplot comparing CRT values at switch (CRT-S) and after 12 months (CRT-12M). The sustained reduction supports a durable anatomical effect of brolucizumab.

demonstrating the spectrum of anatomical responses observed after switching to brolucizumab. These examples include complete resolution of intraretinal fluid, partial reduction of exudative changes, stable cases without fluid, further thinning of already atrophic retina, and one case with persistent or recurrent fluid despite treatment. As in the overall cohort, changes in visual acuity were generally less pronounced than anatomical changes.

Previous Ranibizumab Administration Impact on Post-Switch Results

Linear regression revealed only a very weak positive association between the number of prior ranibizumab injections and the change in visual acuity, with a slope of 0.15 and a low coefficient of determination ($R^2 = 0.024$), indicating that less than 3% of the variability in VA outcomes could be explained by previous treatment burden. This association was not statistically significant ($p = 0.2046$).Similarly, for CRT, regression analysis yielded a non-significant slope of 0.80 with considerable imprecision and low explanatory value ($R^2 = 0.0033$, $p = 0.6386$).

These findings indicate no statistically significant relationship between the number of prior ranibizumab injections and the extent of anatomical or functional change post-switch (see Supplementary Table 5). The minimal observed effects are likely due to random variation. Therefore, the improvement observed in VA and CRT is more plausibly attributed to the pharmacological effect of brolucizumab following the switch.

Safety Profile

Adverse events were reported in 9 patients (9 eyes) during the follow-up: intraocular inflammation (n = 4), retinal pigment epithelium atrophy (n = 2), vitreous opacities (n = 2), and retinal vasculitis (n = 1). All events were managed according to standard clinical protocols. For the remaining 66 patients (70 eyes), no adverse events were reported during the entire follow-up period or at subsequent control visits. These findings underline the limited nature of the adverse event dataset and align with the reviewers' observation that the safety profile should be interpreted with caution.

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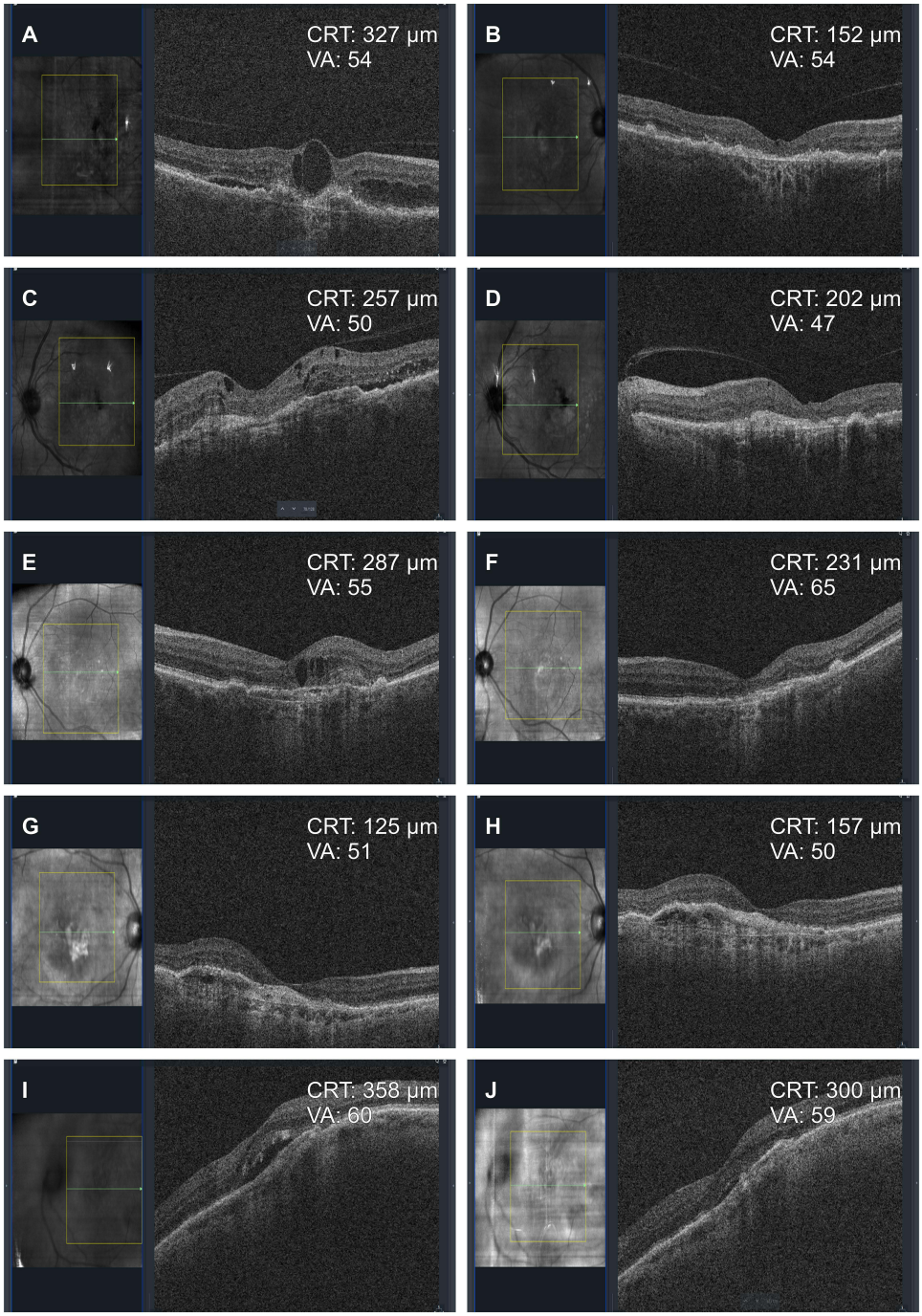

