

Ethnic Differences on Long Term Outcomes of Polypoidal Choroidal Vasculopathy after Predominantly Bevacizumab Monotherapy.

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Abstract

Background: A 3-year single-centre, retrospective, comparative, non-randomized cohort study to describe the long-term outcomes of treatment-naïve, Caucasian and non-Caucasian eyes with polypoidal choroidal vasculopathy (PCV) after treatment with predominantly Bevacizumab monotherapy or in combination with rescue photodynamic therapy (PDT).

Methods: Demographics, visual outcomes, optical coherence tomography (OCT) and treatment data were collected up to 3 years after the first visit. Stratified analysis according to ethnicity and baseline vision was performed to identify factors predictive of long-term visual improvement and maintenance.

Results: A total of 89 eyes with PCV were identified, of which 14 received rescue verteporfin PDT. There was an equal distribution between Caucasian and non-Caucasian individuals. Non-Caucasians present at a younger age (75.4 vs 68.9 years, $p=0.002$), have a higher proportion of foveal involvement (52.1% vs 82.9%, $p=0.003$) and lower baseline visual acuity (62.9 vs. 52.7 letters, $p=0.02$). Mean visual acuity (VA) gain was + 8.8 letters and +5.0 letters at one and three years of follow up, respectively. Non-Caucasian individuals had a lower mean final VA compared to Caucasian individuals (54.7 vs. 70.5, respectively; $P < 0.001$). The mean total number of injections given over three years was 14.

Conclusions: Most patients treated with predominantly Bevacizumab anti-VEGF monotherapy achieved sustained visual acuity gains out to 3 years. Due to ethnic-specific differences in PCV phenotypes, non-Caucasians presented with lower baseline VA and had poorer long-term visual outcomes and may have benefited from early PDT or switch to alternative anti-VEGF agents.

Background

Since its first description in the 1990s,¹ the literature on Polypoidal Choroidal Vasculopathy (PCV) has expanded rapidly. Attempts to categorise PCV according to features observed on multimodal imaging across different contexts have yielded classifications that are increasingly complex and not readily translated to clinical practice.² As a result, PCV is best considered as a wide spectrum of disease, within which there are a number of well recognised and characteristic diagnostic criteria.^{3,4} Whilst the pivotal trials, EVEREST and PLANET, have provided important guidance with respect to the management of PCV, they were predominantly conducted in large Asian centres, raising the possibility that the results may have limited generalisability to mixed populations with wider phenotypic variations of PCV.^{4,5}

It has recently been recognised that there may be distinct differences between the phenotypes of PCV seen in Caucasian and non-Caucasian eyes.⁶ However, little is known about whether this translates into differences in long term visual outcomes and response to available treatments. Auckland, with its diverse ethnic population, facilitates comparison of treatment outcomes across patients from different ethnic groups treated at a single tertiary centre.⁷ The aim of this study was to evaluate the three-year visual outcomes of patients with PCV treated with predominantly Bevacizumab monotherapy and to identify if ethnic-specific differences in PCV phenotypes influenced long-term visual outcome.

Methods

We performed an observational cohort study of the outcomes of eyes diagnosed with PCV, within the Auckland District Health Board, New Zealand (NZ) Fight Retinal Blindness (FRB!) database. The patient selection process is detailed in figure 1. As not all clinicians utilise FRB!, the indocyanine green angiography (ICG) diagnostic logs of the eye department were also reviewed to ensure that all patients diagnosed in the unit with PCV between 2005-2017 were included. All patients had to be treatment naïve and meet either the current standard ICG or OCT diagnostic criteria for PCV.^{3,4} Only eyes with complete three year follow up data were included in the final analysis. Reasons for non-completion and baseline demographics of non-completers were recorded. The cohort was divided into two groups, Caucasian and non-Caucasian, to investigate the influence that ethnicity may play in both the presentation and response to treatment.

