Efficacy and Safety of Brolucizumab in Neovascular Age-Related Macular Degeneration: A Real-World Study

Eficácia e Segurança do Brolucizumab na Degenerescência Macular da Idade Neovascular

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Recebido/Received: 2024-10-16 | **Aceite/Accepted:** 2025-06-17 | **Published online/Publicado online:** 2026-03-17 | **Published/Publicado:** 2026-06-27

DOI: https://doi.org/10.48560/rspo.38267

ABSTRACT

INTRODUCTION: Brolucizumab (Beovu®) is an anti-vascular endothelial growth factor (anti-VEGF) agent approved by the European Medicines Agency (EMA) in 2020 for the treatment of neovascular age-related macular degeneration (nvAMD) and in 2022 for diabetic macular edema. In randomized clinical trials for nvAMD (HAWK and HARRIER), brolucizumab demonstrated visual acuity improvements comparable to aflibercept, with the potential for longer durability. However, post-marketing data raised safety concerns. This study aims to evaluate the real-world safety and efficacy of brolucizumab for nvAMD, focusing on functional and anatomical outcomes, injection intervals, and adverse events.

METHODS: This retrospective study included 42 eyes with nvAMD treated with brolucizumab at Hospital de Braga (2022-2023) that had evaluation with optical coherence tomography (OCT) before and after at least one brolucizumab injection. Outcomes assessed included corrected distance visual acuity (CDVA), central retinal thickness (CRT), macular volume (MV), presence of intraretinal fluid (IRF), subretinal fluid (SRF), serous pigment epithelial detachment (sPED), treatment intervals, and adverse events.

RESULTS: Forty-two eyes from 38 patients (71.1% female, mean age 78±8 years, 57.1% phakic) were included. Most eyes (95.2%) had prior anti-VEGF treatment. CDVA did not significantly change (0.66±0.54 to 0.61±0.46 logMAR, p=0.251), though improvements were seen in the 2 treatment-naïve eyes (25 ETDRS letters in both). Significant improvements were found in CRT (335.6±94.7µm to 301.2±92.1µm, p=0.005) and MV (8.36±1.08 mm^3 to 7.98±0.87 mm^3, p=0.003). The proportion of eyes with IRF decreased from 42.9% to 23.8% (p=0.021), SRF from 69% to 28.6% (p<0.001), and sPED from 33.3% to 19% (p=0.031). The average treatment interval extended from 6.08±2.47 to 8.00±2.71 weeks (p=0.004). Intraocular inflammation occurred in 7.14% of eyes (n=3), with no retinal vasculitis or vascular occlusion.

CONCLUSION: Brolucizumab demonstrated effectiveness in maintaining CDVA and improving anatomical outcomes, with longer treatment intervals, reducing the treatment burden. The incidence of intraocular inflammation was higher than in trials but in accordance with other real-world studies, emphasizing the need for careful patient selection and close monitoring of adverse events.

KEYWORDS: Brolucizumab; Macular Degeneration/Drug therapy; Treatment Outcome.

RESUMO

INTRODUÇÃO: O brolucizumab (Beovu®) é um anti-fator de crescimento endotelial vascular (anti-VEGF), aprovado pela Agência Europeia do Medicamento em 2020 para o tratamento da degenerescência macular da idade neovascular (DMI neovascular) e em 2022 para o edema macular diabético. Nos ensaios clínicos randomizados HAWK e HARRIER, mostrou melhorias da acuidade visual comparáveis ao aflibercept, com potencial para maior durabilidade. Contudo, dados pós-comercialização levantaram preocupações quanto à sua segurança. Este estudo visa avaliar a segurança e eficácia do brolucizumab em ambiente clínico real para a DMI neovascular, analisando resultados funcionais e anatómicos, intervalos entre injeções e eventos adversos.