Figure 6 Optical coherence tomography (OCT) scans before and after anti-VEGF treatment with brolucizumab, illustrating the diversity of anatomical and functional responses in five patients with neovascular age-related macular degeneration. Patient 1: A large foveal intraretinal cyst resolved completely after treatment, accompanied by marked reduction in central retinal thickness; visual acuity remained stable. (**A** and **B**) Patient 2: Multiple small cysts and mild subretinal fluid showed partial regression, with modest anatomical improvement but no functional gain. (**C** and **D**) Patient 3: Mild RPE irregularities progressed to a large intraretinal cyst, resulting in increased central retinal thickness and decline in visual acuity. (**E** and **F**) Patient 4: A thin retina with pigment epithelial detachment thinned further after treatment; despite this anatomical change, visual function was maintained. (**G** and **H**) Patient 5: A large subretinal fluid pocket and hyperreflective material showed partial regression, with anatomical improvement but only minimal functional benefit. (**I** and **J**).

Abbreviations: OCT, optical coherence tomography; RPE, retinal pigment epithelium; VEGF, vascular endothelial growth factor; AMD, age-related macular degeneration.

Discussion

Ranibizumab is a long-standing well-known anti-VEGF drug that has demonstrated excellent efficacy in both clinical trials and real-world use.[28] Ranibizumab has been a cornerstone anti-VEGF therapy with well-documented efficacy in both clinical trials and real-world practice. However, its relatively shorter duration of action often necessitates more frequent dosing compared to newer agents, which can be a limitation in managing chronic conditions like wet AMD.[29,30]

For all anti-VEGF agents, it is common that a certain percentage of patients do not respond optimally to treatment, either anatomically or functionally, necessitating adjustments in the therapeutic approach. Despite ranibizumab's significant role in improving outcomes for many patients, a substantial subset continues to experience limited or inadequate therapeutic effects. This incomplete response often requires clinicians to consider alternative or additional treatment options to better manage disease progression. In real-world practice, non-response rates to ranibizumab in treating wet AMD have been reported to range from approximately 10% to 15% of diagnosed cases, though these figures vary depending on the criteria used to define nonresponse and the specific patient populations studied.[6,31–33]

Studies from routine clinical practice addressing this topic are limited. Haensli describes a 6-month follow-up of only 7 eyes with high baseline visual acuity.[33] Hirayama analyzes data from a Japanese population, highlighting that AMD outcomes may vary among racial and ethnic groups.[31] Our study focuses specifically on a Western European population, which remains underrepresented in the literature. Unlike Hirayama's mixed switching cohort (brolucizumab and aflibercept), our cohort underwent a direct switch from ranibizumab to brolucizumab, enabling clearer conclusions.

