Ophthalmol Ther (2025) 14:2155–2164
https://doi.org/10.1007/s40123-025-01208-w

ORIGINAL RESEARCH

Efficacy of Intravitreal Brolucizumab Switch in Pachychoroid Neovasculopathy

Nicolò Ribarich · Marco Battista · Lisa Checchin · Riccardo Sacconi · Francesco Bandello · Giuseppe Querques

Received: May 26, 2025 / Accepted: July 10, 2025 / Published online: July 17, 2025

ABSTRACT

Introduction: This study aimed to evaluate the anatomical and functional outcomes of switching to intravitreally administered brolucizumab (Beovu®, Novartis) in patients affected by pachychoroid neovasculopathy (PNV) who were considered as non-responders to previous anti-vascular endothelial growth factor (anti-VEGF) therapies, defined as the persistence of intraretinal fluid (IRF), subretinal fluid (SRF), or subretinal hyper-reflective material (SHRM).

Methods: Twenty-three eyes of 21 patients with exudative PNV, who were switched to brolucizumab between April 2021 and December 2023, were retrospectively enrolled. All patients had previously received at least one injection of another anti-VEGF agent. Following the switch (baseline), patients received brolucizumab under a pro re nata regimen and were followed for 12 months. Best-corrected visual acuity (BCVA), central macular thickness (CMT), central choroidal thickness (CT), and height of IRF, SRF, SHRM, and pigment epithelial detachment (PED) were assessed at baseline and at the 12-month follow-up.

Results: At 12 months after the switch to brolucizumab (mean 5.26 injections), BCVA remained stable (20/50, 0.4 logMAR). However, significant anatomical improvements were observed, including a reduction in SRF (97–18 µm, $p=0.002$), SHRM (75–0 µm, $p=0.008$), and CT (379–337 µm, $p<0.001$). Resolution of IRF was achieved in 70% of eyes and SHRM in 87%. A median of 2 brolucizumab injections were required to achieve fluid control (absence of both IRF and SRF). Notably, the number of injections needed for complete SRF resolution predicted final BCVA.

Conclusion: In our cohort of patients with PNV, switching to brolucizumab demonstrated a significant anatomical response, leading to a reduction in exudative features. While BCVA remained stable, the number of brolucizumab injections required to resolve SRF emerged as a predictor of final visual outcome, suggesting that an earlier switch in non-responders might optimize anatomical results. The safety profile of brolucizumab in this study was favourable, with no severe inflammatory adverse events reported.

N. Ribarich · M. Battista · L. Checchin · R. Sacconi · F. Bandello · G. Querques
School of Medicine, Vita-Salute San Raffaele University, Milan, Italy

N. Ribarich · M. Battista · L. Checchin · R. Sacconi · F. Bandello · G. Querques
Division of Head and Neck, Ophthalmology Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy

G. Querques (✉)
Department of Ophthalmology, University Vita-Salute, IRCCS Ospedale San Raffaele, Via Olgettina 60, 20132 Milan, Italy
e-mail: querques.giuseppe@hsr.it; giuseppe.querques@hotmail.it

Keywords: Brolucizumab; Pachychoroid syndrome; Choroidal neovascularization

Key Summary Points

Pachychoroid neovasculopathy (PNV) represents a challenging retinal condition, resulting in persistent subretinal and intraretinal fluid and imposing a significant burden on visual function.

This study aimed to evaluate whether switching to intravitreally administered brolucizumab in anti-VEGF non-responsive patients with PNV would yield superior anatomical and functional outcomes.

The switch to brolucizumab resulted in significant anatomical improvements—namely reductions in subretinal fluid, subretinal hyper-reflective material, and central choroidal thickness—although best-corrected visual acuity remained unchanged.

The findings suggest that brolucizumab may be an effective rescue treatment for anatomical disease control in PNV. Importantly, the number of injections required to resolve subretinal fluid predicted final visual acuity, advocating for earlier intervention in treatment-resistant cases.

These results support the potential role of brolucizumab in the therapeutic algorithm for PNV, particularly in patients unresponsive to standard anti-VEGF agents.

INTRODUCTION

Pachychoroid neovasculopathy (PNV) poses a profound challenge for clinicians. Pachychoroid disorders, characterized by choroidal thickening and consequential alterations in the choroidal vasculature, represent a spectrum of conditions presenting significant diagnostic and therapeutic complexities. When these disorders intersect with the development of choroidal neovascularization (CNV), the clinical landscape becomes substantially more intricate, necessitating urgent and efficacious therapeutic interventions. Recent advancements in the field of ocular therapeutics, notably the emergence of anti-vascular endothelial growth factor (anti-VEGF) molecules, offer a promising treatment for patients suffering from these diseases [1, 2].