MÉTODOS: Este estudo retrospetivo incluiu 42 olhos com DMI neovascular tratados com brolucizumab no Hospital de Braga (2022-2023), que tiveram avaliação clínica com tomografia de coerência ótica (OCT) antes e após, pelo menos, uma injeção de brolucizumab. Foram avaliados a melhor acuidade visual corrigida (MAVC), a espessura central da retina (CRT), o volume macular (MV), a presença de fluido intrarretiniano (IRF), fluido subretiniano (SRF), descolamento seroso do epitélio pigmentar (sPED), intervalos de tratamento e eventos adversos.

RESULTADOS: Este estudo incluiu 42 olhos de 38 doentes (71,1% do sexo feminino, idade média de 78±8 anos, 57,1% fáquicos). A maioria dos olhos (95,2%) tinha sido submetido a tratamento prévio com anti-VEGF. A MAVC não apresentou alterações significativas (de 0,66±0,54 para 0,61±0,46 logMAR, p=0,251), embora os 2 olhos naïve tenham apresentado ambos uma melhoria de 25 letras ETDRS. A CRT melhorou significativamente (de 335,6±94,7 µm para 301,2±92,1 µm, p=0,005) e o MV também reduziu (de 8,36±1,08 mm³ para 7,98±0,87 mm³, p=0,003). A proporção de olhos com IRF diminuiu de 42,9% para 23,8% (p=0,021), com SRF de 69% para 28,6% (p<0,001), e com sPED de 33,3% para 19% (p=0,031). O intervalo médio de tratamento aumentou de 6,08±2,47 para 8,00±2,71 semanas (p=0,004). Foi reportada inflamação intraocular em 7,14% dos olhos (n=3), sem casos de vasculite retiniana ou oclusão vascular.

CONCLUSÃO: O brolucizumab demonstrou eficácia na manutenção da acuidade visual e na melhoria dos parâmetros anatómicos, permitindo intervalos de tratamento superiores e reduzindo o *burden* do tratamento. A incidência de inflamação intraocular deve ser considerada, pelo que os doentes deverão ser cuidadosamente selecionados e monitorizados.

PALAVRAS-CHAVE: Brolucizumab; Degenerescência Macular/tratamento farmacológico; Resultado do Tratamento.

INTRODUCTION

Age-related macular degeneration (AMD) is the leading cause of irreversible blindness in people aged ≥ 50 years of age in the developed world.[1] In its advanced stages, AMD can be either non-neovascular (dry, atrophic or nonexudative) or neovascular (wet or exudative).[1] Neovascular AMD (nvAMD) is characterized by choroidal neovascularization and its potential sequelae, namely intra or subretinal fluid, lipid deposition, hemorrhage, retinal pigment epithelium detachment and fibrotic scars, that result in a significant impairment in visual acuity and quality of life.[1,2]

Intravitreal antiangiogenic therapy is currently the first-line treatment for nvAMD, specifically intravitreal injection (IVI) of an anti-vascular endothelial growth factor (anti-VEGF) agent.[1,3] This therapy has proven effective in reducing pathologic exudation from macular neovascularization, stabilizing the disease and improving vision.[3,4] However, this is usually a prolonged treatment and many patients require frequent injections (eg. monthly) in order to maintain control of the disease, which results in a significant patient and caregiver burden.[5,6] Since 2004, with the introduction of pegaptanib sodium (Macugen®), a number of anti-VEGF agents have been developed in an attempt to improve efficacy or increase the interval of injections, maintaining the same efficacy. Bevacizumab (Avastin®), used off-label since 2005, and ranibizumab (Lucentis®) introduced in 2006, seem to have similar efficacy, with monthly injections.[3] Aflibercept (Eylea®), a pan-VEGF-A and placental growth factor (PGF) blocker, was introduced in 2011, and demonstrated to have similar efficacy to monthly ranibizumab, when administered every 8 weeks, after a loading dose of three monthly injections.[3,7]

