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Real-world efficacy of Brolucizumab in NV-AMD

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REVIEW

Comparative Efficacy of Brolucizumab in the Treatment of Neovascular Age-Related Macular Degeneration: A Systematic Literature Review and Network Meta-Analysis

Robert P. Finger · Natalie Dennis · Rita Freitas · Arthur Quenéchdu · Andreas Clemens · Helene Karcher · Eric H. Souied

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ABSTRACT

Introduction: A systematic literature review (SLR) and network meta-analysis (NMA) were conducted to evaluate the comparative efficacy of brolucizumab relative to other anti-vascular endothelial growth factor (VEGF) treatments for neovascular age-related macular degeneration (nAMD) at 1 and 2 years, and overall safety and injection frequency of each treatment.

Methods: An SLR identifying randomized controlled trials (RCTs) published before June 2021 according to a pre-specified protocol was followed by a Bayesian NMA to compare brolucizumab (6 mg q12w/q8w) against sham and all relevant anti-VEGF regimens. Pooled mean injection frequency, serious adverse ocular events, and discontinuation rates were estimated for each treatment regimen.

Results: Nineteen RCTs were included in NMA base-case analysis. Brolucizumab (6 mg q12w/

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s12325-022-02193-3.

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Adis

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Long term efficacy In treatment-naive Neovascular-AMD

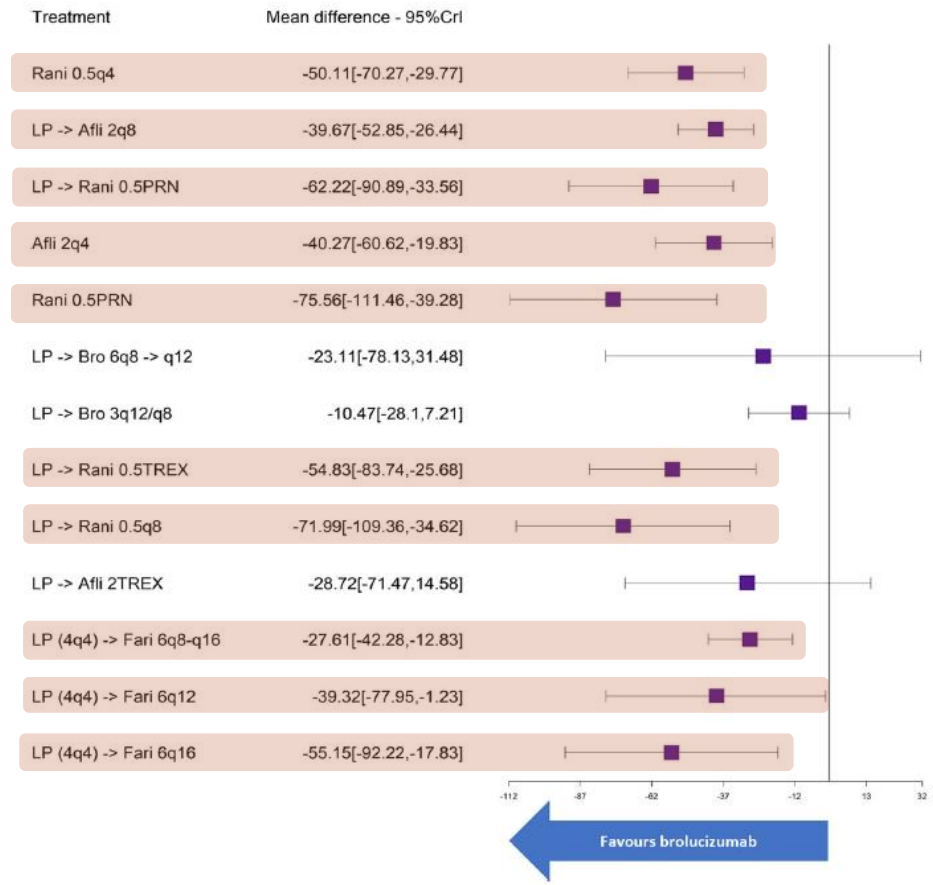
To **evaluate** the **comparative efficacy** of brolucizumab relative to other anti-vascular endothelial growth factor (VEGF) treatments for neovascular age-related macular degeneration (nAMD) **at 1 and 2 years**

- **Brolucizumab** (6 mg q12w/q8w) showed **superior retinal thickness reduction** to most comparators including:
- **Ranibizumab** (0.5 mg **q4w**; **year 1** mean difference **- 50.1**; **year 2** mean difference **- 49.5**)
- **Aflibercept** (2 mg **q8w**; **year 1** mean difference **- 39.7**; **year 2** mean difference **- 35.0**)
- **Faricimab** (6 mg **q16w/q8w**; **year 1** mean difference **- 27.6**)

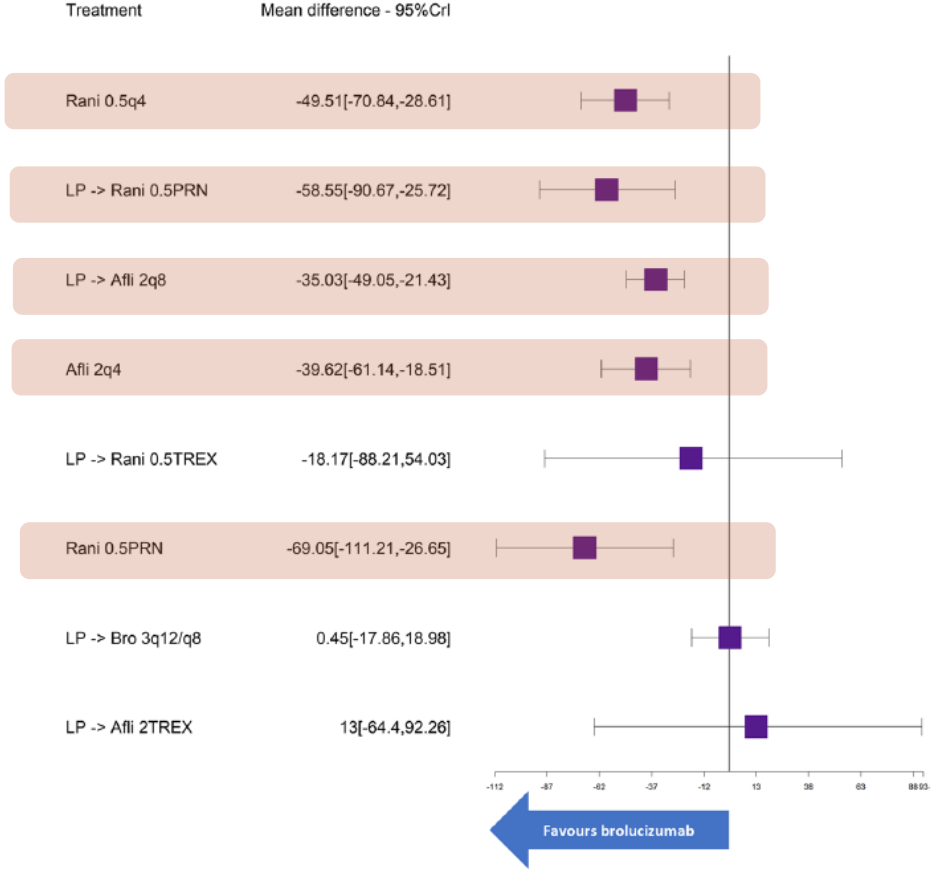
At year 2, pooled annualized **injection frequency** was **lowest for brolucizumab** (6 mg q12w/q8w) and highest for ranibizumab (0.5 mg q4w) at **5.7** and **11.5** injections annually, respectively

Brolucizumab (6 mg q12w/q8w) showed **similar rates** of treatment discontinuation and **serious and overall adverse events** (both years)

CRT y1 **Mean difference in change from baseline of LP -> Bro 6q12/q8 vs.**



CRT y2 **Mean difference in change from baseline of LP -> Bro 6q12/q8 vs.**



Finger RP, et al. Comparative Efficacy of Brolucizumab in the Treatment of Neovascular Age-Related Macular Degeneration: A Systematic Literature Review and Network Meta-Analysis. Adv Ther. 2022 Aug;39(8):3425-3448. doi: 10.1007/s12325-022-02193-3. Epub 2022 Jun 9. PMID: 35678996; PMCID: PMC9309118.

- Among all anti-VEGF treatments, the **visual acuity outcomes were similar**
- Retinal thickness is **a common anatomical measure of disease activity** in nAMD, and greater thickness may be associated with worse visual acuity outcomes
- These measurements **play a key-role in determining dosing intervals** for variable dosing regimens
- **Brolucizumab** showed **greater reductions in retinal thickness** than its comparators

OPEN ACCESS

Short-term real-world outcomes following intravitreal brolucizumab for neovascular AMD: SHIFT study

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ABSTRACT

Background Brolucizumab has recently been approved in Europe as a novel treatment for patients with neovascular age-related macular degeneration (nAMD). We report on early experiences with real-world outcomes of switch to brolucizumab therapy in previously anti-vascular endothelial growth factor (anti-VEGF)-treated patients.

Methods Patients with recalcitrant nAMD were switched to brolucizumab therapy. Functional and structural parameters 4 weeks after first brolucizumab injection were evaluated including best-corrected visual acuity (BCVA (logMAR)), foveal centre point (FCP (µm)), central subfield retinal thickness (CSRT (µm)) and macular volume (mm^3).

Results Sixty-three eyes of 57 patients with nAMD (52.6% females) with a mean (±SD) age of 79.5±6.7 years were included. Mean change of BCVA was 0.03±0.14 logMAR (p=0.115). Significant reductions were recorded for FCP with a mean (±SD) change of −66.81±72.63 µm, −66.76±60.71 µm for CSRT and −0.27±0.24 mm^3 for macular volume (all p<0.001). Intraocular inflammation was observed in seven eyes of seven patients, including one case of retinal vasculitis.

Conclusions The results of the SHIFT study indicate that switch to brolucizumab may represent a treatment option in patients with nAMD poorly responsive to other anti-VEGF agents. Further long-term analyses appear prudent to assess efficacy and safety of brolucizumab in a routine clinical setting.