The spectrum of pachychoroid diseases encompasses a diverse range of ocular conditions combined with the common underlying feature of choroidal thickening, impacting the retinal pigment epithelium (RPE), and often leading to the development of CNV. These conditions include central serous chorioretinopathy (CSCR), pachychoroid pigment epitheliopathy (PPE), PNV, polypoidal choroidal vasculopathy (PCV), peripapillary pachychoroid syndrome (PPS), and pachyvitelliform maculopathy (PVM) [3, 4].

PNV is characterized by the presence of choroidal neovascularization, a critical hallmark of several retinal diseases, complicating the clinical course and significantly affecting the visual prognosis in patients with pachychoroid spectrum disorders. The abnormal growth of blood vessels beneath the retina triggers exudation, haemorrhage, and consequential macular damage, often resulting in impairment of central vision. Effectively managing PNV demands a delicate balance, requiring the simultaneous addressal of the neovascular component and recognition of the distinct underlying pachychoroid pathology, which might manifest differently from the conventional CNV mechanisms observed in other retinal diseases [1, 2].

Conventional treatment modalities, primarily anti-vascular endothelial growth factor (anti-VEGF) agents, have been the mainstay in managing PNV [5]. While these therapies have demonstrated efficacy in controlling CNV activity and enhancing visual outcomes in a substantial number of patients, challenges persist [6–8]. Some individuals exhibit suboptimal responses to anti-VEGF therapy, leading to the necessity for frequent injections and, in certain cases, displaying resistance or limited durability of effects. Additionally, the long-term safety and sustained efficacy of these treatments in pachychoroid disorders remain areas of ongoing research and discussion [9, 10].

In the face of these challenges, the introduction of brolucizumab (Beovu®, Novartis) has introduced a new dimension to the treatment landscape. Brolucizumab is a low molecular weight humanized single-chain variable antibody fragment vascular endothelial growth factor (specifically VEGF-A) inhibitor firstly commercialized in 2019 for the treatment of exudative age-related macular degeneration (AMD) and subsequently extended in 2022 for diabetic macular oedema and macular oedema secondary to retinal vein occlusion [11]. With its distinctive molecular structure and smaller size, brolucizumab holds the potential for enhanced retinal penetration and prolonged durability, potentially addressing the unmet needs of patients grappling with PNV [11].

This article aims to provide an in-depth exploration of the intricate nature of PNV, focusing on the evolving therapeutic landscape and particularly highlighting the potential roles and associated challenges of brolucizumab in managing this complex condition. By delving into the current understanding, clinical evidence, and future directions of brolucizumab utilization, our aim is to evaluate and assess the efficacy in anatomical and functional terms of brolucizumab in PNV in eyes already treated with other anti-VEGF molecules and then switched to brolucizumab.

METHODS

This was a retrospective study enrolling patients from the Medical Retina and Imaging Unit of the Department of Ophthalmology of San Raffaele Scientific Institute, Milan, Italy between April 2021 and December 2023. This retrospective study was performed in accordance with the Helsinki Declaration of 1964, and its later amendments. All subjects provided informed consent to participate in the study and publication of the information. The ethics committee of IRCCS Ospedale San Raffaele was notified about this study. According to Italian law, retrospective studies require the ethics committee to be notified, but do not require its approval.

A cohort of patients diagnosed with exudative PNV who had received at least one intravitreal injection of brolucizumab was selected. Given that the aim of this study was to evaluate the efficacy of brolucizumab in patients undergoing a "therapy switch," our study population had previously received at least one intravitreal injection of another anti-VEGF medication. Enrolled patients were selected to switch to brolucizumab because they were considered non-responders to the previous anti-VEGF therapy, defined by the persistence of intraretinal fluid, subretinal fluid, or subretinal hyper-reflective material after the last three injections. Each patient received brolucizumab therapy following a pro re nata (PRN) regimen after a loading phase of 3 injections every 4 weeks. Patients were followed up for 1 year after the first brolucizumab injection. Anatomical and functional parameters were assessed at 6 and 12 months. All intravitreal injections received by the patients, including brolucizumab, are paid for by the National Healthcare Service of Italy, some patients may have to co-pay a fraction of the cost, but patients who are below a certain income level or above a certain age are exempt from co-pay. Parameters defining the spectrum of pachychoroid and PNV were applied as inclusion criteria: evidence of pachyvessels, focal or diffuse choroidal thickening, inner choroidal attenuation, irregular RPE detachment with heterogeneous hyperreflective material in the sub-RPE space, as well as choroidal vascular hyperpermeability observed on indocyanine green angiography (ICGA) and evidence of intraretinal fluid (IRF) or subretinal fluid (SRF) or SHRM on optical coherence tomography (OCT) [11]. Patients with significant optic media opacities limiting image quality or affected by other ocular pathologies, such as AMD, myopic macular degeneration, diabetic macular oedema or inflammatory, acute central serous chorioretinopathy, were excluded from the study, as were those lacking anatomical follow-up settings in the OCT software.

