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Twenty-four-month real-life treatment outcomes of polypoidal choroidal vasculopathy versus type 1 macular neovascularization in Caucasians

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Abstract

Background: To compare 24-month real-world outcomes of Vascular Endothelial Growth Factor (VEGF) inhibitors for Polypoidal Choroidal Vasculopathy (PCV) and type 1 Macular Neovascularization (MNV) in a Caucasian population.

Methods: Retrospective analysis from a prospectively designed observational database. Data from Italian centres participating in the Fight Retinal Blindness! (FRB!) project were collected. Treatment-naïve PCV or type 1 MNV commencing treatment after January 2009 were included. The primary outcome was 24-month visual acuity (VA) change; other outcomes included baseline characteristics, number of anti-VEGF injections, time to lesion inactivation and proportion of active visits.

Results: A total of 322 eyes (114 PCVs) from 291 patients were included. Median [Q1, Q3] VA at baseline was comparable (70 [55, 75.8] vs. 70 [58.8, 75] letters, $p = 0.95$). Adjusted VA change at 2 years was higher in PCV (mean [95% CI], +1.2 [−1.6, 4.1] vs. −3.6 [−6, −1.2] letters, $p = 0.005$). PCV received fewer anti-VEGF injections over the first 24 months of treatment than type 1 MNV (median [Q1, Q3], 8 [5, 10] vs. 9 [7, 12.2] injections, $p = 0.001$), inactivated earlier (median [Q1, Q3], 235 [184, 308] vs. 252 [169, 343] days, $p = 0.04$) and was less frequently graded 'active' (62% vs. 68% of visits, $p = 0.001$).

Conclusions: PCV had slightly better VA outcomes over 24 months of treatment than type 1 MNV after receiving less anti-VEGF injections. These results suggest a possible overlap of the two clinical entities with similar visual prognosis in Caucasians.

KEYWORDS

age-related macular degeneration, Caucasians, polypoidal choroidal vasculopathy, real-life, type 1 macular neovascularization

1 | INTRODUCTION

Polypoidal choroidal vasculopathy (PCV) represents an estimated 8% of all neovascular Age-related Macular Degeneration (nAMD) cases in the Caucasian population,[1–3] although recent evidence suggests prevalence is as high as 25%–30%.[4–6]

PCV in Caucasians is frequently associated with typical AMD features and its imaging characteristics resemble closely those of type 1 Macular Neovascularization (MNV).[7] Given these similarities, some authors have suggested renaming polypoidal lesions 'aneurysmal type 1 MNV' when they develop in the context of type 1 MNV with AMD-related changes, rather than considering PCV a separate entity.[8–10]

While type 1 MNV has shown better treatment outcomes than the other forms of nAMD,[11] PCV has been classically associated with a severe clinical course and a poor visual prognosis.[6,7,12–14] However, most of the studies focusing on PCV have been conducted on patients of Asian descent, while data on outcomes of PCV treatment in Caucasians come mostly from subanalysis of larger clinical trials and real-world studies,[15,16] with few works focusing specifically on PCV in Caucasians.[17]

The aim of this study was therefore to report 24-month, real-world outcomes of PCV treatment in a large cohort of Caucasian patients from the Fight Retinal Blindness! (FRB!) registry and to compare these results with those of Caucasian patients affected by type 1 MNV.

2 | METHODS

2.1 | Study design and setting

The study included eyes tracked in the Fight Retinal Blindness (FRB!) Registry from Italian practices. Details on the methodology of the FRB! registry have been previously published.[18] Briefly, real-world treatment outcomes of nAMD are prospectively tracked in the nAMD module of the registry, in compliance with the International Consortium for Healthcare Outcome Measurement's minimum standard set of treatment outcomes for macular degeneration.[19]

Institutional ethics approval was obtained from each of the participating sites: the Department of Biomedical and Clinical Science Luigi Sacco, Milan, the Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, the Department of Experimental Medicine, Tor Vergata University, Rome, the University Hospital Maggiore della Caritá, Novara, the Eye Clinic, AOU Maggiore della Carità, and the Ophthalmology Department, San Martino Hospital, Belluno. Informed 'opt-in' consent was obtained from all subjects. The research described adhered to the tenets of the Declaration of Helsinki.

2.2 | Study population

Treatment-naïve eyes affected by either PCV or type 1 MNV commencing treatment with anti-VEGF after 1 January 2009 were considered for the analysis. Eligible eyes received at least three intravitreal anti-VEGF injections during the first 12 months of follow-up and had at least two complete visits registered. Eyes that completed at least 24 months of follow-up were defined as 'completers', while eyes that did not complete 24 months of observations were defined as 'non-completers'.