INTRODUCTION

Age-related macular degeneration (AMD) is the leading cause of blindness in the elderly in industrialised countries.[1] With the advent of anti-vascular endothelial growth factor (VEGF) therapy, the visual outcome of patients with neovascular AMD (nAMD) has been improved and measurable reductions of legal blindness incidence have emerged.[2 3]

Besides the anticipated worldwide increase of AMD prevalence due to demographical changes with longer life expectancy, the burden for both patients and caregivers is high when managing patients with repetitive intravitreal injections and monitoring visits over a long period of time in a chronic disease. Various real-world studies have shown visual outcomes to be inferior compared with the results from prospective randomised clinical trials (RCTs).[4] Undertreatment is one of the major factors in part driven by non-adherence. In addition, some patients and certain subphenotypes of nAMD do not respond favourably.[5–12] Therefore, more efficacious agents with longer durability represent an important unmet need.

Brolucizumab (Novartis), a single-chain antibody fragment, was recently approved for the treatment of nAMD in October 2019 and in February 2020 by the regulatory agencies in the USA and the European Union, respectively, as well as in other countries.[13] Potential benefits of brolucizumab are assumed to be related to its low molecular weight with subsequent better tissue penetration as well as higher molar concentration.[13–15] Two pivotal trials have recently shown non-inferiority of brolucizumab to the comparator aflibercept with regard to visual outcome.[13] Post hoc analyses demonstrated overall favourable anatomical effects.[16–18] However, safety signals have been reported in both RCTs and post-marketing reports, which included the occurrence of intraocular inflammation (IOI) and retinal vasculitis with or without occlusion.[13 18–25]

The aim of the SHIFT study was to report early real-world experiences in a single European clinical centre of brolucizumab treatment for nAMD with regard to both functional and anatomical disease control as well as adverse effects following approval in February 2020 in Europe.

METHODS

The SHIFT study is a retrospective, observational, monocentre study of patients with exudative AMD who received 6 mg brolucizumab intravitreal therapy between 16 March 2020 and 15 October 2020, at the Department of Ophthalmology, University of Bonn, Germany, in routine clinical care. All patients were previously treated repetitively because of recalcitrant fluid accumulations on optical coherence tomography (OCT) despite frequent dosing with other anti-VEGF agents, including ranibizumab, aflibercept and bevacizumab. Recalcitrant fluid was defined as persistent fluid accumulations despite a high frequency of intravitreal injections of other anti-VEGF agents over a longer period of time prior to the switch to brolucizumab. The day of the first intravitreal brolucizumab injection was regarded as the baseline visit.

At each visit, best-corrected visual acuity (BCVA) determination and complete ophthalmic examination, including slit-lamp examination and fundoscopy following pupil dilation, was performed. Signs of IOI and/or retinal vasculitis were recorded if present. Retinal imaging was performed at each visit with combined confocal scanning laser ophthalmoscopy and spectral-domain optical coherence tomography (SD-OCT) (Spectralis HRA2+OCT,

Efficacy in «switch» patients

Aim of the *SHIFT study* was to report **early real-world experiences** in a single European clinical center of Brolucizumab treatment for nAMD with regard to both **functional and anatomical disease control** as well as adverse effects following approval in February 2020 in Europe

All 63 eyes of 57 patients were previously treated repetitively because of recalcitrant fluid accumulations on OCT despite frequent dosing with other anti-VEGF agents, including Ranibizumab, Aflibercept and Bevacizumab

Table 2 Functional and structural outcomes after switch to brolucizumab

Outcome	Mean±SD	95% CI	P value
Change BCVA (logMAR)	0.03±0.14	(−0.01 to 0.06)	0.115
Change FCP (µm)	−66.81±72.63	(−85.10 to −48.52)	<0.001
Change CSRT (µm)	−66.76±60.71	(−82.05 to −51.47)	<0.001
Change macular volume (mm³)	−0.27±0.24	(−0.33 to −0.20)	<0.001

BCVA, best-corrected visual acuity; CSRT, central subfield retinal thickness; FCP, foveal centre point.

- A significant **reduction** on average of **retinal thickness parameters**, including FCP, CSRT and **macular volume**, was observed demonstrating a favorable response on morphological signs for disease activity

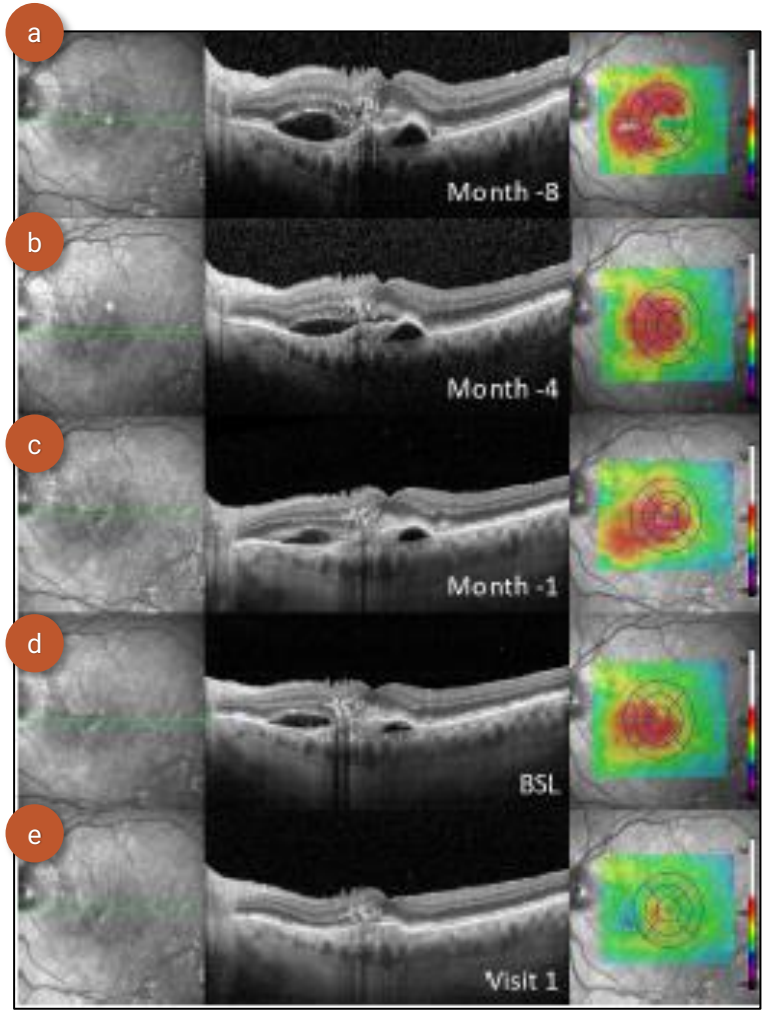
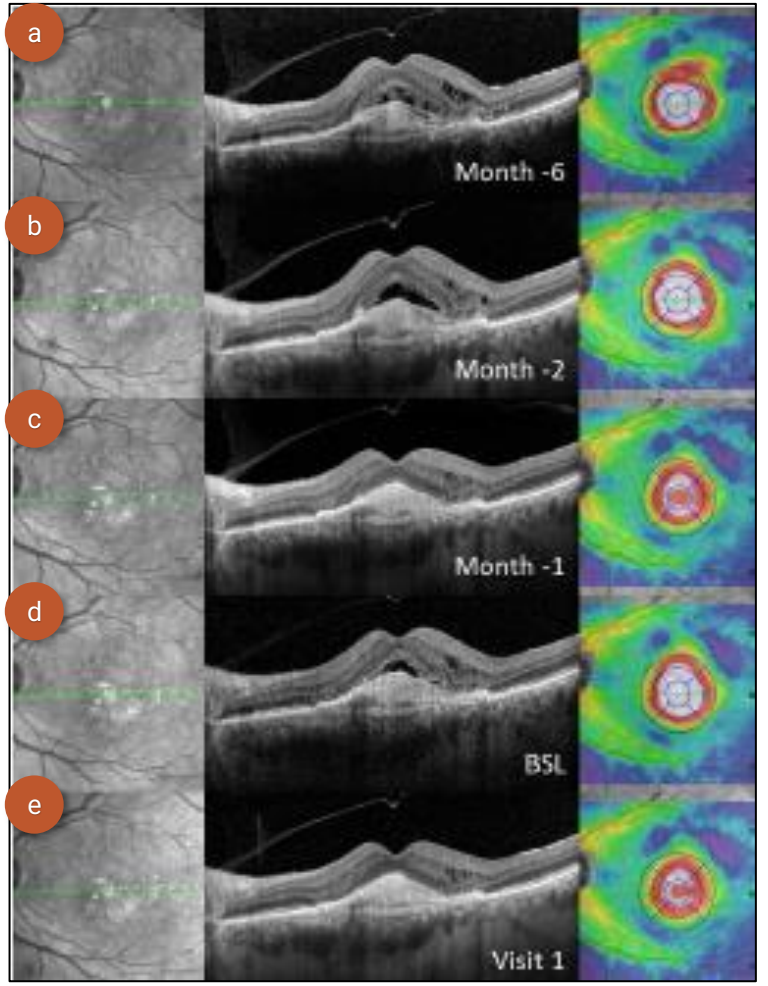


Figure 4 Exemplary case of a patient with subretinal pigment epithelial (sub-RPE) and subretinal fluid at baseline (BSL) (D) as well as in historical imaging up to 8 months (A–C) before switch to brolucizumab as demonstrated in (from left to right) near-infrared imaging, spectral-domain optical coherence tomography through the fovea and colour-coded two-dimensional thickness map for total retinal thickness. Retinal imaging at visit 1 (E) revealed complete resolution of subretinal and sub-RPE fluid. Note: Before switch to brolucizumab, the patient received repetitive, high-frequency intravitreal injections of other anti-vascular endothelial growth factor agents over a longer period of time.

Figure 5 Exemplary case of a patient with intraretinal and subretinal fluid at baseline (BSL) (D) and in historical images 1 (C), 2 (B) and 6 (A) months before switch to brolucizumab as demonstrated in (from left to right) near-infrared imaging, spectral-domain optical coherence tomography through the fovea and colour-coded two-dimensional thickness map for total retinal thickness. One month after switch (E, visit 1), complete resolution of subretinal and incomplete resolution of intraretinal fluid was demonstrated. Note: Before switch to brolucizumab, the patient received repetitive, high-frequency intravitreal injections of other anti-vascular endothelial growth factor agents over a longer period of time.