Baseline was set as the timepoint in which the switch toward brolucizumab happened. The decision to change the drug was made by the physician visiting the patient on the basis of their own clinical judgement. All patients underwent a complete ophthalmological examination, including best-corrected visual acuity (BCVA) on Snellen chart, slit-lamp biomicroscopy,

intraocular pressure measurement, and indirect fundus examination at baseline and at follow-up. BCVA was expressed as the logarithm of the minimum angle of resolution (logMAR) for statistical analyses.

MultiColor imaging, infrared reflectance (IR), fundus autofluorescence (FAF), and structural spectral-domain OCT (SD-OCT) were acquired at each ophthalmological examination. OCT-A was performed in a substantial number of patients. MultiColor imaging, IR, FAF, and SD-OCT were performed using Spectralis HRA + OCT (Heidelberg Engineering, Heidelberg, Germany). Central macular thickness (CMT) in the central 1-mm-diameter circle of the Early Treatment Diabetic Retinopathy Study (ETDRS) thickness map were recorded with Spectralis software (Heidelberg Eye Explorer, Version 1.9.11.0; Heidelberg Engineering). Central choroidal thickness (ChT) was manually measured as the mean of subfoveal ChT and ChT measured 500 and 1000 µm nasally and temporally to the fovea [12].

Analysis involved examination of OCT radial sections centred on the fovea, as well as horizontal sections measuring 20° × 20° and 15° × 5°. Various parameters were assessed, including subfoveal choroidal thickness, CMT pre- and post-injection, and the height of IRF, SRF, SHRM and fibrovascular PED pre- and post-injection. Measurements were performed by two trained ophthalmologists: NR and LC.

Statistical Analysis

Statistical analyses were performed using SPSS Statistics Software version 27.0 (IBM, Armonk, New York, USA). Categorical variables were expressed as absolute count and percentages. Continuous variables were summarized as mean ± standard deviation if normally distributed. If not, median and interquartile range (IQR) were provided. Normal distribution of continuous variables was tested using the Shapiro–Wilk test. We longitudinally explored normally distributed variables using Student's paired samples *t* test and non-normally distributed variables with the Wilcoxon signed-rank test. To assess the statistical association between the various OCT variables and between these variables and visual acuity, logistic regression and binary logistic regression were employed and the results of these tests are reported with their standardized coefficients (β). We set a threshold for statistical significance at $p < 0.05$.

RESULTS

For the study, 21 white patients treated with at least one intravitreal injection of brolucizumab were recruited, accounting for a total of 23 eyes. Among these patients, 14 were male (64%) and 7 were female (35%), with a mean age of 68 ± 11 years (Table 1).

Ten patients received the injection in the right eye (48%) and nine in the left eye (43%); two patients received an injection in both eyes. Eighteen eyes were phakic (78%), and five were pseudophakic (22%).

Before switching to brolucizumab, patients had received an average of 17.65 ± 11.54 (minimum 3) injections of other anti-VEGF medications, divided into an average of 3.5 (0–6 IQR) bevacizumab (Avastin®, Genentech/Roche), 4 (0–7.25 IQR) ranibizumab (Lucentis®, Genentech/Novartis), and 5.5 (1–12 IQR) aflibercept (Eylea®, Regeneron/Bayer) injections.

At baseline, the average BCVA was 20/50, 0.4 logMAR (20/32–20/100, 0.2–0.7 logMAR IQR), with mean heights of IRF, SRF, SHRM, and PED at 0 µm (0–115 µm IQR), 97 µm (64–136 µm IQR), 75 µm (0–148 µm IQR), and 146 µm (105–266 µm IQR), respectively, and a subfoveal choroidal thickness (CT) of 379 µm (± 108 µm).

The patients received an average of 5.26 (3.42–7.10 IQR) injections of brolucizumab over the course of 1 year, with an average of an injection every 70 days. Patients were treated with a PRN regimen; according to the clinician's judgement, patients underwent injections if persistent or recurrence of OCT alterations occurred. All patients underwent a loading phase of 3 injections every 4 weeks.