Brolucizumab (Beovu®, Novartis) is a newer anti-VEGF agent approved by the European Medicines Agency (EMA) in 2020 for the treatment of neovascular AMD and in 2022

for diabetic macular edema.[8] It is a humanized single-chain antibody fragment with high binding affinity for multiple isoforms of VEGF-A and a low molecular weight, which allows for a high concentration in each IVI, potentially increasing the durability of the treatment response.[9]

In randomized clinical trials (HAWK and HARRIER) for nvAMD in treatment naïve patients, brolucizumab demonstrated similar improvements in visual acuity when compared to aflibercept, with superior anatomical outcomes and potential for longer durability.[10,11] In fact, over 50% of eyes were maintained on a 12-week dosing interval through week 48, which would considerably reduce the IVIs burden when compared to the aflibercept's 8-weekly treatment.[10,12] Therefore, the recommended dosing regimen by the EMA involves monthly IVI of 6 mg/0.05 mL for the first 3 doses, then every 8 to 12 weeks, depending on disease activity.[8,13]

Regarding adverse events, the HAWK and HARRIER trials reported a 2.2% rate of mild to moderate intraocular inflammation associated with brolucizumab, 3 cases of retinal vascular occlusion and no cases of retinal vasculitis.[10] However, post-marketing surveillance has raised safety concerns. Later on, a Safety Review Committee reported that 3.3% of eyes had retinal vasculitis and 2.1% had retinal vasculitis with vascular occlusion.[14]

There is growing uncertainty regarding the safety of brolucizumab, particularly since its efficacy and safety in treatment-naïve and highly selected patients from clinical trials may not fully reflect real-world clinical outcomes. Therefore, this study aims to evaluate the real-world safety and efficacy of intravitreal brolucizumab for nvAMD by analysing functional and anatomical outcomes, injection intervals, and the occurrence of adverse events.

METHODS

This retrospective observational study included patients who received intravitreal brolucizumab injections to treat nvAMD at the Ophthalmology Department of Hospital de Braga, Portugal, between January 2022 and December 2023. The present study was approved by the Ethics Committee of Hospital de Braga and conducted in accordance with the tenets of the Declaration of Helsinki.

The inclusion criteria were patients with neovascular AMD who had clinical evaluation and macular optical coherence tomography (OCT) before and after receiving at least one brolucizumab injection. Whenever possible, it was considered the evaluation after three loading doses of intravitreal brolucizumab to evaluate response. Patients were excluded if they lacked follow-up evaluations at the time of data collection, received other ophthalmologic treatments besides brolucizumab between assessments, or had OCT images of insufficient quality or with significant segmentation errors that hindered interpretation.

Data collected from patients' medical records included demographics, past medical and ophthalmologic history. Previous AMD treatments information was also retrieved, such as number of injections and anti-VEGF used, interval between injections, time since last injection to first brolucizumab injection and the reason for the switch. Regarding brolucizumab treatment, data collected included the number of injections completed as the loading dose, time from last brolucizumab injection to evaluation and interval between load injections and afterwards, if available.

Corrected distance visual acuity (CDVA) was the functional outcome evaluated, and data was assessed using decimal scale chart and converted to the logarithm of the minimum angle of resolution (logMAR) for statistical analysis. CDVA of counting fingers was converted into 1.90 logMAR according to Schulze-Bonsel *et al*[15] and Lange *et al*.[16]

Anatomic outcomes were assessed by spectral-domain OCT (Spectralis® OCT, Heidelberg Engineering, Heidelberg, Germany). Macular volume (MV) and central retinal thickness (CRT) were measured automatically by the segmentation software in Heidelberg Eye Explorer. The presence or absence of intraretinal fluid (IRF), subretinal fluid (SRF), and serous pigment epithelial detachment (sPED) was assessed on the foveal line scans only, and if present after treatment they were further classified into three categories: "reduced but persistent fluid", "stable fluid" and "increased fluid" manually by M.V.P and K.S independently, and confirmed by N.L if equivocal.