Briefly, the FRB! database is a cloud-based, record-keeping software that stores data from each clinical visit.⁸ Entry datapoints include best- corrected VA, lesion subtype (classic, occult, PCV), greatest linear diameter (baseline), lesion activity, treatment, and

any ocular adverse events. VA is recorded in equivalent logarithm of the minimum angle of resolution (logMar) letters. Treating physicians determined all management decisions, including frequency of visits and treatment method, thereby reflecting real-world practice. Lesion activity status was graded by the treating physician based on optical coherence tomography (OCT), ICG, or a combination of both, at each visit. Baseline ICG and OCT of all patients so identified were reviewed to determine baseline lesion characteristics. In cases of missed or incomplete entries, data was corroborated by a retrospective review of physical records.

Outcome Measurements

The primary study outcome was the mean VA over three years after initiating treatment. Secondary outcomes were the proportion of eyes that achieved lesion inactivity, time to inactivity, median number of injections per year, and proportion receiving photodynamic therapy (PDT), Aflibercept or Ranibizumab. Self-reported ethnicity data was extracted from the clinical records. Individuals who identified with more than one ethnicity were routinely classified to a single ethnicity based on a defined prioritized order.⁹ Stratified analysis according to Caucasian and non-Caucasian ethnicity, and baseline vision were performed. Patients that were discharged following poor visual prognosis had their last visual acuity measured brought forward for final analysis.

Statistical Analysis

Descriptive data are presented as mean (standard deviation), mean (95% confidence interval), or number (percentage). The Student T-test, Fisher's test, Wilcoxon test was used to compare the differences in baseline characteristics and final visual outcomes between different groups. P-value of less than < 0.05 was considered statistically significant. All statistical analysis was performed using IBM SPSS® Statistics (Release 27.0.1.0).

Kaplan Meier survival curves were used to display the time to inactivity. Locally Weighted Scatterplot Smoothing curves (LOESS) were used to plot the visual acuity trends for different ethnic groups and eyes with varying baseline vision. All graphs were produced using GraphPad Prism® Version 9.2.0 (283).

Results

Study participants

Table 1: Baseline characteristics

	Caucasian	Non-Caucasian	p-value	Total cohort
No. of eyes (%)	48 (53.9%)	41 (46.1%)	-	89
No. bilateral (%)	7 (17.1%)	4 (10.8%)	0.524*	11 (%)
Mean age (SD), yrs	75.4 (9.8)	68.9 (8.0)	0.002**	72.3 (9.5)
Gender, male (%)	14 (34.1%)	19 (51.4%)	0.169*	33 (42.3%)
Mean baseline VA (SD), letters	62.9 (16.3)	52.7 (22.3)	0.02***	58.2 (19.9)
VA \geq 70 letters (20/40 Snellen)	18 (37.5%)	9 (22.0%)	0.165*	27 (30.3%)
VA \leq 35 letters (20/200 Snellen equivalent)	4 (8.3%)	8 (19.5%)	0.212*	12 (13.5%)
Presence of BVN, no (%)	20 (41.7%)	27 (65.9%)	0.033*	47 (52.8%)
Foveal involvement, no. (%)	25 (52.1%)	34 (82.9%)	0.003*	59 (66.3%)
Cluster/String Configuration, no. (%)	24 (50%)	29 (70.7%)	0.054*	53 (59.6%)
Solitary polyp Configuration, no. (%)	13 (27.1%)	5 (12.2%)	0.113*	18 (20.2%)
Early filling [†] , no. (%)	8 (16.7%)	16 (39.0%)	0.03*	24 (27.0%)
Late filling [‡] , no. (%)	24 (50%)	15 (36.6%)	0.284*	39 (43.8%)
Mean (SD) Central Retinal Thickness, microns	385 \pm 160	387 \pm 197	0.659***	386 \pm 176
Mean GLD (SD), microns	2657 (1383)	4216 (1954)	0.008***	3552 (1885)

SD: Standard deviation; GLD: greatest linear diameter; IQR: interquartile range; VA: visual acuity; BVN: Branching vascular network

† Polyp fill during arteriolar phase of ICG

‡ Polyp fill during late venous phase of ICG

* Fisher exact test.