2.3 | Data sources and measurements

Data recorded from each clinical visit by the treating practitioner included the number of letters read on a logarithm of the minimum angle of resolution (logMAR) visual acuity chart (best of corrected, uncorrected, or pinhole), intraocular pressure, presence of macular atrophy or subretinal fibrosis, lesion activity (defined as any combination of subretinal fluid, intraretinal fluid or haemorrhage on optical coherence tomography [OCT] and/or fundoscopic examination), treatments or procedures received and any ocular adverse events.

Previous treatments received, angiographic lesion subtypes and demographic data were recorded at the baseline visit. In particular, neovascular AMD subtypes such as type 1 MNV and PCV were diagnosed by retinal specialists in routine clinical practice using the available imaging which included OCT, fundus fluorescein angiography and indocyanine green angiography at all centres. Treatment decisions, such as the choice of drug and frequency and timing of treatment, were at the discretion of the treating practitioner in consultation with the patient with no intervention by the investigators, reflecting routine clinical practice.

2.4 | Outcomes

The primary outcome was the adjusted VA change from baseline at 24 months. Secondary outcomes included baseline VA, overall final VA, crude VA change, number of injections, the proportion of visits graded as active over 24 months and time to first inactivation.

2.5 | Statistical analysis

Descriptive data were summarised using the mean (standard deviation), median (first and third quartiles), and number (percentages) where appropriate. Two-tailed *t*-tests, Mann–Whitney *U* tests, Fisher's exact tests and Chi-square

tests were used as appropriate according to data distribution to compare baseline characteristics and crude outcomes between PCV and type 1 MNV eyes. Paired *t*-tests were used to compare within-group differences between baseline and 2-year outcomes.

Calculation of raw, unadjusted visual outcomes over 24 months used the last-observation-carried-forward (LOCF) for non-completers. The number of injections was calculated using completers-only data to avoid underestimation of treatment burden.

Predictions from a longitudinal generalised additive model, including data from all eyes up to 24 months of follow-up regardless of whether they completed the follow-up, were used to visualise and compare VA outcomes between PCV and type 1 MNV over 24 months, with the interaction between angiographic subtype and time as the main predictor variable for the comparison.

The proportion of active visits over 24 months was analysed using a linear logistic mixed-effects regression model. Generalised mixed-effects Poisson regression models were used to compare the number of injections and visits over 24 months.

A Cox proportional hazards regression model was used to compare the hazard ratio between the two groups for time to first inactivation (i.e., first visit after baseline where the lesion was graded as inactive); a Kaplan–Meier survival function was used to plot survival curves.

All regression models were adjusted for baseline age and baseline VA (fixed-effects), and clustering by practice and patient (random-effects). This nesting structure helps to account for intra-subject correlation of outcomes. Poisson models also had an offset for log days of follow-up.

A *p*-value of 0.05 was considered statistically significant. All analyses were conducted using R software version 4.1.1 (R Project, R Foundation for Statistical Computing, Vienna, Austria). Packages *mgcv*, *GlmmTMB*, *coxme* and *survival* were used for the analyses.

3 | RESULTS

We identified a total of 363 treatment-naïve eyes from the FRB! Italy database affected by either PCV or type 1 MNV that started anti-VEGF treatment after 1 January 2009. Of these, 41 eyes were excluded because they did not receive at least 3 injections in the first year of treatment. The remaining 322 eyes from 291 subjects fulfilled the inclusion criteria and were included in the study. Among these, 114 (35%) were affected by PCV and 208 (65%) by type 1 MNV. Twenty four months of treatment were completed by a total of 213 (66%) eyes, of which 85 (75%) were in the PCV group and 128 (62%) in the type 1 MNV group.

3.1 | Demographics

Baseline characteristics are summarised in Table 1. Patients in the PCV group were on average significantly younger ($p < 0.001$) compared to those affected by type 1 MNV, and there were more males in the PCV cohort ($p = 0.03$), but all other baseline characteristics were homogeneously distributed. In particular, VA at baseline was similar between the two groups ($p = 0.95$).

3.2 | Visual outcomes

The adjusted VA change at 24 months was higher for PCV compared to Type 1 MNV (mean [95% CI], +1.2 [−1.6, 4.1] vs. −3.6 [−6, −1.2] letters), with a significant difference in the longitudinal trend between the 2 groups ($p = 0.005$, Figure 1A). The difference started being significantly in favour of PCV from approximately day 402 of follow-up (Figure 1B).

The unadjusted final VA at 24 months, using LOCF for dropouts, was not significantly different between the two groups (median [Q1, Q3], 70 [59, 80] vs. 70 [52.5, 75] letters, $p = 0.10$).