Finally, drug-related and clinically significant adverse events were also collected from patients' medical records and their incidence calculated by dividing the number of AE reports attributed to brolucizumab by the total number of eyes receiving brolucizumab during the study period.

Statistical analysis was performed using SPSS software version 26.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were described by their mean (M) ± standard deviation (SD) and categorical variables through absolute (n) and relative (%) frequencies. Normality of sample distribution in each variable was assessed by the Kolmogorov-Smirnov test. Parametric tests were applied to analyse variables that followed a normal distribution (CRT, MV and treatment interval after treatment) and non-parametric tests for the ones that did not (CDVA and treatment interval before treatment). A two-tailed, paired sample t-test was performed to analyse CRT and MV variables; the Wilcoxon signed-rank test for the CDVA and treatment intervals comparison; and the paired McNemar test for categorical variables (IRF, SRF and sPED). Statistical significance was considered when p-value was <0.05 with a 95% confidence interval.

RESULTS

DESCRIPTIVE ANALYSIS

A total of 42 eyes from 38 patients were included in this study. Demographics and baseline sample characteristics are summarized in Table 1. The mean age of patients was 78±8 years, there was a female preponderance (27/42, 71.1%) and 57.1% were phakic. The most common comorbidities reported were cardiovascular risk factors such as arterial hypertension (44.7%), dyslipidemia (34.2%) and diabetes *mellitus* (15.8%). Right (22/42, 52.4%) and left (20/42, 47.6%) eyes were equally represented in the study sample.

The majority of eyes treated with brolucizumab (40/42, 95.2%) had received prior treatment with other anti-VEGF

Table 1. Descriptive analysis.	
Number of patients, N	38
Number of eyes, N	42
Number of brolucizumab IVIs, N	118
Age, M±SD (range)	78 ± 8 (61 to 91) years
Gender, n (%)	
Male	11 patients (28.9%)
Female	27 patients (71.1%)
Laterality, n (%)	
Right eye	22 (52.4%)
Left eye	20 (47.6%)
Lens status, n (%)	
Phakic	24 (57.1%)
Pseudophakic	18 (42.9%)
Comorbidities, n (%)	
Arterial hypertension	17 (44.7%)
Dyslipidemia	13 (34.2%)
Diabetes *mellitus*	6 (15.8%)
Cardiac conditions	4 (10.5%)
Respiratory conditions	5 (13.2%)
Oncologic conditions	5 (13.2%)
Previous treatment	
Naïve eyes, n	2 (4.8%)
Number of IVI, M±SD (range)	20.8 ± 20.5 (0 to 75)
Number of agents, M±SD (range)	1.71 ± 0.86 (0 to 3)
1 agent	40.5%
2 agents	33.3%
3 agents	21.4%
Reason for the switch, n (%)	
Persistent fluid	33 (82.5%)
Increase treatment interval	7 (17.5%)
Time from last injection to switch (months), M±SD	3.56 ± 1.84
Number of brolucizumab loading dose IVIs, n (%)	
3 doses	36 eyes (85.7%)
2 doses	4 eyes (9.5%)
1 dose	2 eyes (4.8%)
Interval between load injections, n (%)	
4 weeks	13 (32.5%)
6 weeks	25 (62.5%)
8 weeks	2 (5%)

IVI, intravitreal injection; M, mean; n, absolute frequencies; SD, standard deviation; %, relative frequencies.

agents, such as aflibercept, ranibizumab, and/or bevacizumab. Only two eyes were treatment naïve. The mean number of previous IVI was 20.8 ± 20.5 (0 to 75) and the mean number of agents used was 1.71 ± 0.86. Most patients had only been treated with 1 agent previously (17/40, 40.5%), 33.3% (14/40) with 2 different drugs and 21.4% (9/40) were previously treated with 3 agents. The majority of patients switched to brolucizumab treatment due to persistent fluid in the retina (33/40, 82.5%) and only 7 patients (7/40, 17.5%) switch in an attempt to increase IVI interval and reduce its burden. The mean time from last IVI to the first brolucizumab injection was 3.56 ± 1.84 months, with 90% of patients respecting the recommended 2 months interval.[8]