At 1 year after the first injection of brolucizumab, the average BCVA remained stable around 20/50, 0.4 logMAR (20/32–20/100, 0.2–0.7 logMAR IQR), as did IRF (0 µm, 0–119

Table 1 Demographic, therapeutical, anatomical and functional characteristics of patients at baseline and at 12-month follow-up

Sex	
Male	14 (66%)
Female	7 (33%)
Age	68 ± 11 years
Lens	
Phakic	18 (78%)
Pseudophakic	5 (22%)
Eyes involved	
One eye	19 (91%)
Both eyes	2 (9%)
Previous injections	17.65 ± 11.54
Bevacizumab	3.5 (0–6)
Ranibizumab	4 (0–7.25)
Aflibercept	5.5 (1–12)
Baseline	
BCVA	20/50 (20/32–20/100)
IRF	8 (35%) | 0 µm (0–115)
SRF	21 (92%) | 97 µm (64–136)
SHRM	11 (48%) | 75 µm (0–148)
PED	23 (100%) | 146 µm (105–266)
Choroidal thickness	379 µm (± 108)
Brolucizumab injections at 12 months	5.26 (3.42–7.10)
1-year follow-up	
BCVA	20/50 (20/32–20/100)
IRF	7 (30%) | 0 µm (0–119)
SRF	11 (48%) | 18 µm (0–50)
SHRM	2 (9%) | 0 µm (0–0)
PED	23 (100%) | 120 µm (55–185)
Choroidal thickness	337 µm (244–430)

For anatomical parameters both the frequency and the median/mean are reported

IQR), and PED (120 µm, 55–185 µm IQR) while there was a reduction in SRF, SHRM, and CT at respectively 18 µm (0–50 µm IQR, $p=0.002$), 0 µm (0–0 µm IQR $p=0.008$), 337 µm (244–430 µm IQR $p<0.001$, Fig. 1). To achieve a fluid control (intended as absence of both IRF and SRF) a median of 2 injections of brolucizumab were needed.

Intermediate results at 6 months showed a significant reduction only in SRF (− 68 µm, $p=0.004$), PED (− 54 µm, $p=0.002$), and CT (− 52 µm, $p=0.001$) (Table 2).

In detail, among all 23 eyes, 16 (70%) achieved complete resolution of IRF, 20 (87%) of SHRM, while only 11 (48%) showed disappearance of SRF.

The final BCVA was statistically linked to BCVA ($\beta=0.83$, $p<0.001$) and IRF ($\beta=-0.46$, $p=0.024$) at baseline, and at 6 months (respectively $\beta=0.88$, $p<0.001$ and $\beta=-0.42$, $p=0.045$). The analysis of other associations did not yield statistically significant results ($p>0.05$). Specifically, the visual acuity at 12 months was not linked to CT, SRF, SHRM, PED, or CMT, either at the initial assessment or at 6 months.

Post hoc power analysis yielded excellent ($p<0.01$) results in all tests which turned out to be significant except for the linear regression between baseline IRF, 6-month IRF and 12-month BCVA (Table 3).

DISCUSSION

We assessed the anatomical and functional efficacy of intravitreal injection of brolucizumab in patients affected by PNV and we found a significant anatomical response 6 months after switching patients to a new treatment regiment, with this effect being sustained at 1-year follow-up. Indeed, we highlighted that this new drug significantly reduced SRF, PED and CT at the first timepoint, with the added benefit of decreasing SHRM after a year of treatment. Besides, 70% achieved complete absorption of IRF, 87% of SHRM, while 48% showed resolution of SRF. However, we did not reveal a clear visual improvement at the conclusion of the cycle, a trend not consistent with the outcomes