Bulirsch LM, et al. Short-term real-world outcomes following intravitreal brolucizumab for neovascular AMD: SHIFT study. Br J Ophthalmol. 2022 Sep;106(9):1288-1294. doi: 10.1136/bjophthalmol-2020-318672. Epub 2021 Apr 12. PMID: 33846161; PMCID: PMC9411904

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CLINICAL INVESTIGATION

Short-term results for brolucizumab in treatment-naïve neovascular age-related macular degeneration: a Japanese multicenter study

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Abstract

Purpose To investigate short-term treatment outcomes of intravitreal brolucizumab (IVBr) for treatment-naïve neovascular age-related macular degeneration (AMD) in a Japanese multicenter study.

Study design Retrospective case control study

Methods The subjects were 58 eyes of 57 patients with neovascular AMD (43 men and 14 women, mean age 74.6 years) of whom 43 eyes of 42 patients completed initial loading of 3 monthly IVBr injections and were followed for more than 3 months. Best-corrected visual acuity (BCVA) changes, anatomical outcomes, and complications were investigated.

Results Of the 43 eyes that completed loading doses, the AMD subtype was type 1 and type 2 macular neovascularization (MNV) in 51%, polypoidal choroidal vasculopathy (PCV) in 42%, and type 3 MNV in 7%. At 3 months after initiating treatment, BCVA significantly improved ($P = 0.002$) and central retinal thickness significantly decreased ($P < 0.0001$). At 3 months, complete retinal and subretinal fluid resolution was achieved in 91% of all eyes and complete regression of polypoidal lesions was achieved in 82% of PCV eyes. Iritis occurred in 8 eyes of 8 patients (14%), but resolved using topical or subtenon corticosteroid injection without visual loss in all cases.

Conclusions IVBr for treatment-naïve neovascular AMD was effective in the short-term, achieving significantly improved BCVA, good retinal fluid resolution, and a high rate of polypoidal lesion regression. However, iritis was noted in 14% of patients which may limit use of this drug.

Keywords Age-related macular degeneration · Polypoidal choroidal vasculopathy · Brolucizumab · Multicenter study · Treatment

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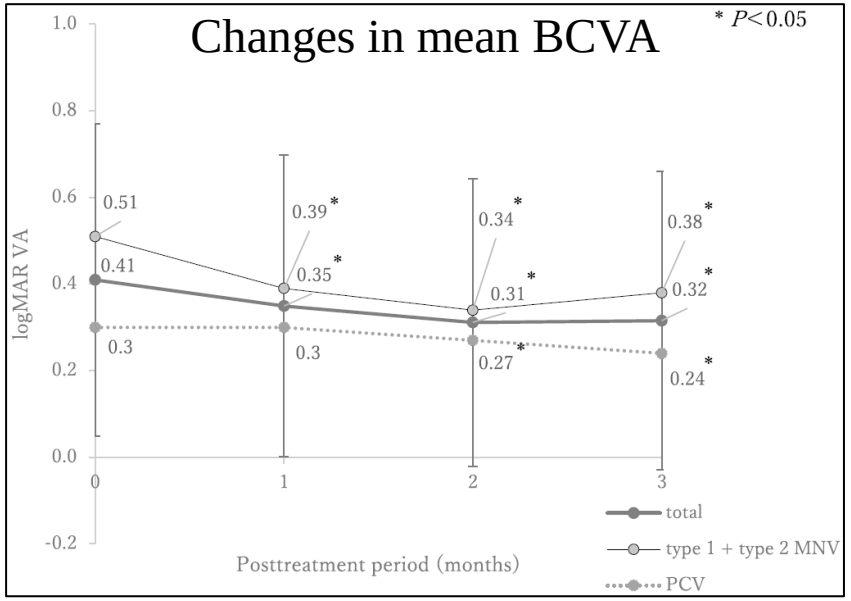
Introduction

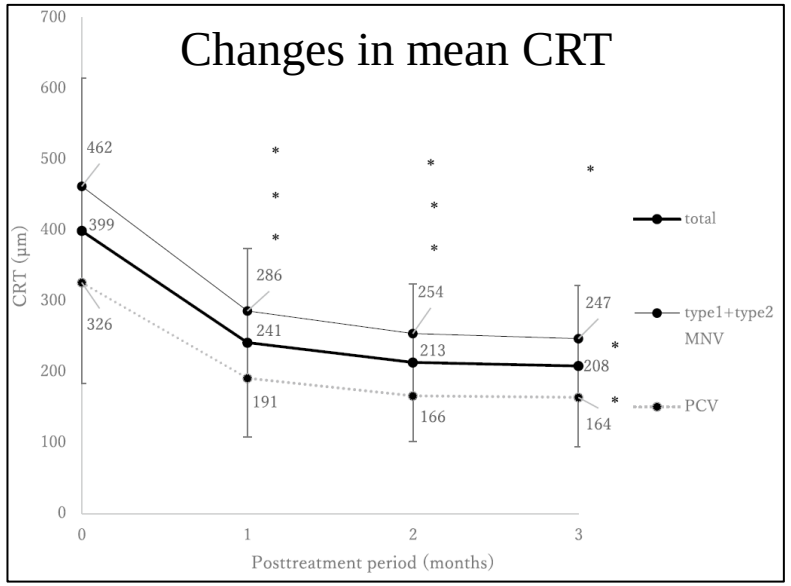
The incidence of neovascular age-related macular degeneration (AMD) is increasing in developed countries [1]. Treatment modalities include bevacizumab (Avastin; Roche Pharma AG), ranibizumab (Lucentis; Genentech) and aflibercept (Eylea; Regeneron and Bayer HealthCare). Since bevacizumab has not been approved for ocular use in Japan, intravitreal injections of two anti-vascular endothelial growth factor (VEGF) drugs, ranibizumab and aflibercept, are the main treatments available. However, treatment-resistance to aflibercept and ranibizumab, and the need for frequent injections, are problematic [2–4].

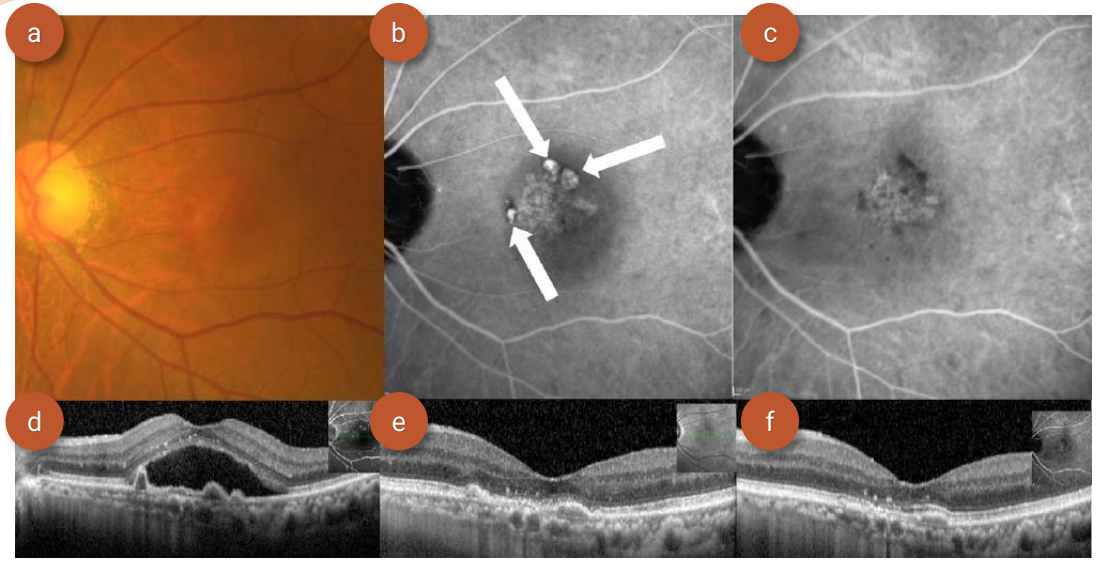
Brolucizumab (Beovu; Novartis) for neovascular AMD was launched in the United States in October 2019, with

Efficacy in naïve neovascular-AMD patients

Outcomes obtained with **three IV Brolucizumab injections at monthly intervals** for **treatment-naive neovascular AMD** in a multicentric study







Multimodal imaging of 75-years-old PCV patient

a. Color fundus photograph at baseline showed orange-reddish lesions in the macula
b. Indocyanine green angiography (ICGA) at baseline showed 3 polypoidal lesions (arrows)
c. ICGA at 3 months demonstrated complete regression of polypoidal lesions
d. OCT at baseline revealed subretinal fluid in the macula and irregular elevation of retinal pigment epithelium
e. OCT at 1 month revealed complete resolution of subretinal fluid
f. OCT still showed dry macula at 3 months

Results in different AMD subtypes

	Type 1 + Type 2 MNV	PCV	Type 3 MNV
Number of eyes, n (%)	22 (51%)	18 (42%)	3 (7%)
Female (%)	5 (23%)	5 (38%)	0 (0%)
Mean age (years)	74.7 ± 5.1	72.5 ± 8.4	80.0 ± 6.5
BCVA at baseline (logMAR)	0.51 ± 0.37	0.30 ± 0.31	0.37 ± 0.23
BCVA at 3 months (logMAR)	0.38* ± 0.35	0.24* ± 0.30	0.30 ± 0.29
Mean CRT at baseline (μm)	462.1 ± 228	326.6 ± 159	372.0 ± 264
Mean CRT at 3 months (μm)	247.1* ± 145	164.3* ± 32	188.3 ± 34
Dry macula at 3 months, n (%)	20 (91%)	16 (89%)	3 (100%)
Complete regression of polypoidal lesion at 3 months, n (%)	–	14 (82%)	–

*P < 0.05 compared with baseline. MNV, macular neovascularization; PCV, polypoidal choroidal vasculopathy; BCVA, best-corrected visual acuity; CRT, central retinal thickness

"Intravitreal **Brolucizumab** for treatment-naive neovascular AMD was **effective in the short-term**, achieving significantly **improved BCVA**, good retinal **fluid resolution**, and a **high rate of polypoidal lesion regression**"