A total of 118 brolucizumab injections were administered during the study period. Thirty six eyes (85.7%, 36/42) completed three injections of brolucizumab before first evaluation, while only 4 eyes received 2 doses and 2 eyes received 1 dose. Regarding the interval between load injections, the most frequent was 6 weeks (13/40, 62.5%), followed by 4 weeks (25/40, 32.5%) and 8 weeks (2/40, 5%). A total of 8 injections (6.8%) were missed and postponed, all in different patients, implying that the patient did not receive all the injections at the correct timing. There were 2 cases of patient non-attendance (one of which was due to the patient being hospitalized for oncological reasons) and 6 injections deferred due to strike of health professionals.

VISUAL AND ANATOMICAL OUTCOMES

CDVA showed no statistically significant change after brolucizumab treatment (from 0.66 ± 0.54 to 0.61 ± 0.46 logMAR, p=0.251), although notably improving in the two naïve eyes – from 1.80 and 1.30 to 1.30 and 0.80 logMAR, respectively. Globally, VA improved in 35.7% of eyes, 50% had no change in VA and 14.3% showed VA deterioration after receiving brolucizumab.

Regarding anatomical outcomes, CRT decreased significantly after treatment with brolucizumab, from 335.6 ± 94.7 µm to 301.2 ± 92.1 µm, p=0.005, with a mean difference of -34.5 µm. Macular volume also decreased, on average, 0.38 mm³, with mean values improving from 8.36 ± 1.08 mm³ to 7.98 ± 0.87 mm³, p=0.003. These functional and anatomical results are summarized in Table 2.

FLUID STATUS

The proportion of eyes with fluid in each of the intraretinal, subretinal, and sub-RPE compartments decreased significantly following treatment with brolucizumab. The proportion of eyes with IRF in the fovea decreased from 42.9% to 23.8% (p=0.021), SRF from 69% to 28.6% (p<0.001), and sPED from 33.3% to 19% (p=0.031) after treatment with brolucizumab. Only 1 eye demonstrated a new occurrence of IRF (2.4%) after treatment, with no such occurrences regarding SRF or sPED. This eye switched from treatment with aflibercept due to fluid maintenance, also increasing the interval from 4 to 6 weeks. This IRF worsening is likely attributed to the outcome evaluation being conducted only four months after the last IVI, as this patient completed another cycle of brolucizumab IVI every six weeks, achieving full fluid resolution.

Of the 18 eyes that presented IRF before treatment, 50% (n=9) showed complete resolution of fluid, 16.7% (n=3) had reduced fluid, 16.7% (n=3) remained stable, and 16.7% (n=3) experienced an increase in IRF. Of the 29 eyes that had SRF before brolucizumab injections, in 58.6% (n=17) it resolved

Table 2. Visual Outcomes, Anatomic Outcomes and Fluid Status after Treatment with Brolucizumab.

	Pre-Brolucizumab M ± SD	**Post-Brolucizumab** M ± SD	**Wilcoxon Signed-Rank Test** *p*-value	
CDVA (logMAR)	0.66 ± 0.54	0.61 ± 0.46	0.251	
			Paired, 2-tailed t-Test Difference (95% CI)	*p*-value
CRT (μm)	335.6 ± 94.7	301.2 ± 92.1	- 34.5 (-11.1 to -57.8)	0.005*
MV (mm^3)	8.36 ± 1.08	7.98 ± 0.87	- 0.38 (-0.14 to -0.62)	0.003*
	n (%)	n (%)	**Paired McNemar Test** *p*-value	
Presence of **IRF**	18 (42.9%)	10 (23.8%)	0.021*	
Presence of **SRF**	29 (69%)	12 (28.6%)	0.000*	
Presence of **sPED**	14 (33.3%)	8 (19%)	0.031*	