** Student t-test

*** Wilcoxon rank-sum test.

From the Auckland DHB FRB! database and ICG diagnostic logs, a total of 89 eyes met all the eligibility criteria specified in Figure 1. Baseline characteristics of the study cohort are outlined in Table 1. Fifty-three percent of patients were NZ European, 27% Asian, 13% Pacific Islander and 5% were NZ Māori. To examine for differences in ethnicity, patients were subcategorised into Caucasian (53%) and non-Caucasian eyes (47%). The mean baseline VA was higher in Caucasian participants compared with non-Caucasian participants (62.9 \pm [SD 16.3 letters] vs. 52.7 \pm [SD 22.3 letters], respectively; P = 0.02). Non-Caucasian individuals were more likely to present at a younger age with larger lesions which were associated with branching vascular networks. Their lesions also had a predilection to involve the fovea. Baseline ICG, where available, revealed that non-Caucasian individuals were also more likely to have string or cluster of polyps, which filled early in the ICG transit.

Non-completion rate

Table 2: Demographics of patients that were lost to follow up and excluded due to incomplete data.

Ethnicity no. (%)	
<i>Caucasian</i>	12 (71%)
<i>Non-Caucasian</i>	5 (29%)
Gender no. (%)	
<i>Male</i>	6 (35%)
<i>Female</i>	11 (65%)
Mean age (SD), years	73.1 (12.5)
Mean baseline VA (SD), letters	61.5 (13.3)
Mean final VA at last visit (SD), letters	71.4 (9.4)
Mean Follow Up Time (SD), months	20.5 (5.7)

SD: Standard deviation; VA: Visual acuity

Seventeen patients were excluded. The reasons included: Patient death, the patient elected to seek care outside of the public hospital, the patient was referred from to Auckland from another unit solely for an ICG, the patient left Auckland during treatment and either moved to a different hospital catchment or left the country (Figure 1). The demographics of this population is outlined in table 2. This represents 17% of all eyes that were commenced on treatment for PCV in our unit. The mean duration of follow up of the non-completers was 20.5 months and the final mean VA was 71.4 letters. Of those that were discharged, three patients had their last measured VA brought forward after discharge with futile visual prognosis ($VA \leq 35$ letters). The remaining four patients were discharged after a long period of inactivity. These patients, along with those deceased, all had a last measured VA of greater than 60 letters. Given the unpredictability of their future visual outcome, their last measured VA was not carried forward for final analysis. The baseline demographics of those eyes that were excluded were broadly comparable to the study cohort [Table 2 vs Table 1], including mean baseline vision ($61.5 \pm SD 13.3$ vs. $58.2 \pm SD 19.9$, $p=0.641$).

Visual outcomes

The mean visual acuity for all eyes for each year is displayed in Table 1 and Figure 2A. Overall, there was a 8.9 letter gain from baseline at 12 months. At three years, there was a mean gain of 5.0 letters compared to baseline ($63.2 \pm [SD 21.0]$ letters vs $58.2 \pm [SD 19.9]$ letters), respectively, $p=0.021$). All other visual outcomes are outlined in table 2. The only significant difference between ethnicities was that non-Caucasian individuals ($54.7 \pm SD 25.8$ letters) had a lower mean final VA compared to Caucasian individuals ($70.5 \pm [SD 25.0]$ letters), $P < 0.001$). Figure 2B plots the mean visual change over three years for Caucasian and non-Caucasian individuals. The largest gains in vision occurred within the first year for both Caucasian and non-Caucasian individuals, with both groups achieving a mean improvement in visual acuity gain of 8.8 letters.

The mean visual change over three years, stratified according to baseline visual acuity, is shown in figure 2C. Eyes were stratified into 3 groups according to their presenting baseline VA: (1) good baseline vision of 70 letters or more (27 eyes), (2) moderate baseline vision of between 36 and 69 letters (50 eyes), and (3) low baseline vision of 35 letters or fewer (12 eyes). The mean VA of eyes with good baseline vision was initially 74.3 letters (SD 7.2), dropping down to 70.2 (SD 17.4) letters at year three. The presenting mean VA and final VA of eyes with intermediate baseline VA was similar to that of the entire cohort, increasing from 58.0 letters (SD 12.3) at baseline to 65.6 letters (SD 18.5) at 3 years; an increase of 7.6 letters. Eyes with poor baseline vision had a mean baseline VA of 22.4 letters ($\sim 20/400$) and experienced an increase of 23.1 letters ($\sim 20/160$) at 3 years; all improvement occurred in the first year of treatment. Overall, those who presented with good vision had a better final VA at 3 years compared to those who started off with poor vision. ($70.2 \pm [SD 17.4]$ vs. $45.5 \pm [SD 28.8]$, $p= 0.007$).