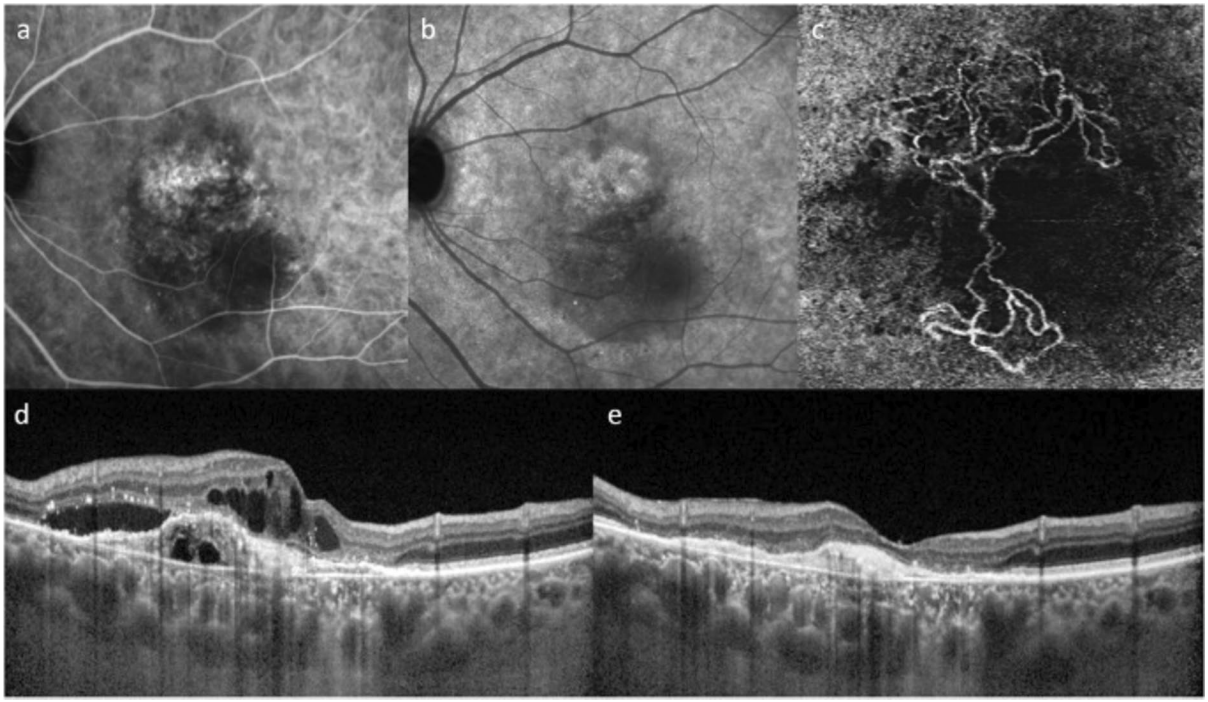

Fig. 1 Left eye of a 59-year-old woman affected by pachychoroid neovasculopathy (PNV). The early (**a**) and late (**b**) phases of indocyanine green angiography (ICGA) revealed the presence of a vascular net in the parafoveal area, just above a hypofluorescent area in the inferior part of the macula. The 3 × 3 optical coherence tomography-angiography (OCT-A) scan confirmed the presence of a type 1 choroidal neovascularization (CNV). The OCT scan after 30 days from the last injection of a triplet of monthly aflibercept (9 in total) showed the relapse of significant exudation (intraretinal, subretinal fluid and pigment epithelium detachment (PED)) with an increase of macular thickness in the subfoveal and nasal parafoveal area. A switch toward brolucizumab was then decided: the OCT scan after 30 days from the second monthly brolucizumab treatment demonstrated a great improvement of the macular thickness with a complete resolution of the exudative features; of note, also the thickness of PED was reduced with an increase of the inner hyperreflectivity

observed with the same molecule in other diseases, such as diabetic macular oedema (DME) and AMD. This result needs to be confirmed with larger studies, but it is already informative with regards to treatment objectives that we can try to achieve in patients with PNV. This will also shift how we counsel these patients and what expectations they might have from the treatment with a new drug.

All three KINGFISHER, KESTREL and KITE trials on DME, as well as the HAWK and HARRIER studies on AMD, revealed that this molecule can lead to a more pronounced and long-lasting anatomical response compared to aflibercept, while functional improvement, although present, was comparable between the two compounds [13–17]. The major drawback in the acceptance of this new drug as first-line therapy among anti-VEGFs was the relatively high incidence of intraocular inflammation events, such as vasculitis, with sight-threatening severe cases [18]. This led to the investigation of the use of this drug in other diseases that were already treated with other anti-VEGF agents and sometimes were unresponsive to currently available therapies. In fact, Ueda-Consolvo et al. studied the use of intravitreally administered brolucizumab in 23 eyes with PCV, likewise affected by AMD, and observed a significant extension of the interval between 2 injections in both the illnesses [19].

Table 2 Statistical analysis

Parameter	Value	*p* value
Change from baseline[a]		
6-month BCVA	0	0.412
6-month IRF	0 µm	0.263
6-month SRF	− 68 µm	0.004*
6-month SHRM	− 75 µm	0.074
6-month PED	− 54 µm	0.002*
6-month CT	− 52 µm	0.001*
12-month BCVA	0	0.413
12-month IRF	0 µm	0.575
12-month SRF	− 79 µm	0.002*
12-month SHRM	− 75 µm	0.008*
12-month PED	− 26 µm	0.263
12-month CT	− 42 µm	0.001*
12-month BCVA[b]		
Baseline BCVA	$\beta = 0.83$	< 0.001*
Baseline IRF	$\beta = -0.46$	0.024*
Baseline SRF	$\beta = -0.04$	0.848
Baseline SHRM	$\beta = -0.25$	0.231
Baseline PED	$\beta = -0.29$	0.166
Baseline CT	$\beta = -0.24$	0.265
6-month BCVA	$\beta = 0.88$	< 0.001*
6-month IRF	$\beta = -0.42$	0.045*
6-month SRF	$\beta = -0.04$	0.848
6-month SHRM	$\beta = -0.40$	0.057
6-month PED	$\beta = -0.15$	0.492
6-month CT	$\beta = -0.17$	0.435