Tanaka K, et al. Short-term results for brolucizumab in treatment-naïve neovascular age-related macular degeneration: a Japanese multicenter study. Jpn J Ophthalmol. 2022 Jul;66(4):379-385. doi: 10.1007/s10384-022-00922-3. Epub 2022 May 21. PMID: 35595951

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Ophthalmic Research

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Brolucizumab intravitreal injection in macular neovascularization type 1: VA, SD-OCT and OCTA parameters changes during a 16-weeks follow up

Toto L, Ruggeri ML, D'Aloisio R, De Nicola C, Trivigno C, Cerino L, Di Marzio G, Di Nicola M, Porreca A, Mastropasqua R

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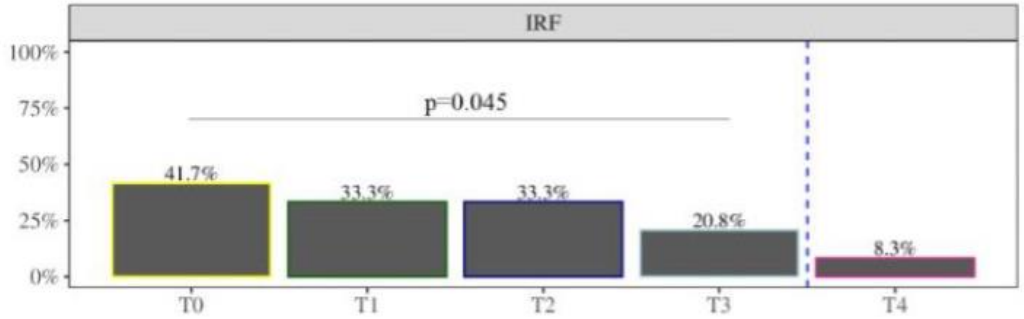
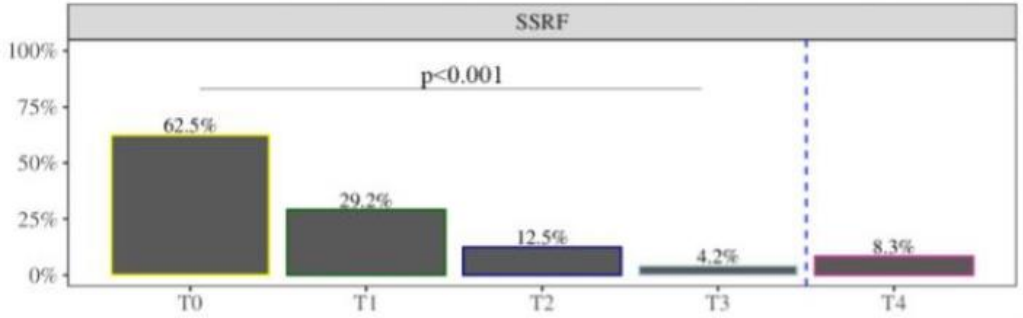
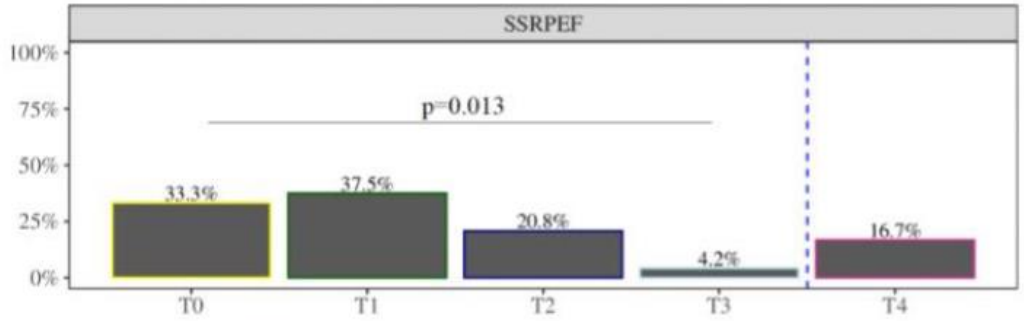
Ophthalmic Research

Efficacy in Type 1 MNVs

Early anatomical and functional changes after brolucizumab intravitreal injection (BIVI) in **24 eyes** of 24 **naïve** patients with age-related macular degeneration (AMD) and macular neovascularization **type 1 (MNV1)** candidates to intravitreal Brolucizumb injections **as per label** with q12/q8 dosing regimen after the loading dose







At week 16 DDA 75% of eyes were shifted in the q12 interval and only a minority of eyes shifted in a q8 interval (6 eyes, 25%).

- **Brolucizumab** is **efficient in improving** anatomical parameters such as **macular thickness**, **choroidal thickness** and **PED height**, which may be predictive factors
- The new drug is successful in obtaining a dry macula

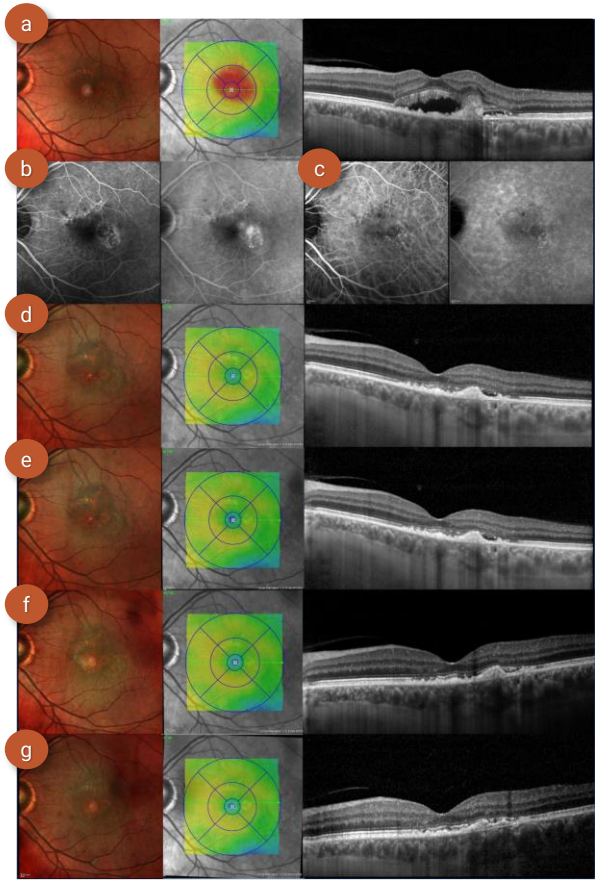
Table 1. Mean and standard deviation (SD) of functional and anatomical parameters reported at each time point.

	T0	T1	T2	T3	p-value[a]	T4	p-value[b]
BCVA (logMAR)	0.61 (0.37)	0.56 (0.33)	0.48 (0.29)	0.36 (0.24)	*0.028*	0.33 (0.21)	*0.721*
CMT (µm)	456.0 (123.0)	370.0 (105.0)	318.0 (85.3)	265.0 (85.0)	*<0.001*	293.0 (61.0)	*0.282*
SSRFT (µm)	105.0 (102.0)	43.5 (83.7)	12.2 (33.3)	1.4 (6.1)	*<0.001*	17.5 (52.6)	*0.260*
SSRPEFT (µm)	64.0 (107.0)	31.3 (52.9)	26.0 (51.2)	4.9 (21.0)	*0.049*	39.6 (79.6)	*0.121*
PED-MH (µm)	162.0 (110.0)	139.0 (84.9)	102.0 (48.7)	94.1 (38.9)	*0.020*	115.0 (66.4)	*0.290*
SFCT (µm)	203.0 (56.9)	186.0 (55.0)	155.0 (55.9)	146.0 (64.2)	*0.006*	149.0 (51.7)	*0.902*
CC Flow (mm^2)	0.31 (0.27)	0.23 (0.16)	0.20 (0.13)	0.22 (0.13)	*0.208*	0.21 (0.05)	*0.815*
ORCC Flow (mm^2)	0.22 (0.11)	0.19 (0.08)	0.18 (0.08)	0.20 (0.12)	*0.147*	0.19 (0.09)	*0.185*
FDSCP	20.2 (9.2)	21.6 (12.5)	20.2 (11.7)	20.1 (14.2)	*0.974*	19.7 (11.5)	*0.924*
FDDCP	37.8 (11.7)	34.9 (9.5)	30.1 (10.1)	32.2 (14.8)	*0.174*	28.2 (9.0)	*0.386*
PDSCP	41.5 (8.5)	38.0 (7.6)	40.7 (6.6)	38.6 (9.2)	*0.492*	38.8 (6.9)	*0.960*
PDDCP	47.2 (6.3)	46.5 (7.2)	47.7 (7.5)	46.1 (7.8)	*0.917*	46.9 (7.0)	*0.788*

BCVA, best corrected visual acuity; CMT, central macular thickness; SSRFT, subfoveal subretinal fluid thickness; SSRPEFT, subfoveal sub-RPE fluid thickness; PED-MH, pigment epithelial detachment maximum high; FDSCP, foveal density of superficial capillary plexus; FDDCP, foveal density of deep capillary plexus; PDSCP, parafoveal density of superficial capillary plexus; PDDCP, parafoveal density of deep capillary plexus.
[a]p-value derived from one-way repeated measures ANOVA models for repeated measures
[b]p-value derived from paired t-test for T3 *vs* T4.

Toto L, et al. Brolucizumab intravitreal injection in macular neovascularization type 1: VA, SD-OCT and OCTA parameters changes during a 16-weeks follow up. Ophthalmic Res. 2022 Sep 26. doi: 10.1159/000526851. Epub ahead of print. PMID: 36162382

Multimodal retinal imaging of a 70 years-old man with naïve macular neovascularization type 1 in the left eye at baseline and after brolucizumab intravitreal injection during 16-week follow up



At baseline best corrected visual acuity (BCVA) was 0.2 logarithm of the minimum angle of resolution (logMAR).

a. Multicolor fundus image (MCI) (left image) shows retinal pigment epithelium (RPE) degeneration and serous retinal detachment (SRD) at the macular area, volume optical coherence tomography (OCT) map (middle image) shows increased central macular thickness (CMT) of 406 µm, central foveal horizontal OCT scan (right image) shows irregular RPE elevation with medium to high reflectivity and sub retinal fluid in the macular area

b. Fluorescein angiography (f. - a.) images (left images) show ill-defined areas of hyperfluorescence (early phase) with late leakage (late phase).

c. Indocyanine green angiography (ICGA) images (right images) show neovascular network (early phase) with late spot of hypercyanescence (late phase). At 4 weeks after brolucizumab injection BCVA was 0.1 logMAR

d MCI (left image) shows RPE degeneration, volume OCT map shows reduced CMT compared to baseline of 241 µm (central image), central foveal OCT scan (right image) shows almost complete reabsorption of sub retinal fluid with persistence of RPE elevation. At 8 BCVA remined stable at 0.1 logMAR

e. MCI (left image) shows RPE degeneration, volume OCT maps show stable CMT (central image), central foveal OCT scan (right image) shows RPE elevation with unchanged subretinal fluid compared to 4 weeks. At 12 and 16 weeks BCVA was still at 0.1 logMAR.

f. - g. MCI images (left images) show RPE degeneration, volume OCT maps show stable CMT (central images), central foveal OCT scan images (right images) shows RPE elevation with complete reabsorption of subretinal fluid (right images).