Table 3: Comparison of visual outcomes between different ethnic groups.

	12 months	36 months	36 months (Caucasian)	36 months (Non- Caucasian)	p-value
No. of eyes	89	89	48	41	-
Mean \pm SD final VA, letters	67.0 \pm 16.4	63.2 \pm 21.0	70.5 \pm 12.0	54.7 \pm 25.8	<0.001*
Mean \pm SD CRT, microns	307.3 \pm 146.5	295.4 \pm 122.2	269.9 \pm 77.0	327.0 \pm 157.2	0.269*
Mean change in VA letters (95% CI)	+8.9 (2.7 to 10.5)	+5.0 (-2.7 to 8.8)	+7.6 (3.2 to 12.0)	+2.0 (-5.8 to 9.8)	0.581*
Proportion with \geq 15-letter gain	24 (27.0%)	29 (32.6%)	17 (35.4%)	12 (29.3%)	0.651**
Proportion with \leq 15-letter loss	84 (94.4%)	78 (87.6%)	44 (91.7%)	34 (82.9%)	0.333**
VA \geq 70 letters (20/40 Snellen equivalent)	48 (53.9%)	47 (52.8%)	33 (68.8%)	14 (34.1%)	0.001**
Mean total \pm SD, no. of injections	5.8 \pm 2.9	13.8 \pm 8.1	14.0 \pm 8.1	13.6 \pm 8.1	0.833***
Received PDT, no. (%)	5 (5.6%)	14 (15.7%)	4 (8.3%)	10 (24.4%)	0.08**
Mean time to PDT (SD), months	-	-	30 (15.2)	19.1 (15.6)	0.185***
Received Aflibercept or Ranibizumab, no. (%)	6 (6.7%)	15 (16.9%)	11 (22.9%)	4 (9.8%)	0.155**

CRT: Central Retinal Thickness; VA : visual acuity; CI : confidence interval; SD: Standard deviation; PDT: photodynamic therapy

* Wilcoxon Rank-Sum test.

** Fisher's exact test.

*** Student t-test

Secondary outcomes

Kaplan-Meier survival curve representing the proportion of eyes achieving inactivity is shown in Figure 3. Seventy-four percent of patients achieved lesion inactivity by 12 months, rising to 88% at 24 months. Overall, the mean central retinal thickness dropped by 82 microns within the first year ($386 \pm$ [SD 176 microns] vs $307 \pm$ [SD 147 microns], paired T-test $p < 0.001$) and remained stable until year three ($295 \pm$ [SD 122 microns]). [Table 3]

The median number of injections delivered in the first year was 6 and ranged between 3 to 4 injections during maintenance years. The total mean number of injections given to study completers at the end of 3-years was 13.8. There was a higher mean total number of injections given to those that had a final vision of greater than 70 letters at three years, compared to those with vision worse than 35 letters (13.2 ± 7.9 vs 9.6 ± 5.9 , $p = 0.182$, respectively). The majority of Caucasian eyes received Bevacizumab anti-VEGF monotherapy, with just 8% of eyes receiving PDT. A higher proportion of non-Caucasian eyes received PDT (24%), but this trend did not achieve statistical significance. The mean time to application of PDT (30 months for Caucasians vs 19 months for Non-Caucasians) indicates it was being used for late, rescue treatment in both cohorts.

Discussion

This study evaluates the real-world outcomes of patients with PCV in a single tertiary unit that serves an ethnically diverse population. Overall, there was a sustained visual benefit up to three years. Most patients were treated with Bevacizumab anti-VEGF monotherapy, with a proportion of both cohorts receiving late, rescue PDT. There was an initial mean VA gain of 8.8 and

5.0 letters at years one and three respectively. Stratified analysis according to baseline visual acuity, revealed that a poor VA at presentation was predictive of a poor visual outcome at 3 years, despite significant improvements being achieved in the first year of treatment.