*Statistically significant (as $p < 0.05$)

[a]The first section reports the mean difference of parameters from baseline and the associated statistical significance

[b]The second section reports logistic regression between various parameters and final BCVA

Table 3 Post hoc power analysis: post hoc powers, expressed as *p* values, for the associations proven to be statistically significant in Table 2 are shown

Parameters[a]	Post hoc power (*p* value)
Baseline vs 6-month SRF	< 0.01
Baseline vs 6-month PED	< 0.01
Baseline vs 6-month CT	< 0.01
Baseline vs 12-month SRF	< 0.01
Baseline vs 12-month SHRM	< 0.01
Baseline vs 12-month CT	< 0.01
Baseline BCVA and 12-month BCVA LR	< 0.01
Baseline IRF and 12-month BCVA LR	0.34
6-month BCVA and 12-month BCVA LR	< 0.01
6-month IRF and 12-month BCVA LR	0.44

[a]Variations of parameters from baseline are reported first, followed by results of one linear regression (LR) between various parameters and final BCVA

The absence of a statistically significant functional improvement in our study may be attributed to the characteristics of our sample. Specifically, the selected patients already had a long-standing disease and had received an average of 17.65 ± 11.54 SD previous injections of other anti-VEGF agents. It is recognized that both the persistence of subretinal or intraretinal fluid and a high number of injections can promote photoreceptor damage, potentially explaining our limited visual acuity recovery despite the robust anatomical response [20–22].

Furthermore, our analysis revealed that patients required a median of 2 brolucizumab injections to achieve fluid control, defined as the absence of both IRF and SRF. Nonetheless, only the number of injections needed to induce a complete resolution of SRF significantly predicted the final BCVA.

Additionally, as expected, we showed that the BCVA and IRF reached by patients at the end of the 3 injections were respectively associated with both the baseline BCVA and IRF, as well as those obtained after a single treatment.

Overall, our results are consistent with two studies recently published in the literature. Carosielli et al. retrospectively examined 34 eyes with PCV and found resolution of SRF or IRF in 65% of eyes and a functional response in 80% of cases, with a mean number of brolucizumab injections of 2.8 ± 1.8 [23]. Cho et al. retrospectively compared the anatomical and functional response at 12 months in 62 eyes with PCV treated with aflibercept or brolucizumab. They found that, despite the absence of a statistically significant functional improvement compared to aflibercept at the end of the follow-up period, brolucizumab induced a more accentuated anatomical response than aflibercept [24].

However, compared to these studies, our analysis has highlighted the existence of a predictive factor for final BCVA, which is represented by the number of injections required to achieve complete resolution of SRF. In this sense, considering an early switch toward brolucizumab could be appropriate to optimize the anatomical results. Surprisingly, the same remarkable outcome was not observed with IRF alone or in combination with SRF. This result could be attributed to two factors: firstly, the influence of intraretinal fluid, rather than subretinal fluid, on BCVA at the end of treatment [21, 22]; and secondly, the predominant presence of subretinal fluid within the pachychoroid spectrum. In fact, there may be a transudative accumulation of subretinal fluid due to dysfunction in the retinal pigment epithelium (RPE) pump function, resulting in dysfunctional yet partially viable photoreceptors. Additionally, the pachychoroid spectrum more commonly presents with type 1 CNV, which typically exhibits subretinal fluid accumulation. This contrasts with the other two types of macular neovascularization often seen in AMD, which involve both intra- and subretinal fluid accumulation [11, 22, 25].

Finally, none of our patients developed severe inflammatory adverse reaction; specifically, no cases of retinal occlusion, uveitis and retinal vasculitis were recorded. This finding is consistent with previous data produced during clinical trials [10, 13, 17].

Despite the small size of our sample, most of the tests were shown to have excellent power. The associations between baseline IRF, 6-month IRF and 12-month BCVA had a lower power compared to the others, indicating that these results may be harder to replicate in further studies.

CONCLUSION

Our study reveals that intravitreally administered brolucizumab could be a promising and safe therapeutic option for cases affected by PNV which do not respond to currently available commercial treatments. These findings warrant further investigation through prospective studies. Indeed, our study has several limitations, including the small sample size, its retrospective design, the absence of a control group, and the inclusion of patients previously treated with other intravitreal medications or having undergone PDT before starting brolucizumab. Indeed, a chronic macular condition unresponsive to various other intravitreal treatments may have compromised the potential for functional recovery in our cohort. Furthermore, a control group, such as patients who were switched to a drug other than brolucizumab, could provide some useful information in future studies.