Recent studies by Coney, Bilgic, and Holz have also examined switching to brolucizumab, though most included multiple prior agents and ethnically diverse populations.[32,33,34] For instance, Bilgic's dataset, although drawn from German centers, included both Caucasian and Asian patients, which may introduce population bias.

We further compared our findings with the Phase III HAWK and HARRIER trials. While these reported higher VA gains, the difference is likely attributable to trial conditions, treatment-naïve status, and better baseline VA.[18,23]

Our results, while more modest, primarily reflect functional stabilization rather than marked functional improvement in treatment-experienced eyes. Therefore, the clinical effect should be interpreted more as maintenance of vision with concurrent anatomical improvement, rather than as a substantial visual gain. Anatomical outcomes support this conclusion. The median CRT reduction observed in our study was smaller than in HAWK and HARRIER, which again is consistent with the real-world nature and lower initial CRT in our patients. Nevertheless, continuous positive effects were present over 12 months, supporting brolucizumab's sustained anatomical efficacy. Regression analysis did not identify any statistically significant association between the number of prior ranibizumab injections and post-switch changes in VA or CRT. This indicates that even patients with long-term exposure to ranibizumab may benefit from switching. Importantly, correlations in VA and CRT over time suggest a stable, durable treatment effect after the switch. All outcomes were analyzed using nonparametric statistics, as the data were not normally distributed.

In summary, this real-world Western European study supports the use of brolucizumab as a safe and effective alternative in patients with a suboptimal response to ranibizumab. However, given the modest magnitude of functional benefit and the occurrence of adverse events in a subset of patients, caution is warranted in generalizing these results. The findings underscore the importance of timely switching in suboptimal responders and suggest a potential benefit of not delaying treatment adjustment. While our results concern branded ranibizumab, similar outcomes might be expected with biosimilars, though further studies are needed to confirm this hypothesis.

Although a few real-world studies have previously addressed this switch, they are generally limited by small sample sizes, short follow-up periods, mixed populations, or geographic/ethnic specificity. These factors restrict their generalizability. In contrast, our study focuses solely on switching from ranibizumab to brolucizumab in a clearly defined Western European population under standardized treatment and imaging protocols. We believe that this makes our study both original and clinically valuable—offering meaningful evidence for therapeutic decision-making and forming a solid foundation for future research in this area.

This study has several limitations. First, its retrospective design is inherently subject to potential selection bias. Specifically, the exclusion criteria omitted patients with advanced disease or very poor baseline visual acuity, as these individuals would not have met the therapeutic continuation criteria. In the Czech Republic, under Bismarck model, anti-

VEGF therapy is no longer reimbursed from public health insurance when treatment outcomes fall below these thresholds. Given the high cost of therapy, continuation is generally not feasible for elderly patients on a self-pay basis, and treatment is therefore discontinued. While this approach ensured a more homogeneous study population for evaluating anatomical and functional change, it may limit the generalizability of the findings to all patients switched from ranibizumab to brolucizumab. Secondly, attrition bias is possible, since only eyes that completed the 6-month or 12-month follow-up were included in the respective analyses, although this approach ensured consistent and comparable datasets at each time point.

Conclusion

In this real-world multicenter study, switching from ranibizumab to brolucizumab in patients with suboptimal response led to a statistically significant reduction in central retinal thickness and statistically significant, but clinically modest, visual acuity stabilization or improvement, accompanied by a meaningful decrease in injection burden. Prior exposure to ranibizumab did not significantly influence post-switch outcomes, suggesting that the observed benefits are largely attributable to the pharmacological characteristics of brolucizumab itself. These results support the potential clinical utility of timely switching in refractory wet AMD, but the functional benefit should be interpreted with caution given its limited magnitude.

Nevertheless, due to the limited sample size, potential bias introduced by the retrospective design and attrition, and the restricted adverse event dataset, safety conclusions should be considered preliminary. Larger prospective studies focused specifically on the switch from ranibizumab to brolucizumab are warranted to confirm and expand upon these findings. Furthermore, considering the growing role of biosimilars in clinical practice, it is important to conduct studies evaluating whether the safety and efficacy of this switch can also be expected when transitioning from ranibizumab biosimilars. Such biosimilar-focused studies are, with rare exceptions, not typically included in registration trials, highlighting the need for dedicated real-world evidence to guide therapeutic strategies in this context.

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Disclosure

The authors report no conflicts of interest in this work.

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