Table 4 compares the clinical outcomes observed in the current study with previously published real-world observational studies for PCV. Whilst the data is very heterogenous, three key themes emerge; 1. All long-term studies demonstrate peak visual gains at 1 year, with a subsequent decline in the following maintenance years, regardless of therapeutic regimen.¹⁰⁻¹⁴ 2. There is a paucity of long-term data from Caucasian populations with PCV and thus there are few comparisons of visual outcomes based on ethnicity. 3. Consistent with the EVEREST trials, combination therapy, at least in non-Caucasians is associated with superior visual outcomes, despite fewer injections.¹⁴⁻¹⁷

Table 4. Comparison of Clinical Outcomes in the Current Study with Previously Published Real-World Observational Studies for Polypoidal Choroidal Vasculopathy Composing Different Ethnic Compositions Treated with Anti-Vascular Endothelial Growth Factor Monotherapy or Combination Therapy with Verteporfin Photodynamic Therapy.

Author, number of eyes	Ethnicity of Population	Baseline VA, logMar letters	VA 1 year, logMar letters	VA 3 years, logMar letters	Mean total number of injections, follow up duration, anti-VEGF agent	Photodynamic therapy
Teo, 193 ²⁵	Caucasian 65 Non-Caucasian 115 Undisclosed 13	46 [†] - 60 [‡]	67.5 [†] - 70 [‡]	-	4.3 [‡] – 6.4 [†] over 12 months Predominantly bevacuzimab	Mean of 1.23 treatments within initial 3 months
Current cohort, 48	Caucasian	62.9	71.7	70.5	14 over 3 years	4 had PDT, none in the first year
Chehab, 50 ²⁶	Caucasian	59.9 [¶]	60.4 [¶]	-	8.4-8.6 over 24 months Ranibuzimab/Aflibercept	15 had PDT, with 6 in the first 6 months.
Gharehbagh, 29 ¹²	Caucasian	62 [¶]	66 ^{¶§}	-	7.6 over 22 months Aflibercept	7 had PDT
Current cohort, 41	Non-caucasian	52.7	61.5	54.7	13.6 over 3 years	10 had PDT, 5 in the first year
Fenner, 199 ¹⁶	Non-caucasian	41.6 [†] – 45.1 [‡]	48.2 [†] –55.9 [‡]	-	5.0 [†] -5.6 [‡] over 12 months Predominantly bevacuzimab	100 had PDT, 66 in the first 3 months
Miyata, 61 ²⁷	Non-caucasian	~65 (0.4 [†] -0.41 [‡])	~70-73 (0.26 [‡] -0.29 [†])	~68 (0.32 [†] -0.33 [‡])	5.3 [‡] – 9.2 [†] over 5 years Ranibuzimab	20 had initial PDT
Wataru, 53 ¹⁵	Non-caucasian	~57 (0.55)	~70 [§]	~70 [§]	7.51 over 5 years Ranibuzimab/Aflibercept	All had initial PDT
Chang, 31 ¹¹	Non-caucasian	~60 (0.52)	~63 (0.46)	~47 (0.76)	8.8 over 53 months Ranibuzimab/bevacuzimab	-
Kang, 42 ¹⁴	Non-caucasian	~45 (0.78)	~53 [§]	~53 [§]	6.42 over 5 years Ranibuzimab/bevacuzimab	All had initial PDT
Hikichi, 66 ¹³	Non-caucasian	~67 (0.34)	~75 [§]	~70 (0.32)	21.5 over 6 years Ranibuzimab	-

~ Converted from logMar decimal to logMar letters

† Combination anti-VEGF and PDT therapy group

‡ Anti-VEGF monotherapy group

§ Inferred from plotted points on graph

¶ Early Treatment Diabetic Retinopathy Study (ETDRS) letters

The total median number of six injections in the first year in our cohort lies upon the upper range of studies which enrolled Non-Caucasians, but is consistent with Singaporean and Australian studies [Table 4]. Gillies et. al. has demonstrated a strong

relationship between the number of anti-VEGF intravitreal injections and final visual outcome in long term observation studies for neovascular age-related macular degeneration (nAMD).^{18,19} In the multivariate analysis by Fenner et. al, poor baseline vision and higher number of injections were also strongly predictive of visual improvement.