Author Contributions. Nicolò Ribarich: Data collection, Drafting of Manuscript, Statistical Analysis. Marco Battista: Drafting of Manuscript, Statistical Analysis, Review of the manuscript. Lisa Checchin: Data collection, Drafting of Manuscript. Riccardo Sacconi: Concept and design, Review of the manuscript. Francesco Bandello: Supervision. Giuseppe Querques: Concept and design, Review of the manuscript.

Funding. No funding or sponsorship was received for this study or publication of this article.

Data Availability. The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of Interest. Nicolò Ribarich, Marco Battista, Lisa Checchin: none. Riccardo Sacconi is consultant for Allergan Inc, Bayer Shering-Pharma, Medivis, Novartis, and Zeiss. Francesco Bandello consultant for: Alcon (Fort Worth, Texas, USA), Alimera Sciences (Alpharetta, Georgia, USA), Allergan Inc (Irvine, California, USA), Farmila-Thea (Clermont-Ferrand, France), Bayer Shering-Pharma (Berlin, Germany), Bausch And Lomb (Rochester, New York, USA), Genentech (San Francisco, California, USA), Hoffmann-La-Roche (Basel, Switzerland), NovagaliPharma (Évry, France), Novartis (Basel, Switzerland), Sanofi-Aventis (Paris, France), Thrombogenics (Heverlee, Belgium), Zeiss (Dublin, USA). Giuseppe Querques is consultant for Alimera Sciences, Allergan Inc, Amgen, Bayer Shering-Pharma, Heidelberg, KBH, LEH Pharma, Lumithera, Novartis, Sandoz, Sifi, Sooft-Fidea, and Zeiss. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed. Giuseppe Querques and Riccardo Sacconi are Editorial Board members of *Ophthalmology and Therapy*. They were not involved in the selection of peer reviewers for the manuscript nor any of the subsequent editorial decisions.

Ethical Approval. This retrospective study was performed in accordance with the Helsinki Declaration of 1964, and its later amendments. All subjects provided informed consent to participate in the study and publication of the information. The ethics committee of IRCCS Ospedale San Raffaele was notified about this study. According to Italian law, retrospective studies require the ethics committee to be notified, but do not require its approval.

REFERENCES

1. Sagar P, Sodhi PS, Roy S, Takkar B, Azad SV. Pachychoroid neovasculopathy: a comparative review on pathology, clinical features, and therapy. Eur J Ophthalmol. 2021;32(2):767–80. https://doi.org/10.1177/11206721211036290.

2. Yanagi Y. Pachychoroid disease: a new perspective on exudative maculopathy. Jpn J Ophthalmol. 2020;64(4):323–37. https://doi.org/10.1007/S10384-020-00740-5/METRICS.

3. Brown RB, Mohan S, Chhablani J. Pachychoroid spectrum disorders: an updated review. J Ophthalmic Vis Res. 2023;18(2):212–29. https://doi.org/10.18502/JOVR.V18I2.13188.

4. Cheung CMG, Dansingani KK, Koizumi H, et al. Pachychoroid disease: review and update. Eye (Lond). 2025;39(5):819–34. https://doi.org/10.1038/s41433-024-03253-4.

5. Sacconi R, Tomasso L, Corbelli E, et al. Early response to the treatment of choroidal neovascularization complicating central serous chorioretinopathy: a OCT-angiography study. Eye (Lond). 2019;33(11):1809–17. https://doi.org/10.1038/s41433-019-0511-2.

6. Ferrara N, Adamis AP. Ten years of anti-vascular endothelial growth factor therapy. Nat Rev Drug Discov. 2016;15(6):385–403. https://doi.org/10.1038/NRD.2015.17.

7. Wykoff CC, Ou WC, Brown DM, et al. Randomized trial of treat-and-extend versus monthly dosing for neovascular age-related macular degeneration: 2-year results of the TREX-AMD study. Ophthalmol Retina. 2017;1(4):314–21. https://doi.org/10.1016/J.ORET.2016.12.004.

8. Sacconi R, Baldin G, Carnevali A, et al. Response of central serous chorioretinopathy evaluated by multimodal retinal imaging. Eye (Lond).

2018;32(4):734–42. https://doi.org/10.1038/eye.2017.295.

9. Cheung CMG, Lee WK, Koizumi H, Dansingani K, Lai TYY, Freund KB. Pachychoroid disease. Eye (Lond). 2019;33(1):14–33. https://doi.org/10.1038/S41433-018-0158-4.