Toto L, et al. Brolucizumab intravitreal injection in macular neovascularization type 1: VA, SD-OCT and OCTA parameters changes during a 16-weeks follow up. Ophthalmic Res. 2022 Sep 26. doi: 10.1159/000526851. Epub ahead of print. PMID: 36162382

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Article

Comparison of Outcomes between 3 Monthly Brolucizumab and Aflibercept Injections for Polypoidal Choroidal Vasculopathy

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Abstract: We compared the short-term outcomes between 3-monthly aflibercept and brolucizumab injections for treatment-naïve polypoidal choroidal vasculopathy (PCV). A total of 52 eyes were included. Patients received 3 monthly intravitreal aflibercept (n = 38) or intravitreal brolucizumab (n = 14). Indocyanine green angiography (ICGA) was performed at baseline and at the 3-month visit. Selection of anti-VEGF agents depended on time. In the brolucizumab-treated group, best-corrected visual acuity (BCVA) improved from 0.27 ± 0.34 (log MAR unit) at baseline to 0.20 ± 0.24 at 3-month visit, which is comparable with the aflibercept-treated group (p = 0.87), after adjustment of confounding factors. Central retinal thickness significantly decreased by 43%—44% in both groups. Subfoveal choroidal thickness also significantly decreased by 20.5% during this interval in the brolucizumab-treated group, which was greater than the aflibercept-treated group. The complete resolution rate of polypoidal lesions on ICGA was significantly higher (p = 0.043) in the brolucizumab-treated group (78.6%) than in the aflibercept-treated group (42.1%). Intraocular inflammation was observed in 14.3% (2/14) in the brolucizumab-treated group only. In short-term follow-up, intravitreal injection of 3-monthly brolucizumab was comparable with aflibercept in terms of BCVA and morphological improvement along with higher resolution of polypoidal lesion(s) on ICGA.

Keywords: polypoidal choroidal vasculopathy; brolucizumab; aflibercept; intraocular inflammation; resolution of polypoidal lesion(s)

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1. Introduction

Polypoidal choroidal vasculopathy (PCV), a variant of type 1 neovascularization secondary to neovascular age-related macular neovascularization (AMD), is characterized by aneurysmal dilation with or without branching vascular networks on indocyanine green angiography (ICGA) [1,2]. PCV accounts for approximately half of advanced AMD according to a clinic-based study undertaken in Japan [3].

Vascular endothelial growth factor (VEGF) is a key factor in the development and progression of neovascular AMD, and intravitreal injection of VEGF inhibitors has revolutionized the treatment of neovascular AMD [4,5]. To date, intravitreal injection of VEGF inhibitors has been the standard treatment for PCV as well as combined therapy involving photodynamic therapy and intravitreal injection of anti-VEGF agents [6–9]. Currently, in 2021, three anti-VEGF agents are commercially available in Japan: ranibizumab, aflibercept, and brolucizumab. Brolucizumab, an approximately 26 kDa single-chain antibody fragment, is the most recently approved anti-VEGF agent for the treatment of neovascular AMD [10]. In phase 3 HAWK/HARRIER, intravitreal administration of 6.0 mg brolucizumab demonstrated an equivalent visual improvement and a superior morphological

Efficacy in PCV: short-term outcomes

Short-term visual, morphological, and angiographic outcomes in 52 **naive** patients treated for **Polypoidal Choroidal Vasculopathy** after **3-monthly injections** of **Brolucizumab** in comparison with Aflibercept

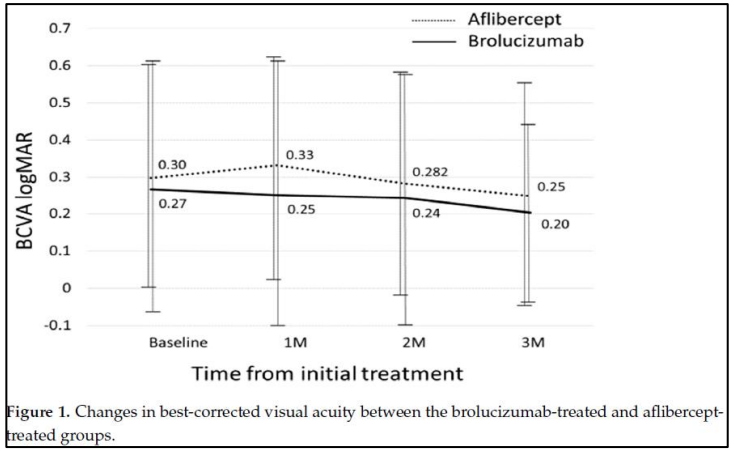


Figure 1. Changes in best-corrected visual acuity between the brolucizumab-treated and aflibercept-treated groups.

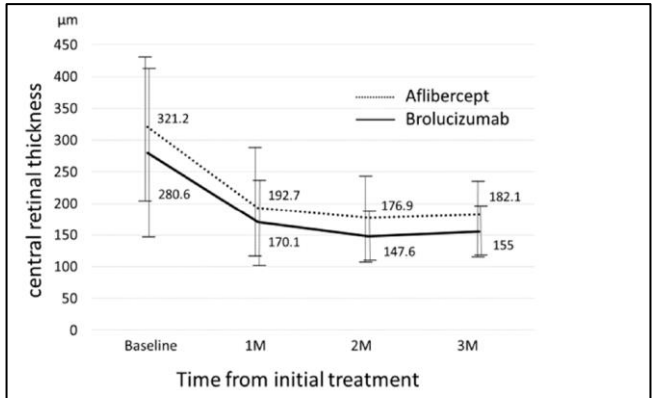


Figure 2. Changes in central retinal thickness between the brolucizumab-treated and aflibercept-treated groups.

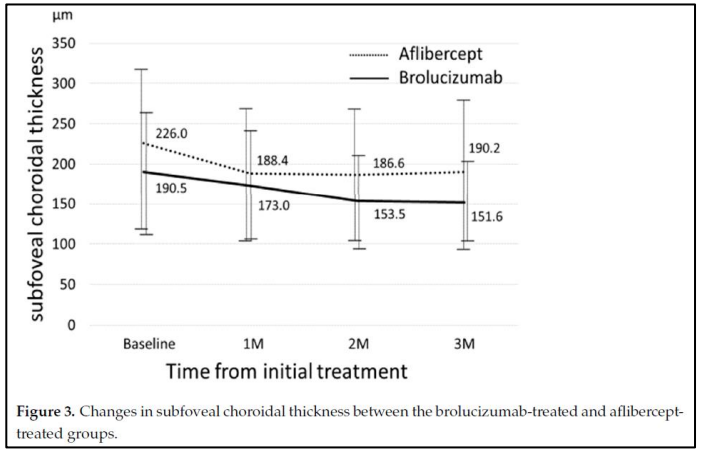


Figure 3. Changes in subfoveal choroidal thickness between the brolucizumab-treated and aflibercept-treated groups.

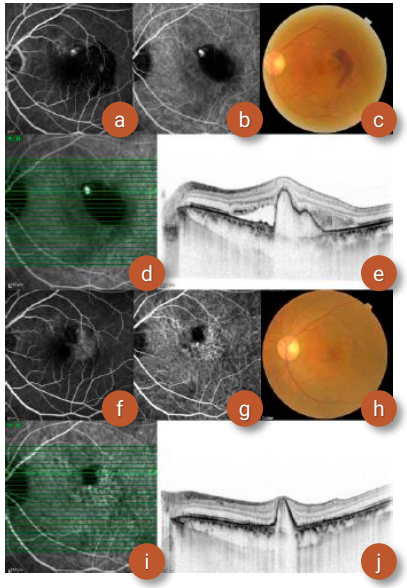


Table 2. Prevalence of subretinal fluid at each visit between two groups.

	Aflibercept (n = 38)	Brolucizumab (n = 14)	p-Value
Baseline SRF (%)	38 (100%)	14 (100%)	1.0
SRF at 1-month visit (%)	21 (55.3%)	5 (35.7%)	0.35
95%CI	38.7–71.8%	7.0–64.4%	
SRF at 2-month visit (%)	9 (23.7%)	2 (14.3%)	0.72
95%CI	9.5–37.9%	0–35.3%	
SRF at 3-month visit (%)	6 (15.8%)	0 (0%)	0.27
95%CI	3.6–27.9%	0%	

SRF: subretinal fluid.