Head-to-head comparison with landmark trials, such as EVEREST and PLANET, is confounded by differences in baseline characteristics, choice of anti-VEGF agent, dosing intervals and timing of PDT. Whilst PLANET found Aflibercept monotherapy was non-inferior to Aflibercept combined with PDT rescue, EVEREST II demonstrated superior visual gains with combination therapy compared with Ranibuzimab monotherapy.^{4,5} In spite of these differences, a higher proportion of patients in the monotherapy arm of PLANET achieved disease inactivity after three injections compared to EVEREST, suggesting that Aflibercept may be more effective in treating individuals with PCV than Ranibuzimab.^{4,5} It is also inferable from other major trials on diabetic macular oedema and retinal vein occlusions, that Bevacuzimab may be inferior to Ranibuzimab and Aflibercept in the treatment of PCV.²⁰⁻²³ Hence, the conclusion from PLANET that anti-VEGF monotherapy is non-inferior to anti-VEGF with PDT rescue may not generalisable towards Bevacuzimab. Despite this, Bevacuzimab remains the first-line agent to treat nAMD and PCV in many health economies due to its cost-effectiveness. This study provides reassurance that Bevacuzimab monotherapy with rescue PDT or Aflibercept reserved for non-responders, yielded good visual outcomes in the long-term.

Consistent with other published data, we found that both the demographics and the morphological characteristics of PCV differed according to ethnicity. It is well described that the prevalence of PCV among those diagnosed with nAMD is higher in Asians (20-60%)²⁴⁻²⁶ compared to Caucasians (4-10%).²⁷⁻³⁰ PCV also tends to present a decade later in Caucasians^{27,29-31} compared to Asians^{25,32-37} and whilst there is a male predominance in Asians,^{25,33-36} the opposite is seen in Caucasians.^{29,31,37,38} In addition to the demographic differences, there also appears to be distinct anatomical differences between ethnic groups. Whilst Asians tend to present with large lesions and BVNs that have a predilection to involve the central macula,^{25,34,35,39} Caucasians tend to present with smaller lesions which often spare the fovea.^{28-31,37,38,40} Our findings mirror those previously reported; Caucasians tended to be older, presenting with solitary macular polyps or clusters which filled in the venous phase, with no accompanying BVN, while Asians were more likely to have strings or clusters in the central macula area with large associated BVNs. In the current study, Caucasian patients tend to manifest a different disease phenotype, presented with better visual acuity and reported superior long-term visual outcomes compared to Non-Caucasian patients. These findings then raise the possibility that the observed differences in clinical presentation of PCV may influence how the two ethnic groups respond to treatment. If so, whilst Bevacuzimab is favoured for its cost-effectiveness and appears to deliver acceptable results to Caucasians with PCV, our results suggest that PDT or alternative anti-VEGF agents should be considered earlier in Non-Caucasian eyes with PCV.

This study has limitations inherent to observational studies that should be acknowledged. The recruitment of patients using ICG logs and a separate analysis of excluded patients were purposefully done to mitigate selection bias. Unlike randomised controlled trials, case and treatment selection were performed without reference to an adjudication centre or study protocols. The data presented therefore has a lower internal validity but is still meaningful because they are an accurate representation of decisions made in real-world practice. ICG is not routinely performed on all individuals who present with nAMD and is instead only performed if PCV is suspected. This practice is likely to have led to the unjustified exclusion of some patients with PCV being managed in our unit. It could have also resulted in an underestimation of ICG biomarkers such as branching vascular networks and polyp clusters. Our study included patients that were diagnosed using non-ICG criteria, which has a specificity of 0.86 – 0.91. Although these figures allow for a small proportion of false positive cases, it is another reflection of real-world practice where access to ICG is limited.

In conclusion, Caucasian patients have a preponderance to present with solitary, peripapillary polypoid lesions and have good visual outcomes up to three years with predominately Bevacuzimab anti-VEGF monotherapy. Conversely, Non-Caucasian patients, who are more likely to present with PCV at a younger age with poor visual acuity and foveal involvement, had poorer visual outcomes and may have benefited from early PDT or switching to an alternative anti-VEGF agent.