Secondary visual outcomes such as the crude VA change, the percentage of subjects with final VA ≥ 70 or <35 letters and VA loss/gain ≥15 letters were also comparable. Final VA at 24 months did also not appear to change significantly depending on the year of first diagnosis in either group, suggesting no significant change of trend over time (both $p > 0.05$). Detailed 24-month outcomes are presented in Table 2.

3.3 | Visits, treatments, and lesion activity

The number of visits was similar between the two groups over the 24 months of follow-up (median [Q1, Q3], 17 [15, 21] vs. 17.5 [14, 20], $p = 0.07$), while PCV received comparable, yet significantly fewer, anti-VEGF injections (median [Q1, Q3], 8 [5, 10] vs. 9 [7, 12.2] injections; $p < 0.001$). Over a third of PCV subjects (38%) also received at least one session of photodynamic therapy (PDT); 8% and 0.9% of the PCV eyes were administered 2 and 3 sessions of PDT over 24 months of follow-up, respectively.

More visits were graded as 'active' in the type 1 MNV group (68% vs. 62%, $p = 0.001$). The time (median [Q1, Q3]) to first physician grading as 'inactive' was 235 (184, 308) days for PCV and 252 (169, 343) for type 1 MNV ($p = 0.04$, Figure 2). The adjusted hazard ratio indicated that PCV lesions became inactive earlier than

TABLE 1 Baseline characteristics by lesion subtype.

	Total	PCV	Type 1 MNV	*p*
Eyes, *n*	322	114	208	
Patients, *n*	291	103	188	
Females, *n* (%)	161 (55.3%)	48 (46.6%)	113 (60.1%)	0.03
Baseline age, years, mean (SD)	74.7 (8.2)	71.6 (9.2)	76.4 (7)	<0.001
Ethnicity				
White/Caucasian, *n* (%)	322 (100%)	114 (100%)	208 (100%)	1
Baseline visual acuity				
Baseline VA, LogMAR letters, median (Q1, Q3)	70 (57.2, 75)	70 (55, 75.8)	70 (58.8, 75)	0.94
Baseline VA ≥ 70 LogMAR letters, *n* (%)	30 (9.3%)	9 (7.9%)	21 (10.1%)	0.65
Baseline VA ≤ 35 LogMAR letters, *n* (%)	169 (52.5%)	59 (51.8%)	110 (52.9%)	0.94
Presence of subretinal fibrosis, *n* (%)	18 (5.6%)	5 (4.4%)	13 (6.2%)	0.66
Subfoveal	13 (4.0%)	4 (3.5%)	9 (4.3%)	0.95
Presence of macular atrophy, *n* (%)	47 (14.6%)	16 (14.0%)	31 (14.9%)	0.96
Subfoveal	11 (3.4%)	3 (2.6%)	8 (3.8%)	0.75
Angiographic lesion subtype				
Type 1 MNV, *n* (%)	208 (64.6%)			
PCV, *n* (%)	114 (35.4%)			

Abbreviations: MNV, macular neovascularization; *n*, number; PCV, polypoidal choroidal vasculopathy; Q1–Q3, interquantile range; SD, standard deviation; VA, visual acuity.