PCV case (76-year-old man) treated with a 3-monthly intravitreal injection of brolucizumab

a. - b. Fluorescein angiography (left) and indocyanine angiography (ICGA) (middle) demonstrated a hyperfluorescent spot corresponding to a polypoidal lesion at baseline

c. Color fundus photography showed an orange-red lesion and subretinal hemorrhage before treatment

d. - e. Horizontal optical coherence tomography (OCT) demonstrated retinal pigment protrusion with subretinal fluid and hemorrhage corresponding to a polypoidal lesion on ICGA at baseline

f. - h. Fluorescein angiography (left) showed staining on the temporal side at the 3-month visit. The polypoidal lesion disappeared on ICGA at the 3-month visit (middle). Subretinal hemorrhage also disappeared on color fundus photography at the 3-month visit (left)

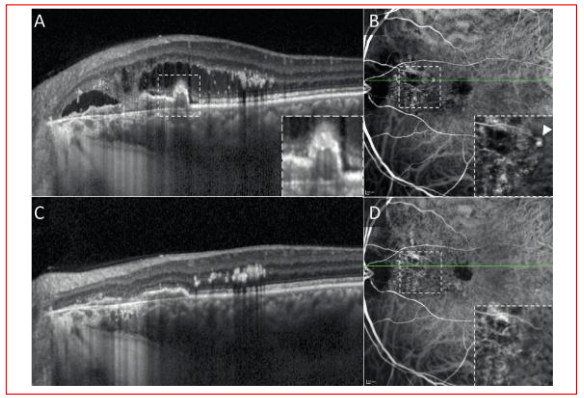
i. - j. On a horizontal OCT scan corresponding to an original polypoidal lesion, retinal pigment epithelial protrusion remained without subretinal fluid

- "The rate of **polypoidal lesion(s) resolution** on ICGA at the 3-month visit was significantly **higher in the brolucizumab-treated group (78.6%, 11/14) than in the aflibercept treated group (42.1%, 16/38)**"
- "**Brolucizumab has a higher binding capacity to VEGF** and a stronger effect on choroidal thickness than aflibercept"

Fukuda Y,et al. Comparison of Outcomes between 3 Monthly Brolucizumab and Aflibercept Injections for Polypoidal Choroidal Vasculopathy. Biomedicines. 2021 Sep 5;9(9):1164. doi: 10.3390/biomedicines9091164. PMID: 34572350; PMCID: PMC8469297

Photo Essay

Regression of aneurysmal type 1 neovascularization after brolucizumab injections



A 68-year-old man presented with progressive visual acuity decline OS. Optical coherence tomography revealed an irregular pigment epithelial detachment (PED) and a ring-like lesion enclosed in a peaked PED (inlet) with intra- and subretinal fluid (A). Early-phase indocyanine green angiography showed a branching vascular network (BVN) with an aneurysmal dilation (arrowhead) at the temporal margin of the BVN (B). One month after 2 brolucizumab intravitreal injections, complete resorption of fluid, flattening of the PED, and disappearance of the aneurysmal dilation were observed (C, D), along with reduced vascular density of the BVN. Brolucizumab could have a prominent role in the management of aneurysmal type 1 neovascularization. Fig.

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Footnotes and Disclosure

The authors declare the following financial interests/personal relationships that may be considered potential competing interests: Matteo Airaldi: none; Mariano Cozzi: Nidek and Bayer; and Giovanni Staurenghi: Heidelberg Engineering, Optos, Centervue, Zeiss, Bayer, Apellis Pharmaceuticals, Allergan, Astrellas, Boehringer Ingelheim, Genentech, Graybug, Novartis, Roche, Chengdu Kanghong Biotech, Kyoto Drug Discovery and Development, Biogen, and Ocular Instruments. Q3

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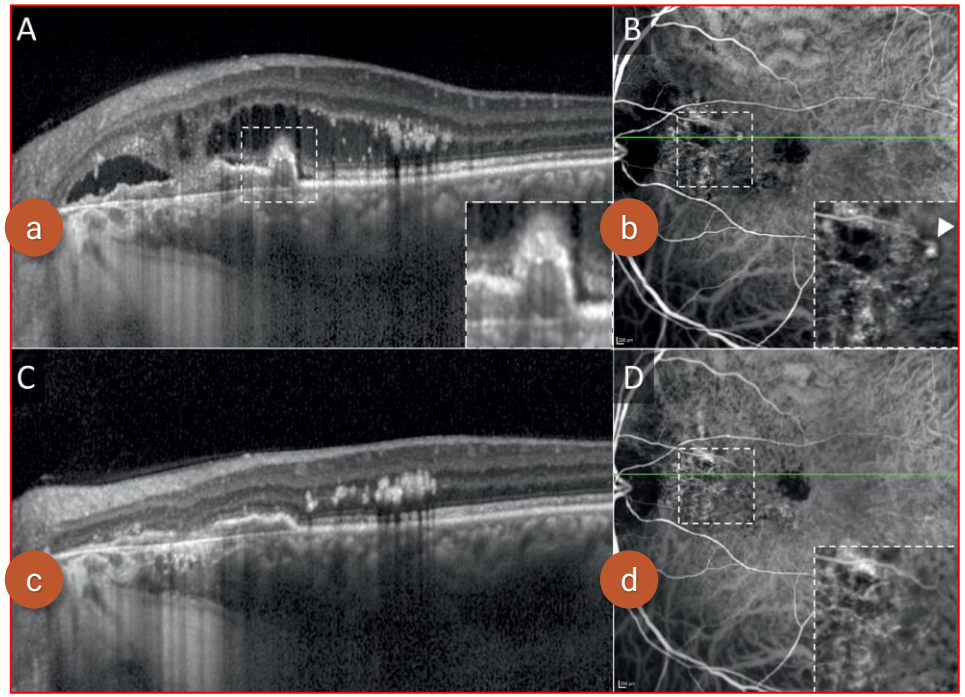
Efficacy in PCV

- OCT revealed an irregular pigment epithelial detachment (PED) and a “ring-like” lesion enclosed in a peaked PED (inlet) with intra- and subretinal fluid a.
- Early-phase ICGA showed a **branching vascular network** (BVN) with an **aneurysmal dilation** (arrowhead) at the temporal margin of the BVN b.
- One month after 2 **Brolucizumab** intravitreal injections c. - d.:
  - **complete resorption of fluid**
  - **flattening of the PED**
  - **disappearance of the aneurysmal dilation were observed**
  - **reduced vascular density of the BVN**

- **Brolucizumab could have a prominent role in the management of aneurysmal type 1 neovascularization**



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One-year outcomes of intravitreal brolucizumab injections in patients with polypoidal choroidal vasculopathy

Arisa Ito[1], Maiko Maruyama-Inoue[1✉], Yoko Kitajima[2], Shoko Ikeda[1], Tatsuya Inoue[1] & Kazuaki Kadonosono[1]

To evaluate the 1-year visual outcomes and anatomic responses of Japanese patients who received intravitreal brolucizumab (IVBr) injections for polypoidal choroidal vasculopathy (PCV). This was a retrospective study of 17 treatment-naïve eyes with PCV that were treated with IVBr. We evaluated the best-corrected visual acuity (BCVA), central macular thickness (CMT), central choroidal thickness (CCT) and number of injections for 1 year. The eradication of polypoidal lesions was also evaluated using by indocyanine green angiography during the 1-year follow-up. Non-infectious intraocular inflammation developed in two (11.8%) eyes; 15 eyes were assessed at the 1-year follow-up examination. The mean BCVA improved significantly from 0.28 at baseline to 0.13 ($P < 0.05$) at 1 year. The CMT and CCT decreased significantly after 1 year. The mean number of injections was 6.4 ± 0.13. The rate of complete resolution of polypoidal lesions at 1 year was 93.3%. A dry macula was achieved in 13 eyes (86.6%) after the loading phase and in 11 eyes (73.3%) at 1 year. The IVBr injections appeared to be effective for improving both functional and anatomic outcomes in Japanese patients with PCV, with a high regression rate of polypoidal lesions.

Polypoidal choroidal vasculopathy (PCV) was originally described by Yannuzzi et al.[1,2] as a distinct subtype of wet age-related macular degeneration (AMD). Recently, Spaide et al.[3] described that PCV is a variant of type 1 macular neovascularization that is more prevalent in Asian individuals. Indocyanine green angiography (ICGA) visualized a branching vascular network and various numbers of aneurysmal dilations at the outer edge of the expanding lesion. In Japan, it has been reported that approximately half of the patients with wet AMD have PCV[4].

In eyes with PCV, massive hemorrhages and significant loss of vision are evident after a long-term follow-up period[5]. Previous studies have reported that anti-vascular endothelial growth factor (VEGF) agents, such as ranibizumab (Lucentis, Genentech, Inc., South San Francisco, CA) and aflibercept (Eylea, Bayer Health Care, Berlin, Germany) have had been effective in the treatment of PCV, although numerous injections are needed to stabilize patients' visual acuity (VA)[6–13]. Moreover, aflibercept is more effective than ranibizumab for achieving eradication of polypoidal lesions. However, the eradication rate of polypoidal lesions at 1 year in Japanese patients was not as high as the 13% to 39% reported with ranibizumab[6–9] and the 39% to 55% reported with aflibercept[10–12].

Recently, brolucizumab was sanctioned as a new anti-VEGF agent for the treatment of AMD. Brolucizumab is a roughly 26-kDa single-chain antibody fragment[14]. The HAWK and HARRIER studies[15,16], worldwide phase 3 clinical trials, showed that intravitreal brolucizumab (IVBr) injections administered at every-12-week/every-8-week intervals were effective for improving and stabilizing VA for 96 weeks and were not inferior to the every-8-week dosing interval for intravitreal aflibercept. Moreover, IVBr injections provided better intraretinal, subretinal, and sub-retinal pigment epithelial fluid control than intravitreal aflibercept.

However, the results of IVBr injections for treating PCV in a real-world clinical setting have not been reported. The purpose of this study was to evaluate the 1-year visual outcomes and anatomic responses of Japanese patients with PCV treated with IVBr injections.

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Efficacy in PCV: long-term outcomes

To evaluate the **1-year visual outcomes and anatomic responses** of 17 **naive** Japanese patients with **PCV** treated with Intravitreal Brolucizumab injections (3 every 4weeks followed with q8/q12 regimen)

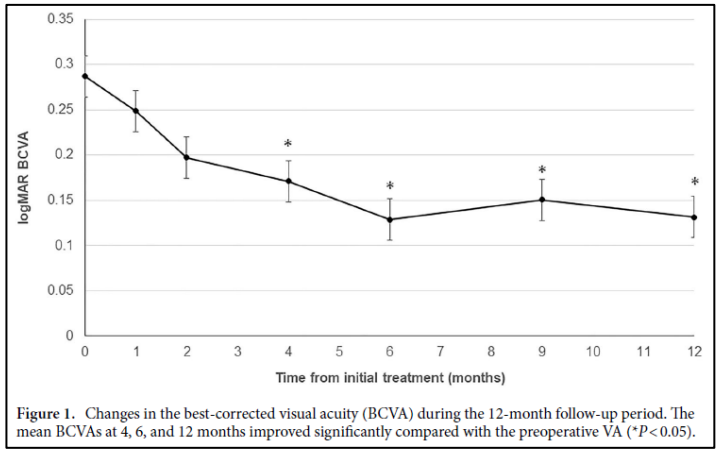


Figure 1. Changes in the best-corrected visual acuity (BCVA) during the 12-month follow-up period. The mean BCVAs at 4, 6, and 12 months improved significantly compared with the preoperative VA (*$P < 0.05$).