Abbreviations

Anti-VEGF: anti vascular endothelial growth factor

BVN: branching vascular network

CI: confidence interval

CNVM: Choroidal neovascular membrane

CRT: central retinal thickness

FRB!: Fight Retinal Blindness

ICG: Indocyanine green angiography

IQR: interquartile range

LOESS: locally weighted smoothing

nAMD: neovascular age related macular degeneration

PCV: polypoidal choroidal vasculopathy

PDT: photodynamic therapy

OCT: optical coherence tomography

RPE: Retinal Pigment Epithelium

SD: Standard deviation

VA: visual acuity

Declarations

Ethics approval and consent to participate

The study protocols was approved by the Auckland District Health Board Research Review committee, approval number A+9628.

This study was conducted in accordance with the tenets of the Declaration of Helsinki. The Auckland District Health Board Research Review committee waived the requirements for informed consent because of the retrospective nature of the study and use of anonymized retinal images and clinical data. All methods were carried out in accordance with relevant guidelines and regulations

Consent for publication

Not applicable

Availability of data and materials

The datasets generated and analysed during the current study are not publicly available due to potential compromise to individual privacy but are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

Funding

There are no sources of funding to declare.

Authors' contributions

AY and NW performed data collection, interpretation, and analysis. AY and DS wrote the main manuscript text. All authors read and approved the final manuscript.

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Figures

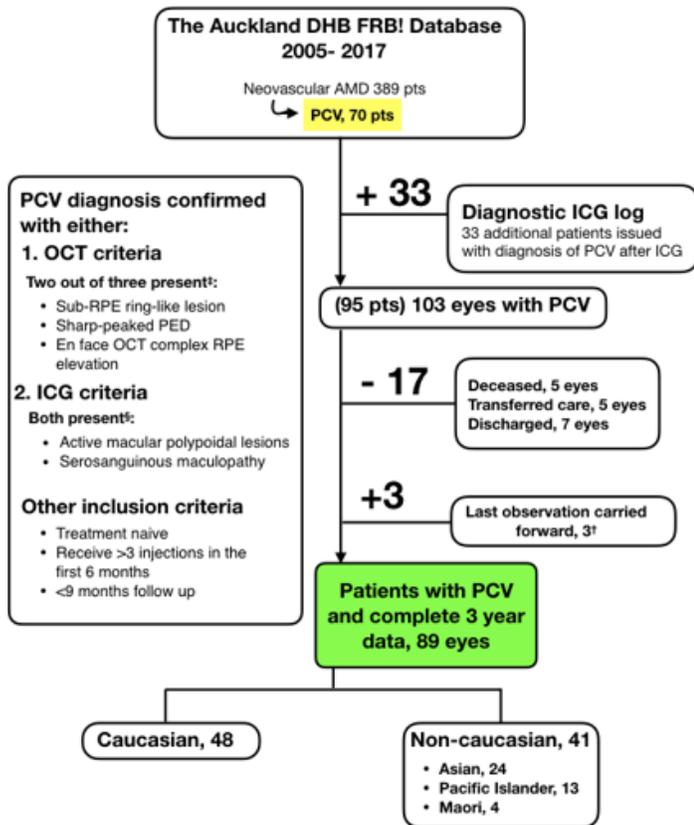


Figure 1

Flowchart Outlining the Patient Selection Process and Reasons for Patient Exclusion and Lost to Follow Up.

FRB! : Fight Retinal Blindness, RPE: Retinal Pigment Epithelium, PCV: Polypoidal choroidal vasculopathy, CNVM: Choroidal neovascular membrane, ICG: Indocyanine green angiography, OCT: Optical coherence tomography.