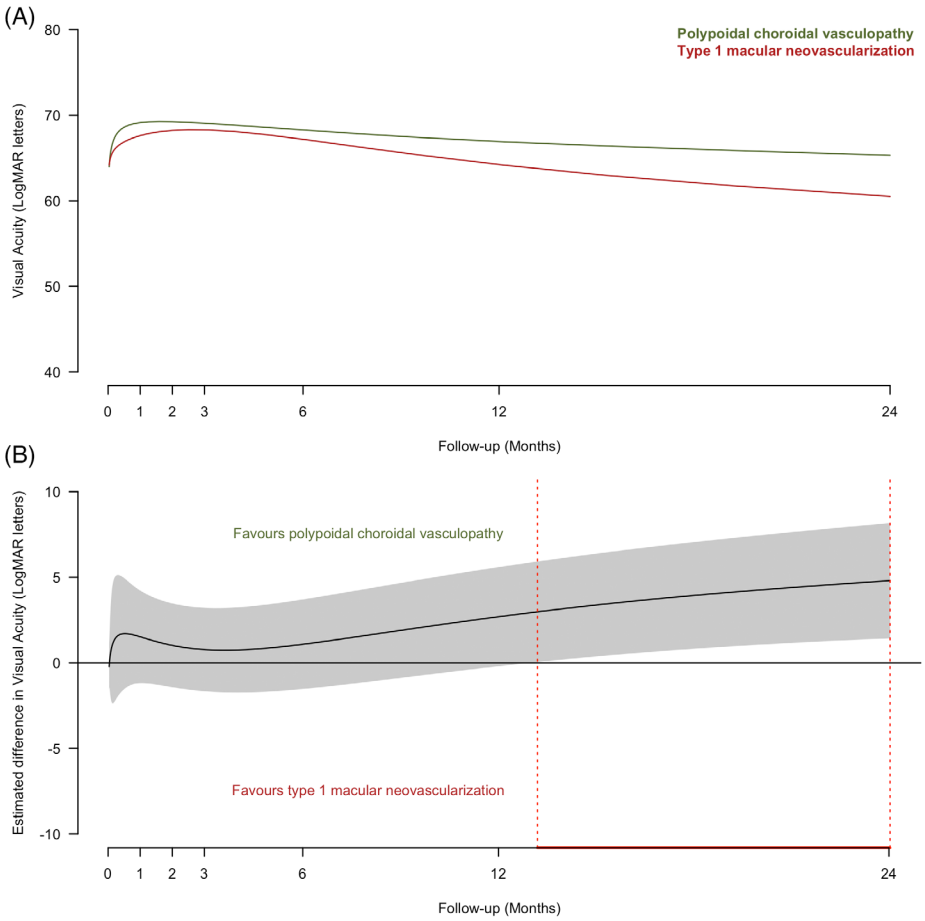

FIGURE 1 (A) Mean estimated VA (solid lines) in LogMAR letters over time in PCV (green) and type 1 MNV (red) eyes. (B) Difference in the mean change in VA between PCV and type 1 MNV eyes over 24 months in all eyes irrespective of whether they completed 24 months of follow-up. The grey shaded area in (B) represents the 95% confidence interval; the red dotted line in (B) represents the window of time in which the 95% CI does not cross zero. Predictions were made from a generalised additive model adjusted for age, baseline VA (fixed effects), and practice and intrapatient correlation for bilateral cases (random effects).

TABLE 2 Twenty-four-month outcomes by lesion subtype.

	Total	PCV	Type 1 MNV	*p*
Eyes, *n*	322	114	208	
Patients, *n*	291	103	188	
Completers, *n* (%)	213 (66.1%)	85 (74.6%)	128 (61.5%)	
Months of follow-up, median (Q1, Q3)	29.8 (16.5, 52.6)	45.8 (22, 65.3)	26 (15.1, 46.2)	<0.001
Baseline VA, median (Q1, Q3)	70 (57.2, 75)	70 (55, 75.8)	70 (58.8, 75)	0.94
Final VA[a], median (Q1, Q3)	70 (55, 76)	70 (59, 80)	70 (52.5, 75)	0.10
Crude VA change[a], mean (95% CI)	−0.3 (−2, 1.5)	1.6 (−1.4, 4.6)	−1.3 (−3.5, 0.9)	0.13
Adjusted VA change[b], mean (95% CI)	−1.6 (−3.6, 0.4)	1.2 (−1.6, 4.1)	−3.6 (−6, −1.2)	0.005
VA ≤ 35, baseline/final	9.3%/11.2%	7.9%/7.9%	10.1%/13%	0.65/0.23
VA ≥ 70, baseline/final	52.5%/52.8%	51.8%/56.1%	52.9%/51%	0.94/0.44
Final VA 15 letters change, loss/gain	12.4%/11.5%	14%/15.8%	11.5%/9.1%	0.64/0.11
24-month number of injections, median (Q1, Q3)	9 (6, 12)	8 (5, 10)	9 (7, 12.2)	0.08
Adjusted ratio[c], PCV versus type 1 MNV (95% CI)			0.78 (0.68, 0.88)	<0.001
Bevacizumab, %	19.3%	18.6%	19.6%	
Ranibizumab, %	50.3%	41.1%	54.9%	
Aflibercept, %	30.3%	40.0%	25.5%	
Photodynamic therapy, %	13.7%	37.7%	0.5%	
24-month number of visits, median (Q1, Q3)	17 (14, 20)	17 (15, 21)	17.5 (14, 20)	0.04
Adjusted ratio[c], PCV versus type 1 MNV (95% CI)			0.95 (0.89, 1.01)	0.07
Time to inactivation, days, median (Q1, Q3)	235 (208, 308)	235 (184, 308)	252 (169, 343)	0.04
Adjusted hazard ratio[d], PCV versus type 1 MNV (95% CI)			0.68 (0.48, 0.95)	0.03
Proportion of active visits, %	65.5%	61.8%	68.0%	0.001

Abbreviations: CI, confidence interval; MNV, macular neovascularization; *n*, number; PCV, polypoidal choroidal vasculopathy; Q1–Q3, interquartile range; SD, standard deviation; VA, visual acuity.

[a]Last observation carried forward for non-completers.