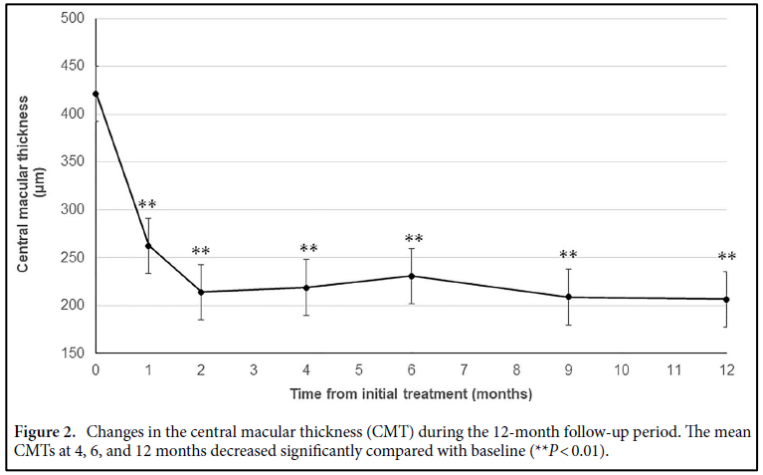
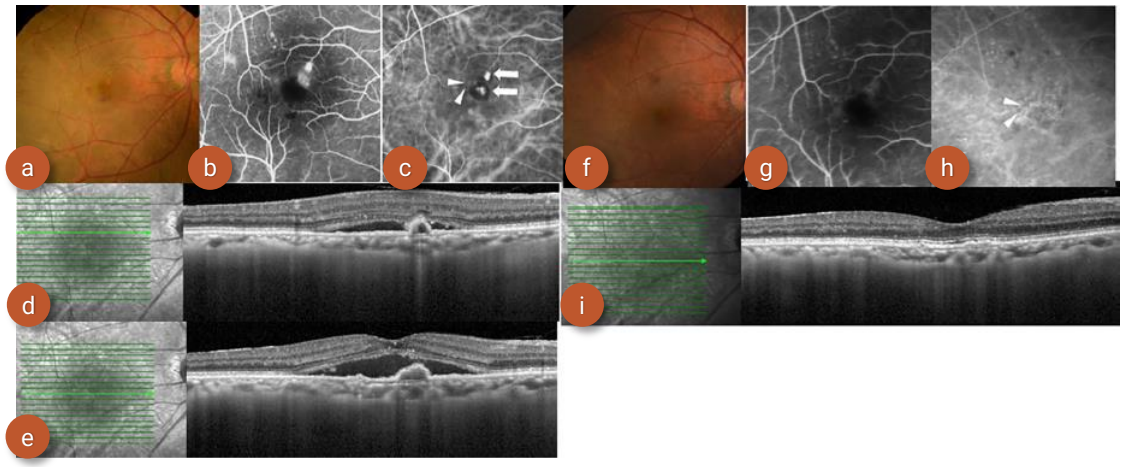


Figure 2. Changes in the central macular thickness (CMT) during the 12-month follow-up period. The mean CMTs at 4, 6, and 12 months decreased significantly compared with baseline (**$P < 0.01$).



The case of an 86-year-old man who presented with reduced visual acuity in his right eye

a. A color fundus photograph shows reddish-orange polypoidal lesions, submacular hemorrhage, and a large area of subretinal fluid (SRF)

b. Fluorescein angiography (FA) demonstrates occult leakage

c. Indocyanine green angiography (ICGA) shows two polypoidal lesions (white arrows) and an abnormal vascular network (arrow heads)

d. - e. OCT images obtained at baseline show SRF with polypoidal lesions. The visual acuity (VA) was 0.39 logarithm of the minimum angle of resolution (logMAR) in the right eye, and the patient was diagnosed with PCV. The patient received IVBr injections during the loading phase and during the maintenance phase, he was treated every 3 months IVBr injections. The exudative changes did not recur for 1 year. Twelve months after VA improved to 0.045 logMAR.

f. - g. - h. A color fundus photograph shows no reddish-orange lesion or hemorrhage at the macula and FA shows staining with no leakage. ICGA shows complete polyp regression, although an abnormal vascular network (arrow heads) remained

i. OCT shows no polypoidal lesion or SRF. Irregular retinal pigment epithelium elevation was observed where the abnormal vascular network was located.

A **dry macula** was achieved in **73.3%** after 1

The polypoidal lesions **regressed completely** after 1 year in **93.3% of eyes**

- The persistence of **brolucizumab** might derive from its high affinity for VEGF
- Its **low molecular weight** allows **more delivery of drug** per injection compared with other available anti-VEGFs and offers the potential for **more effective tissue penetration** and **increased duration** of action
- Brolucizumab **might reduce the treatment burden** for patients with PCV.

Ito A, et al. One-year outcomes of intravitreal brolucizumab injections in patients with polypoidal choroidal vasculopathy. Sci Rep. 2022 May 14;12(1):7987. doi: 10.1038/s41598-022-12216-2. PMID: 35568780; PMCID: PMC9107469

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Article

Biomarkers in Early Response to Brolucizumab on Pigment Epithelium Detachment Associated with Exudative Age-Related Macular Degeneration

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Abstract: Background: The purpose of this study was to describe early changes in the morphology of pigment epithelium detachments (PED) after an intravitreal injection of Brolucizumab into eyes with macular neovascularization secondary to exudative age-related macular degeneration (e-AMD). Method: We included twelve eyes of 12 patients with PED secondary to e-AMD which were not responding to prior anti-VEGF treatments. An ophthalmic examination and an assessment of PED-horizontal maximal diameter (PED-HMD), PED-maximum high (PED-MH) and macular neovascularization (MNV) flow area (MNV-FA) by the means of structural optical coherence tomography (OCT) and OCT Angiography (OCT-A) were performed at baseline, as well as 1, 7, 14 and 30 days after the injection. Results: The mean age of the population of study was 78.4 (SD ± 4.8). The mean number of previous Ranibizumab or Aflibercept injections was 13 (SD ± 8). At the last follow-up visit, the PED-HMD did not significantly change ($p = 0.16$; F(DF:1.94, 20,85) = 1.9), the PED-MH showed a significant reduction [$p = 0.01$; F(DF:1.31, 14.13) = 6.84.] and the MNV-FA did not significantly differ ($p = 0.1$; F(1.97, 21.67) = 2.54) from baseline. No signs of ocular inflammation were observed during follow-up. Conclusions: A single Brolucizumab injection was able to determine the short-term effects on PEDs' anatomical features of eyes with an unresponsive e-AMD.

Keywords: age-related macular degeneration; innovative biotechnologies; Brolucizumab; exudative AMD; OCT angiography; personalized medicine

1. Introduction

Worldwide, the incidence and prevalence of age-related macular degeneration (e-AMD) are relentlessly growing [1,2]. Over the age of 75, the risk of developing early and late AMD is 25% and 8%, respectively [3]. It was not a long time ago when the first anti-vascular endothelial growth factor (VEGF) drug received FDA approval for the treatment of e-AMD, and many steps forward have been made ever since [4]. As the median age of the general population keeps on growing, the burden associated with the treatment of AMD is expected to rise consistently. In fact, the overall number of patients with AMD is

Efficacy on Pigment Epithelium Detachments

Case series reporting the short-term results of intravitreal **Brolucizumab** on **PEDs** in 12 patients with neovascular-AMD

A single **Brolucizumab** injection was able to determine the **short-term effects on PEDs anatomical features** of eyes with an **unresponsive neovascular-AMD**

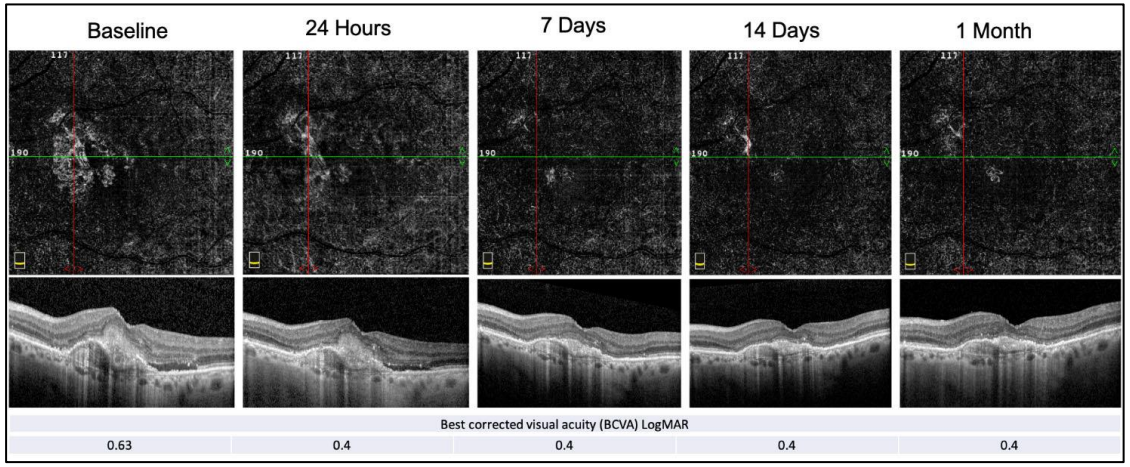

Table 2. Characteristics of structural OCT and OCT-A at baseline, after 24 h, at 7 days, at 14 days and 1 month after the Brolucizumab injection.

	PED-HMD (±SD) µm	PED-MH (±SD) µm	OCTA MNV-FA (mm^2)	BCVA (LogMAR)
Baseline	1548.36 (±1041.96)	207.36 (±82.89)	0.25 (±0.45)	0.48 (±0.42)
24 h	1588.41 (±897.41)	195.75 (±85.65)	0.22 (±0.41)	0.44 (±0.33)
7 days	1638.72 (±1022.77)	163.25 (±69.53)	0.17 (±0.37)	0.49 (±0.40)
14 days	1398.66 (±959.67)	145.66 (±80.34)	0.12 (±0.34)	0.48 (±0.41)
1 Month	1322.63 (±905.88)	127.5 (±77.79)	0.12 (±0.33)	0.46 (±0.41)

PED: pigment epithelium detachment; PED-HMD: pigment epithelium detachment-horizontal maximal diameter; PED-MH: pigment epithelium detachment-maximum high; OCTA: optical tomography angiography; MNV-FA: macular neovascularization-flow area; LogMAR: logarithm of the minimum angle of resolution.