CDVA, corrected distance visual acuity; CRT, central retinal thickness; IRF, intraretinal fluid; M, mean; MV, macular volume; n, absolute frequencies; SD, standard deviation; sPED, serous pigment epithelial detachment; SRF, subretinal fluid; %, relative frequencies; *, statistical significance..

completely, in 13.8% (n=4) it reduced, in 10.3% (n=3) it remained stable and in 17.2% (n=5) there was increased SRF after treatment. Finally, 14 eyes had serous pigment epithelial detachment before treatment and, of these, 42.9% (n=6) resolved with brolucizumab IVIs, 21.4% (n=3) reduced and 35.7% (n=5) remained stable, with no cases of increased sPED (Fig. 1).

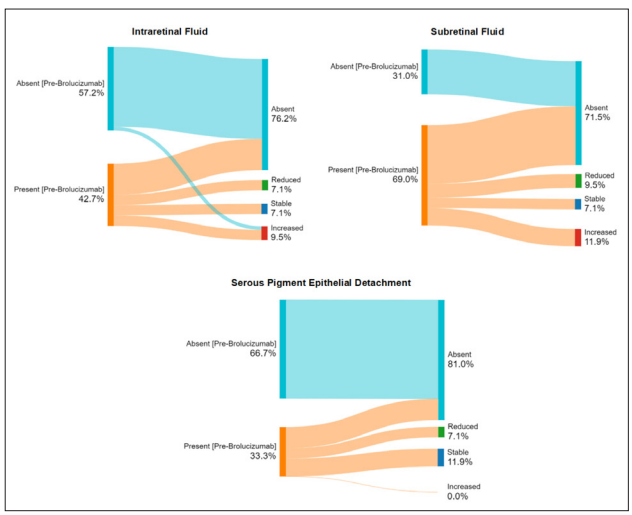

Figure 1. Sankey charts representing IRF, SRF and sPED status – Proportion of patients with ("present") or without ("absent") fluid before treatment with brolucizumab; and their evolution into one of four categories ("absent", "reduced fluid", "stable fluid" or "increased fluid") after treatment with brolucizumab. Made at SankeyMATIC.com IRF, intraretinal fluid; sPED, serous pigment epithelial detachment; SRF, subretinal fluid; %, relative frequencies.

TREATMENT INTERVALS

The interval between injections after the first load cycle was only possible to evaluate in 25 eyes, as 38% of eyes had no data following first evaluation (absence of further follow-up, switched to other anti-VEGF or suspended treatment). Treatment was continued every 6, 8 and 10 weeks in the same proportion of eyes (14.3%), followed by 4 and 12 weeks, both in 9.5% of eyes (Fig. 2). The average treatment interval extended from 6.08 ± 2.47 weeks to 8.00 ± 2.71 weeks (p=0.004) after switching to brolucizumab.

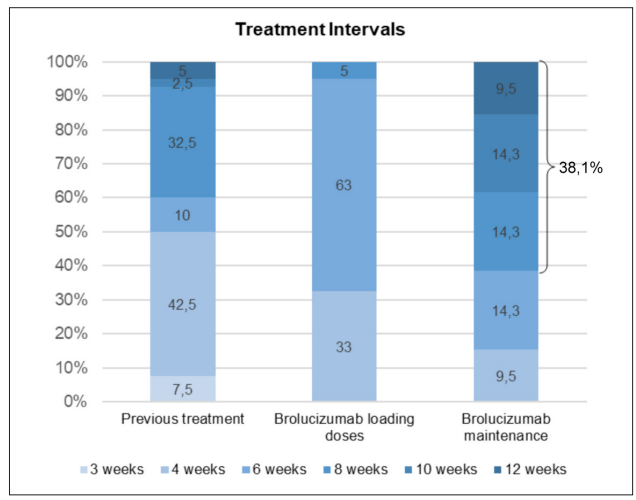

Figure 2. Bar chart – Proportion of eyes in each treatment interval (3, 4, 6, 8, 10 and 12 weeks) before treatment with brolucizumab, during loading doses of brolucizumab and during maintenance phase of treatment with brolucizumab.