[b]Calculated from a longitudinal additive model adjusted for age, baseline VA (fixed effects), and practice and intrapatient correlation for bilateral cases (random effects).

[c]Calculated from a Poisson regression model adjusted for age, baseline VA (fixed effects), nesting of outcomes within practice and patient (random effects) with an offset for log days of follow-up.

[d]Calculated from a Cox proportional hazards regression model adjusted for age, baseline VA (fixed effects), and practice and intrapatient correlation for bilateral cases (random effects).

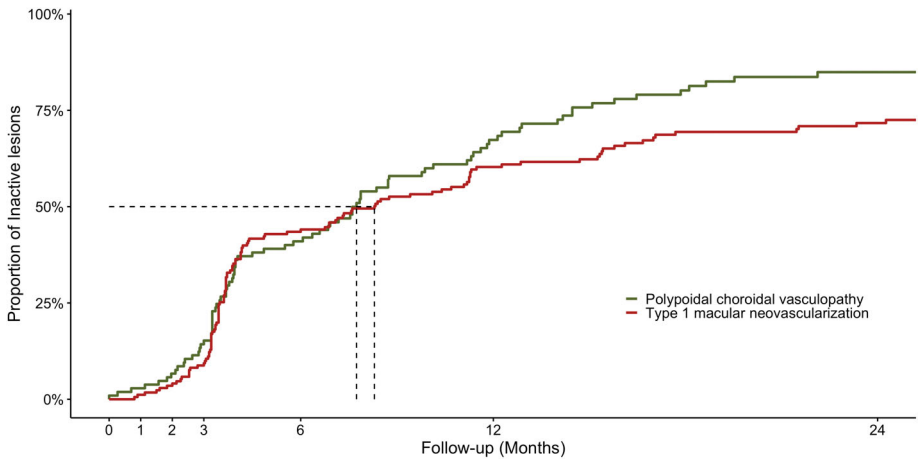

FIGURE 2 Kaplan–Meier survival curves for time from starting treatment to inactivity in PCV (green) and type 1 MNV (red) eyes over 24 months.

type 1 MNV lesions (hazard ratio [95% CI] = 0.68 [0.48, 0.95], $p = 0.03$).

4 | DISCUSSION

In this study, we found that 24-month treatment outcomes were similar between PCV and type 1 MNV in a Caucasian population. To the best of our knowledge, no previous study has reported 2-year, real-life treatment outcomes of eyes affected by PCV exclusively in patients of Caucasian descent.

We chose to compare the outcomes of PCV to those of type 1 MNV in Caucasians for two main reasons. First, a previous real-world, long-term analysis of treatment outcomes of 1929 eyes affected by macular neovascularization reported that type 1 MNV had better visual and anatomical outcomes than other MNV types after 5 years of treatment.[11] Second, imaging studies have suggested that the features of PCV in Caucasians might overlap with those of type 1 MNV.[7–9] In the present study, visual outcomes of PCV were comparable yet slightly better than those of type 1 MNV after adjusting for confounding variables. The number of injections during the 24 months was significantly less in the PCV group as well as the proportion of visits with a lesion graded as 'active'.

Our VA outcomes in PCV are inferior to those reported both in large clinical trials and in similar real-world studies.[15,17,20] The ATLANTIC study reported an overall 2-year BCVA gain of 6 LogMAR letters in a Caucasian population with PCV.[17] This discrepancy may be due to the treat & extend (T&E) regimen with or without adjunct PDT used in ATLANTIC, a regimen known to achieve better visual outcomes than the pro-re-nata (PRN) approach that was used to treat most of our cohort. A treat and extend regimen generally delivers treatments at ≥80% of visits,[21] whereas eyes in the present study received injections at around 9/17 (53%) of visits, which independently confirms that a reactive (PRN) regimen was used. Real-world analyses have also found better outcomes than ours, especially in terms of VA change.[16,22,23] However, VA at presentation in all these studies was consistently lower than that of our subjects, allowing for a higher chance of gain in response to treatment.[16,22,23]

We observed an overall maintenance of baseline VA at 24 months in eyes with PCV and type 1 MNV, with an adjusted VA change slightly favouring PCV (mean [95% CI], +1.2 [−1.6, 4.1] vs. −3.6 [−6, −1.2], $p = 0.005$). This result is consistent with a recent report by Fenner et al.[23] comparing nAMD other than PCV versus PCV in an Asian population treated with anti-VEGF monotherapy or combination therapy during 12 months of follow-up. Similar to our findings, in their study Fenner et al. found that eyes with PCV generally had better VA gains compared to other nAMD types (+10.8/+6.6 vs. +4.7 letters) while receiving similar numbers of anti-VEGF injections with or without adjunct PDT (5.6/5.0 vs. 5.3) over 1 year of follow-up. Nevertheless, all three groups had a mean final VA lower than 56 letters. This may explain why the vision gains in that study were greater than we report here since it is widely accepted that eyes with poor vision have more to gain.[11]