10. Cho HJ, Jung SH, Cho S, Han JO, Park S, Kim JW. Intravitreal anti-vascular endothelial growth factor treatment for pachychoroid neovasculopathy. J Ocul Pharmacol Ther. 2019;35(3):174–81. https://doi.org/10.1089/JOP.2018.0107.

11. Dugel PU, Koh A, Ogura Y, et al. HAWK and HARRIER: phase 3, multicenter, randomized, double-masked trials of brolucizumab for neovascular age-related macular degeneration. Ophthalmology. 2020;127(1):72–84. https://doi.org/10.1016/J.OPHTHA.2019.04.017.

12. Sacconi R, Deotto N, Merz T, Morbio R, Casati S, Marchini G. SD-OCT choroidal thickness in advanced primary open-angle glaucoma. J Glaucoma. 2017;26:523–7.

13. Markham A. Brolucizumab: first approval. Drugs. 2019;79(18):1997–2000. https://doi.org/10.1007/S40265-019-01231-9.

14. Wykoff CC, Garweg JG, Regillo C, et al. KESTREL and KITE phase 3 studies: 100-week results with brolucizumab in patients with diabetic macular edema. Am J Ophthalmol. 2023. https://doi.org/10.1016/J.AJO.2023.07.012.

15. Dugel PU, Singh RP, Koh A, et al. HAWK and HARRIER: ninety-six-week outcomes from the phase 3 trials of brolucizumab for neovascular age-related macular degeneration. Ophthalmology. 2021;128(1):89–99. https://doi.org/10.1016/J.OPHTHA.2020.06.028.

16. Khanani AM, Brown DM, Jaffe GJ, et al. MERLIN: phase 3a, multicenter, randomized, double-masked trial of brolucizumab in participants with neovascular age-related macular degeneration and persistent retinal fluid. Ophthalmology. 2022;129(9):974–85. https://doi.org/10.1016/j.ophtha.2022.04.028.

17. Singh RP, Barakat MR, Ip MS, et al. Efficacy and safety of brolucizumab for diabetic macular edema: the KINGFISHER randomized clinical trial. JAMA Ophthalmol. 2023. https://doi.org/10.1001/JAMAOPHTHALMOL.2023.5248.

18. Pakravan P, Patel V, Lai J, et al. Intraocular inflammation incidence after intravitreal brolucizumab injection for exudative age-related macular degeneration. Retina. 2023;43(10):1717–22. https://doi.org/10.1097/IAE.0000000000003862.

19. Ueda-Consolvo T, Tanigichi A, Numata A, et al. Switching to brolucizumab from aflibercept in age-related macular degeneration with type 1 macular neovascularization and polypoidal choroidal vasculopathy: an 18-month follow-up study. Graefes Arch Clin Exp Ophthalmol. 2023;261(2):345–52. https://doi.org/10.1007/S00417-022-05793-5.

20. Eshtiaghi A, Issa M, Popovic MM, Muni RH, Kertes PJ. Geographic atrophy incidence and progression after intravitreal injections of anti-vascular endothelial growth factor agents for age-related macular degeneration: a meta-analysis. Retina. 2021;41(12):2424–35. https://doi.org/10.1097/IAE.0000000000003207.

21. Sharma A, Kumar N, Parachuri N, et al. Understanding the mechanisms of fluid development in age-related macular degeneration. Ophthalmol Retina. 2021;5(2):105–7. https://doi.org/10.1016/J.ORET.2020.09.016.

22. Core JQ, Pistilli M, Hua P, et al. Predominantly persistent intraretinal fluid in the comparison of age-related macular degeneration treatments trials. Ophthalmol Retina. 2022;6(9):771. https://doi.org/10.1016/J.ORET.2022.03.024.

23. Carosielli M, Carnevali A, Fallico M, et al. Intravitreal brolucizumab for pachychoroid neovasculopathy associated with chronic central serous chorioretinopathy. Transl Vis Sci Technol. 2023. https://doi.org/10.1167/TVST.12.12.17.

24. Cho HJ, Kang KH, Yoon W, Lee J, Kim CG, Kim JW. Intravitreal brolucizumab and aflibercept for polypoidal choroidal vasculopathy. J Ocul Pharmacol Ther. 2023;39(9):653–60. https://doi.org/10.1089/JOP.2023.0030.

25. Core JQ, Pistilli M, Daniel E, et al. Predominantly persistent subretinal fluid in the comparison of age-related macular degeneration treatments trials (CATT). Ophthalmol Retina. 2021;5(10):962. https://doi.org/10.1016/J.ORET.2021.06.003.