† last observation carried forward for three patients that were discharged due to poor visual prognosis

‡ per Non-ICG Diagnostic Criteria from the Asia-Pacific Ocular Imaging Society PCV Workgroup³

§ as per ICG diagnostic criteria in EVEREST⁴

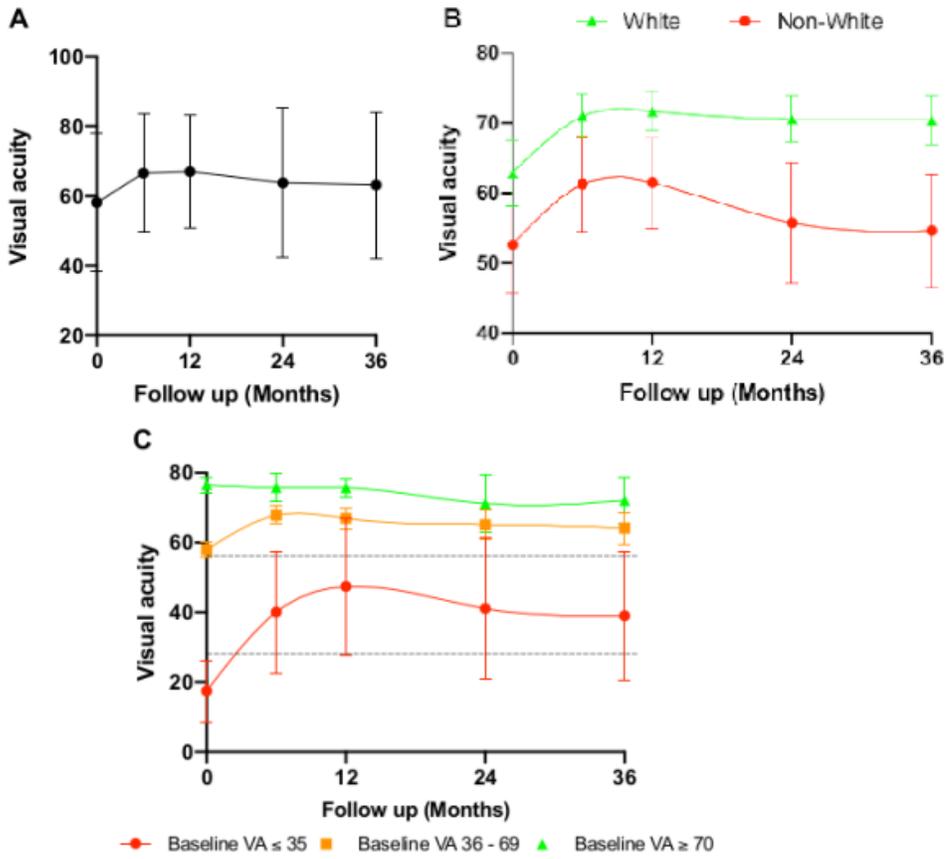


Figure 2

A: Mean \pm standard deviation, best corrected visual acuity in LogMar Letters over the 3 years of follow up. B: LOESS regression curve of mean visual acuity (VA) \pm 95% confidence interval, stratified according to ethnicity. C: LOESS regression curve of mean visual acuity (VA) \pm 95% confidence interval, stratified according to baseline VA, the dotted lines represent the cut-off values of 70 and 35 letters.

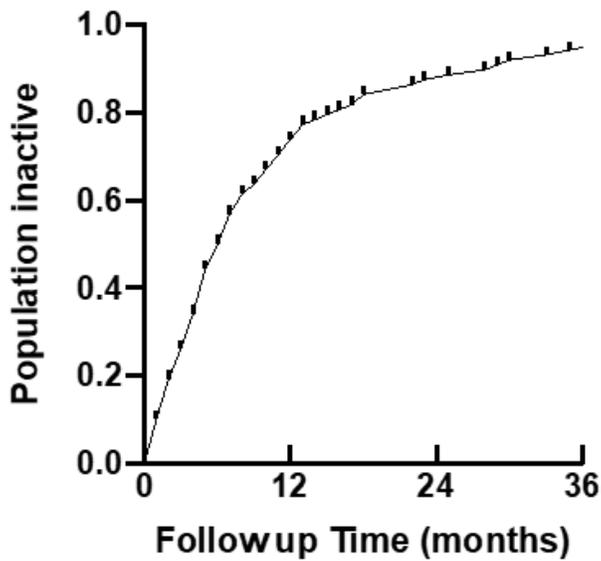


Figure 3

Kaplan Meier Survival Curve showing the proportion of patients achieving lesion inactivity.