PCV has previously been associated with worse visual outcomes and a more severe clinical course, particularly in people of Asian descent.[6,7,12–14] The better outcomes of the study by Fenner et al. and the cohort described in the present analysis may be due to several factors. A higher anti-VEGF treatment load could have provided better visual outcomes than what observed in the earlier years of the anti-VEGF era, since the level of undertreatment has decreased with time.[24–26] PCV patients in our study were significantly younger, and age at diagnosis is known to be negatively correlated with VA gain. Finally, while PCV and type 1 MNV group received a similar number of anti-VEGF injections, over a third of PCV patients in our cohort also received at least one session of adjunct PDT, which may provide better VA gains than anti-VEGF monotherapy.[16,20,23] Since our study is based on a real-world outcomes registry, PDT was administered at the discretion of the treating practitioners and its availability at their respective clinics.

Most of the lesions included in the present study (85% of PCV and 72% type 1 MNV) received a physician-graded 'inactive' status at least once over 24 months of follow-up, consistent with data from RCTs and large real-world studies.[15,16,20] PCV tended to inactivate earlier than type 1 MNV despite the fewer injections received. While differences in lesion subtype may be the reason for this difference, the role of PDT cannot be ignored as a substantial proportion of eyes in the PCV group received at least one session during the follow-up.

Lesions in both groups were graded by their practitioner as 'active' at over 60% of visits. This is likely a direct consequence of the PRN treatment approach adopted in most Italian centres during the study period, calling for close follow-up of the lesion and re-treatment only when there was new exudative activity.[27,28] Treatment paradigms have shifted towards the T&E regimen in recent years as evidence of its long-term benefits became available.[29,30]

Unlike PCV in Asian populations, which has been associated with worse treatment outcomes and is more likely part of the pachychoroid spectrum,[6,7,12–14,31,32] features of typical AMD are much more frequent in PCV affecting Caucasian patients,[7,10,32] placing PCV on a continuum of possible nAMD presentations rather than constituting a clearly separate entity.[8,9] Genetic polymorphisms conferring

susceptibility to type 1 MNV—including alleles of the ARMS2 gene—have also been associated with PCV, possibly accounting for the stronger association of typical AMD features with PCV in Caucasians.[7,8,32–34] Our finding of similar outcomes between PCV and type 1 MNV supports the hypothesis that PCV might not represent a separate entity, but rather an adjunctive feature of the MNV subtypes that have already been well characterised, at least in Caucasian patients, and that PCV in Caucasians might have a milder disease course and better clinical outcomes that are more similar to those of type 1 MNV than PCV in Asians.[11]

This study has some limitations. According to the FRB! registry procedures, the classification of lesions was based on physicians' judgement without a standardised imaging protocol or a centralised reading centre, possibly resulting in misdiagnosis of neovascular lesions. Given the nature of the data collected in the FRB! registry as specified in the methods section, we could not report baseline imaging features that might help to better stratify patients at presentation, nor can we make conclusions on important structural outcomes such as polyp closure rate. Contributors to the FRB database are mostly retinal specialists who would generally be able to distinguish between the two conditions.

The drop-out rate was around 30% at 24 months. This is consistent with other observational studies, but still may have affected the calculation of crude VA outcomes as LOCF was used to account for non-completers. To account as much as possible for this issue, the adjusted VA change from baseline at 24 months—the primary outcome of the study—was calculated using a generalised additive model which makes estimations based on all the available data.

Finally, treatment decisions in routine clinical practice were made according to the treating physician's decision in consultation with the patient. This may have resulted in differences in outcomes across the centres. It also prevented us comparing different anti-VEGF drugs since practitioners could switch between drugs according to their judgement. In addition, most of the eyes were treated with a PRN approach which also makes comparisons more challenging. We mitigated the effect of the possible variability in retreatment criteria across the different practices by including eyes in both groups (PCV and Type 1) from all centres. This was possible thanks to the multicentric nature of the FRB! registry which has provided a diverse representation of real-world treatment outcomes for over a decade.

To conclude, 24-month real-world treatment outcomes of PCV were slightly better compared to those of type 1 MNV in Caucasians. PCV required similar yet significantly fewer anti-VEGF injections through 2 years using a PRN regimen, with 38% of PCV also receiving at least one PDT session. These findings add useful knowledge on the behaviour and management of PCV in Caucasians in the anti-VEGF era. The overall favourable outcomes lower the concerns about the poor prognosis once associated with this condition and support the hypothesis that PCV could represent just a different phenotype of type 1 MNV in most Caucasian patients.