ADVERSE EVENTS

During the study period, after performing a total of 118 brolucizumab IVIs, 3 eyes (7.14%) of 2 patients (5.26%) developed clinically significant intraocular inflammation, yielding a 2.54% incidence on a per injection basis. There was one patient that developed bilateral acute anterior uveitis after brolucizumab and other patient with both anterior segment inflammation and mild vitritis. Both suspended treatment with brolucizumab and inflammation was successfully treated. No cases of retinal vasculitis or vascular occlusion were documented. There were no other extraocular or systemic adverse events during the study period that were attributed to brolucizumab.

DISCUSSION

In this real-world study, there was no significant change in visual acuity after treatment with brolucizumab, which is coincident with most real-world studies, as is shown in a 2023 review by Baumal *et al*, unlike previous studies that only included treatment-naïve patients.[2] This may be due to the fact that switch patients have more severe and unresponsive disease, with more chronic retinal changes and worse visual acuity. Furthermore, real-world visual acuity records are not as rigorous as in clinical trials. Our results reveal a VA deterioration in 14.3% of eyes after the loading dose of brolucizumab. When analysing the individual cases, we verify that 2 eyes are of the same patient and correspond to the 2 cases of anterior uveitis. Another patient had anatomical improvement but had corneal pathology that affects VA (Fuchs dystrophy and keratoconus) and the second IVI was deferred due to an oncology hospitalization; one patient had increased IRF associated, probably due to late evaluation, only 5 months after the last injection; and finally, 2 eyes had AV deterioration despite anatomical improvement, not having a heavy IVI history, being already pseudophakic and having complied with the proposed IVI schedule – perhaps the baseline VA was not updated, or there was loss of photoreceptor cells despite fluid status improvement.

Anatomical improvements have been demonstrated in clinical trials[10,11] and confirmed by Baumal *et al* in their real-world review, both in naïve and in switch eyes.[2] The present study also showed significant improvement in both CRT and MV after treatment with brolucizumab, even considering the fact that 82.5% of our eyes have switched to brolucizumab for having incomplete response to other anti-VEGF agents. The difference in CRT in this study (- 34.5 μm, range -11.1 to -57.8) falls in the range of improvement in switch eyes reported by Baumal *et al* (-26 to -185.7 μm).[2] Likewise, IRF, SRF and sPED all demonstrated a significant improvement after brolucizumab IVIs, and in those that maintained some fluid, a considerable proportion showed some reduction. There were 7 eyes with increased IRF and/or SRF. When analysing potential causes for this fluid worsening, we identified several contributing factors: an extended interval from the last IVI to evaluation in three cases (4 and 5 months); a heavy burden of previous injections (>45) with associated chronicity in two cases; a doubtful diagnosis with suspected polypoidal choroidal vasculopathy in three eyes; and a postponed injection due to a strike in two eyes.

Average injection interval was successfully enlarged from 6 to 8 weeks after switching to brolucizumab in these patients. In the HAWK and HARRIER trials, after 3 monthly loading doses, patients were injected every 12 weeks with adjustments to 8 weeks if disease activity was present.[10] More than 50% of patients in these trials extended treatment interval to 12 weeks,[11] but real-world studies have shown lower percentages, such as 30.8% in the recent Yeom *et al* study.[17] In our study, this percentage was 9.5%. In fact, real-world studies demonstrate that there is an increase in injection interval, but of lower extent. Rave *et al* reported an extension on average treatment interval from 4 weeks to 8 weeks (p<0.001)[18] and Walter *et al* reported a smaller change, from 6.3 weeks to 6.8 weeks (p=0.001).[19] There seems to be a real benefit of brolucizumab in reducing the burden of IVIs, although these reported values may be variable due to different patient demographics and small sample size.