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CONFLICT OF INTEREST STATEMENT

Matteo Airaldi, Vuong Nguyen, Marco Nassisi, and Pietro Monaco: no financial disclosure. Alessandro Invernizzi: consultancy fees, grants, travel support, and speaker fees from Bayer, Allergan, and Novartis outside the submitted work. Stela Vujosevic: consultancy fees and speaker fees from Allergan, Alimera, Bayer, Novartis and Roche outside the submitted work. Federico Ricci: grants and personal fees from Novartis, Genentech, Bayer, Biogen, Regeneron, Allergan, Roche, Merck Sharp & Dohme, Alimera Sciences, and SIFI outside the submitted work. Daniel Barthelmes: consultancy fees, grants, and speaker fees from Bayer, Alcon and Novartis outside the submitted work. Mark Gilles: grants from NHMRC, grants form RANZCO Eye Foundation, grants and others from Novartis, grants and other from Bayer and is an inventor of the software used to track real-world outcomes in this study. Francesco Viola: consultancy fees, honorarium, grants, travel support, and speaker fees from Bayer, Novartis, Allergan, and Roche outside the submitted work.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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REFERENCES

1. Cheung CMG, Lai TYY, Ruamviboonsuk P, et al. Polypoidal choroidal vasculopathy: definition, pathogenesis, diagnosis, and management. *Ophthalmology*. 2018;125(5):708-724.
2. Lorentzen TD, Subhi Y, Sørensen TL. prevalence of polypoidal choroidal vasculopathy in white patients with exudative age-related macular degeneration: systematic review and meta-analysis. *Retina*. 2018;38(12):2363-2371.
3. Yannuzzi LA, Wong DW, Sforzolini BS, et al. Polypoidal choroidal vasculopathy and neovascularized age-related macular degeneration. *Arch Ophthalmol*. 1999;117(11):1503-1510.
4. Yadav S, Parry DG, Beare NAV, Pearce IA. Polypoidal choroidal vasculopathy: a common type of neovascular age-related macular degeneration in Caucasians. *Brit J Ophthalmol*. 2017;101(10):1377-1380.
5. Chen YN, Devenyi RG, Brent MH, et al. Age-related macular degeneration: is polypoidal choroidal vasculopathy recognized and treated? *Can J Ophthalmol*. 2017;52(5):475-479.
6. Kokame GT, de Carlo TE, Kaneko KN, et al. Anti-vascular endothelial growth factor resistance in exudative macular degeneration and polypoidal choroidal vasculopathy. *Ophthalmol Retina*. 2019;3(9):744-752.
7. Corvi F, Chandra S, Invernizzi A, et al. Multimodal imaging comparison of polypoidal choroidal vasculopathy between Asian and Caucasian populations. *Am J Ophthalmol*. 2022;234:108-116.
8. Dansingani KK, Gal-Or O, Sadda SR, Yannuzzi LA, Freund KB. Understanding aneurysmal type 1 neovascularization (polypoidal choroidal vasculopathy): a lesson in the taxonomy of 'expanded spectra' – a review. *Clin Exp Ophthalmol*. 2018;46(2):189-200.
9. Spaide RF, Jaffe GJ, Sarraf D, et al. Consensus nomenclature for reporting neovascular age-related macular degeneration data: consensus on neovascular age-related macular degeneration nomenclature study group. *Ophthalmology*. 2020;127(5):616-636.
10. Airaldi M, Cozzi M, Staurenghi G. Regression of aneurysmal type 1 neovascularization after brolucizumab injections. *Can J Ophthalmol*. 2022;57(5):e163.
11. Invernizzi A, Nguyen V, Teo K, et al. Five-year real-world outcomes of occult and classic choroidal neovascularization: data from the Fight Retinal Blindness! Project. *Am J Ophthalmol*. 2019;204:105-112.
12. Kuroda Y, Yamashiro K, Miyake M, et al. Factors associated with recurrence of age-related macular degeneration after anti-vascular endothelial growth factor treatment: a retrospective cohort study. *Ophthalmology*. 2015;122(11):2303-2310.
13. Maruko I, Iida T, Saito M, Nagayama D, Saito K. Clinical characteristics of exudative age-related macular degeneration in Japanese patients. *Am J Ophthalmol*. 2007;144(1):15-22.
14. Cho JH, Park YJ, Cho SC, et al. Posttreatment polyp regression and risk of massive submacular hemorrhage in eyes with polypoidal choroidal vasculopathy. *Retina*. 2020;40(3):468-476.
15. Lee WK, Iida T, Ogura Y, et al. Efficacy and safety of intravitreal aflibercept for polypoidal choroidal vasculopathy in the PLANET study: a randomized clinical trial. *JAMA Ophthalmol*. 2018;136(7):786-793.
16. Chong Teo KY, Squirrell DM, Nguyen V, et al. A multicountry comparison of real-world management and outcomes of polypoidal choroidal vasculopathy: Fight Retinal Blindness! Cohort. *Ophthalmol Retina*. 2019;3(3):220-229.
17. Silva R, Arias L, Nunes S, et al. Efficacy and safety of intravitreal aflibercept treat and extend for polypoidal choroidal vasculopathy in the ATLANTIC study: a randomized clinical trial. *Ophthalmologica*. 2022;245(1):80-90.
18. Gillies MC, Walton R, Liong J, et al. Efficient capture of high-quality data on outcomes of treatment for macular diseases: the Fight Retinal Blindness! Project. *Retina*. 2014;34(1):188-195.
19. Rodrigues IA, Sprinkhuizen SM, Barthelmes D, et al. Defining a minimum set of standardized patient-centered outcome measures for macular degeneration. *Am J Ophthalmol*. 2016;168:1-12.
20. Lim TH, Lai TYY, Takahashi K, et al. Comparison of ranibizumab with or without verteporfin photodynamic therapy for polypoidal choroidal vasculopathy: the EVEREST II randomized clinical trial. *JAMA Ophthalmol*. 2020;138(9):935-942.
21. Arnold JJ, Campain A, Barthelmes D, et al. Two-year outcomes of "treat and extend" intravitreal therapy for neovascular age-related macular degeneration. *Ophthalmology*. 2015;122(6):1212-1219.
22. Chen SN, Cheng CK, Yeung L, et al. One-year real-world outcomes of ranibizumab 0.5 mg treatment in Taiwanese patients with polypoidal choroidal vasculopathy: a subgroup analysis of the REAL study. *Int J Ophthalmol*. 2018;11(11):1802-1808.
23. Fenner BJ, Ting DSW, Tan ACS, et al. Real-world treatment outcomes of age-related macular degeneration and polypoidal choroidal vasculopathy in Asians. *Ophthalmol Retina*. 2020;4(4):403-414.
24. Ng WY, Cheung CMG, Mathur R, et al. Trends in age-related macular degeneration management in Singapore. *Optom Vis Sci*. 2014;91(8):872-877.
25. Cheung CMG, Li X, Mathur R, et al. A prospective study of treatment patterns and 1-year outcome of Asian age-related macular degeneration and polypoidal choroidal vasculopathy. *PloS One*. 2014;9(6):e101057.
26. Mehta H, Tufail A, Daien V, et al. Real-world outcomes in patients with neovascular age-related macular degeneration treated with intravitreal vascular endothelial growth factor inhibitors. *Prog Retin Eye Res*. 2018;65:127-146.
27. Romano F, Cozzi E, Airaldi M, et al. Ten-year incidence of fibrosis and risk factors for its development in neovascular age-related macular degeneration. *Am J Ophthalmol*. 2023;7:170-181.
28. Airaldi M, Corvi F, Cozzi M, Nittala MG, Staurenghi G, Sadda SVR. Differences in long-term progression of atrophy between neovascular and non-neovascular age-related macular degeneration. *Ophthalmol Retina*. 2022;6:914-921.