The incidence of intraocular inflammation (IOI) in this study was 7.14% and no cases of retinal vasculitis or vascular occlusion were reported. Safety events report in real-world studies is heterogenous and follow-up is highly variable.[2] Incidence of IOI ranged from 0% to 19% in the studies reviewed, and there was no CDVA deterioration as a consequence of any of these events, possibly due to the peripheral location of the retinal vasculitis.[2,20,21] The incidence of occlusive vasculitis ranged from 0% to 16.7%, with loss of visual field loss in one case.[2] Our results are in concordance with these real-world studies. It is of utmost importance the close monitoring, early detection and timely management of these adverse events, informing patients and educating them to be aware of alarm signs and symptoms.[2,22]

There are several limitations in this study that may have influenced results and conclusions. The retrospective nature of this design study limits data collection as timing of injections and evaluations may be heterogenous, real-world clinical records may not be as rigorous as in clinical trials and there may be variability in visual acuity evaluations depending on room facilities. Also, the small sample size may introduce bias when interpreting these results, and, along with the short follow-up period, are two important aspects that should be addressed in future studies to validate these conclusions. Nevertheless, the favourable anatomical outcomes and the extended intervals between injections, resulting in reduced treatment burden, are already promising.

CONCLUSION

In conclusion, this study provides real-world evidence on the efficacy and safety of brolucizumab for treating neovascular AMD. While visual acuity remained largely unchanged, there were significant anatomical improvements in CRT and MV, with substantial reductions in IRF, SRF and sPED. These findings align with prior real-world studies, highlighting brolucizumab's potential to extend treatment intervals, although the increase was more modest when compared to clinical trials. Intraocular inflammation was reported in a small percentage of cases, reinforcing the need for close monitoring and patient education on adverse events. Despite its limitations, including its retrospective design and a small sample size, this study supports brolucizumab as a viable option for treating refractory cases and reducing injection burden in nvAMD patients, with manageable safety concerns. Further research with larger cohorts is recommended to confirm these findings.

CONTRIBUTORSHIP STATEMENT / DECLARAÇÃO DE CONTRIBUIÇÃO

MVP: Study design, data collection and analysis, manuscript writing.

MAS, AS, and RS: Data collection and analysis.

GCS: Interpretation of results, review of the manuscript and its scientific content.

KS: Study design, interpretation of results, and review of the manuscript and its scientific content.

All authors approved the final version of the manuscript for publication.

MVP: Desenho do estudo, colheita e análise de dados, escrita do manuscrito.

MAS, AS e RS: Colheita e análise de dados.

GCS: Interpretação de resultados, revisão do manuscrito e seus conteúdos científicos.

KS: Desenho do estudo, interpretação de resultados e revisão do manuscrito e seus conteúdos científicos.

Todos os autores aprovaram a versão final do manuscrito para publicação.

RESPONSABILIDADES ÉTICAS

Conflitos de Interesse: Os autores declaram a inexistência de conflitos de interesse na realização do presente trabalho.

Fontes de Financiamento: Não existiram fontes externas de financiamento para a realização deste artigo.

Confidencialidade dos Dados: Os autores declaram ter seguido os protocolos da sua instituição acerca da publicação dos dados de doentes.

Proteção de Pessoas e Animais: Os autores declaram que os procedimentos seguidos estavam de acordo com os regulamentos estabelecidos pela Comissão de Ética responsável e de acordo com a Declaração de Helsínquia revista em 2024 e da Associação Médica Mundial.

Proveniência e Revisão por Pares: Não comissionado; revisão externa por pares.

ETHICAL DISCLOSURES

Conflicts of Interest: The authors have no conflicts of interest to declare.

Financing Support: This work has not received any contribution, grant or scholarship

Confidentiality of Data: The authors declare that they have followed the protocols of their work center on the publication of patient data.

Protection of Human and Animal Subjects: The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and those of the Code of Ethics of the World Medical Association (Declaration of Helsinki as revised in 2024).

Provenance and Peer Review: Not commissioned; externally peer-reviewed.

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