29. Gillies M, Arnold J, Bhandari S, et al. Ten-year treatment outcomes of neovascular age-related macular degeneration from two regions. *Am J Ophthalmol*. 2020;210:116-124.
30. Spooner KL, Fraser-Bell S, Cozzi M, et al. Macular atrophy incidence and progression in eyes with neovascular age-related macular degeneration treated with vascular endothelial growth factor inhibitors using a treat-and-extend or a Pro Re Nata regimen: four-year results of the MANEX study. *Ophthalmology*. 2020;127(12):1663-1673.
31. Shimizu Y, Miyata M, Ooto S, et al. Pachychoroid-phenotype effects on 5-year visual outcomes of anti-VEGF monotherapy in polypoidal choroidal vasculopathy. *Acta Ophthalmol*. 2022;100(4):e943-e949.
32. Cheung CMG, Gan A, Yanagi Y, Wong TY, Spaide R. Association between choroidal thickness and drusen subtypes in age-related macular degeneration. *Ophthalmol Retina*. 2018;2(12):1196-1205.
33. Chen LJ. Genetic association of age-related macular degeneration and polypoidal choroidal vasculopathy. *Asia-Pacif J Ophthalmol*. 2020;9(2):104-109.
34. Dansingani KK, Perlee LT, Hamon S, et al. Risk alleles associated with neovascularization in a pachychoroid phenotype. *Ophthalmology*. 2016;123(12):2628-2630.

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