Mukai et al. BMC Ophthalmology (2022) 22:387
https://doi.org/10.1186/s12886-022-02617-2

BMC Ophthalmology

RESEARCH Open Access

Comparison of the regressive effects of aflibercept and brolucizumab on pigment epithelial detachment

Ryo Mukai*, Hidetaka Matsumoto, Kazuki Nagai and Hideo Akiyama

Abstract

Background: To compare the regressive effects of aflibercept and brolucizumab on pigment epithelial detachment (PED) in age-related macular degeneration.

Methods: Eighty-three eyes of 83 patients diagnosed with type 1 macular neovascularization were included and retrospectively analysed using multimodal imaging. Forty-nine eyes were treated with intravitreal aflibercept injections (IVA group), and 34 eyes were treated with brolucizumab (IVBr group), with three consecutive injections administered as induction therapy. Before treatment and 1, 2, and 3 months after the first treatment, the maximum height (MH) and maximum diameter (MD) of the PED were measured using optical coherence tomography in each treatment group.

Results: In the IVA group, MH at baseline (228 ± 169 μm) diminished to 180 ± 150 ($P = 0.2558$), 165 ± 140 ($P = 0.0962$), and 150 ± 129 μm ($P = 0.0284$) at 1, 2, and 3 months after treatment, respectively; the reduction at 3 months was significant. In contrast, in the IVBr group, the MH was 307 ± 254 μm before treatment, and it decreased to 183 ± 156 μm ($P = 0.0113$), 139 ± 114 μm ($P = 0.0003$), and 125 ± 126 μm ($P < 0.0001$) at 1, 2, and 3 months after treatment, respectively, and the reduction at 1 month was significant. In both groups, the MD did not regress significantly.

Conclusions: The results suggested that the MH of PED after IVBr treatment regressed faster than that after IVA treatment.

Keywords: Aflibercept, Age-related macular degeneration, Brolucizumab, Pigment epithelial detachment

Background

Age-related macular degeneration (AMD) is a significant cause of blindness worldwide. Since 2000, anti-vascular endothelial growth factor (VEGF) drugs have been used to treat exudative lesions of AMD. To date, formulations of bevacizumab [1], pegaptanib [2, 3], ranibizumab [4], and aflibercept [5] have been used to stabilize the disease and thus improve vision. Intensive research has also yielded more potent and longer-acting drugs to treat this disease. One such drug, brolucizumab [6, 7], was launched in the United States in 2020 and is now available worldwide. Pigment epithelial detachment (PED) is closely associated with neovascular AMD. Exudative change in the retina with shallow PED indicates the presence of macular neovascularization, especially in the elderly [8]. The presence of a PED which develops due to macular neovascularization (MNV) can cause subretinal fluid, intraretinal fluid, subretinal pigmental epithelial fluid and subretinal or subretinal pigment epithelial (sub-RPE) haemorrhage, with loss of visual acuity [9]. In addition, a large PED associated with MNV can lead to the emergence of RPE tear [10]. Brolucizumab has a strong effect on subretinal pigment epithelial choroidal

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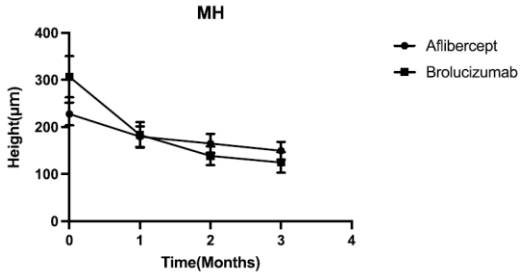
Efficacy on PEfficacy on Pigment Epithelium Detachments (PED)

Focus on the regressive effect of brolucizumab on **PEDs** and the effects of **Intravitreal Aflibercept** and **Brolucizumab** in a real-world setting

Three monthly injections of Brolucizumab (Beovu; 6.0 mg/0.05 mL; Novartis) or Aflibercept (Eylea; 2 mg/0.05 mL; Bayer) were administered as a loading-phase treatment



MH(μm)	Pretreatment	1 month	2 months	3 months
IVA group	228 ± 169	180 ± 150	165 ± 140	150 ± 129*
P value		0.2558	0.0962	0.0284
IVBr group	307 ± 254	183 ± 150*	139 ± 114***	125 ± 126****
P value		0.0113	0.0003	< 0.0001

Fig. 1 Changes in the maximum height (MH) of pigment epithelial detachment measured in the intravitreal aflibercept (IVA) and intravitreal brolucizumab (IVBr) groups before and at 1, 2, and 3 months after the first treatment. *: $P < 0.05$, ***: $P < 0.001$, ****: $P < 0.0001$

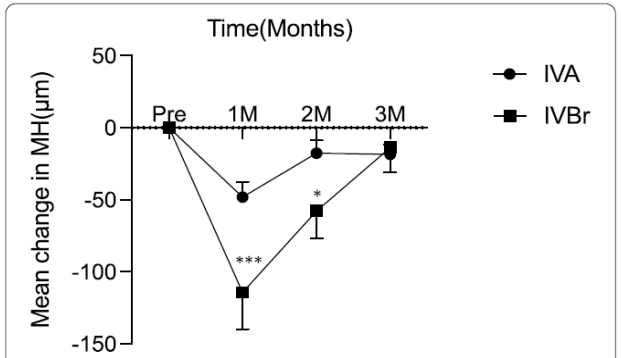
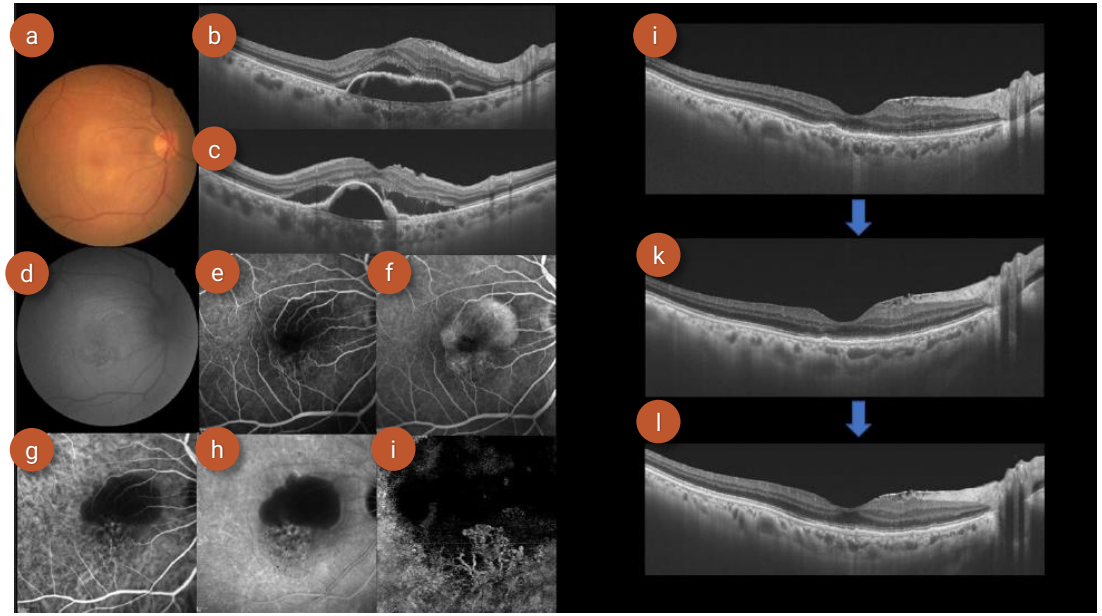


Fig. 2 Mean changes from baseline in the maximum height (MH) of pigment epithelial detachment measured in the intravitreal aflibercept (IVA) and intravitreal brolucizumab (IVBr) groups before and at 1, 2, and 3 months after the first treatment. *: $P < 0.05$, ***: $P < 0.001$



75-year-old male in the intravitreal Brolucizumab treatment group at base line (a. - i.)

a. Fundus photograph showed pigment epithelial detachment (PED) at the macula

b. - c. OCT; horizontal (b.) and vertical images (c.) revealed PED with subretinal fluid

d. Fundus autofluorescence image

e. - f. Early and late phase of fluorescein angiography detected occult macular neovascularization (MNV) at the macula

g. - h. Early and late phase of indocyanine green angiography identified MNV at the bottom of PED

i. OCT-angiography showed MNV at the bottom of the lesion. OCT images of the case at 1,2 and 3 months after IVBr treatment

j. - l. At 1 month after treatment, PED dramatically regressed

j. - k. At 2 months, the PED gradually reduced and almost disappeared at 3 months (l.)

- **Intravitreal Brolucizumab** treatment for type 1 MNV can achieve **faster regression of PED** than intravitreal Aflibercept treatment
- In comparison with intravitreal Aflibercept, **intravitreal Brolucizumab** can potentially contribute to the **stability of sub-RPE lesions**

Mukai R, et al. Comparison of the regressive effects of aflibercept and brolucizumab on pigment epithelial detachment. BMC Ophthalmol. 2022 Sep 29;22(1):387. doi: 10.1186/s12886-022-02617-2. PMID: 36175862; PMCID: PMC9520796

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Article

Early OCTA Changes of Type 3 Macular Neovascularization Following Brolucizumab Intravitreal Injections

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Abstract: Background and Objectives: Brolucizumab is a novel anti-vascular endothelial growth factor (VEGF), whose efficacy has been shown in the Hawk and Harrier phase 3 clinical studies. The goal of the present case series is to report initial results of brolucizumab intravitreal injections (IVI) on type 3 neovascularization in neovascular age-related macular degeneration (nAMD), evaluated by optical coherence tomography angiography (OCTA). Materials and Methods: This is a bicentric retrospective case series. Patients with newly diagnosed type 3 MNV treated with brolucizumab IVI and at least 6 months follow-up were enrolled. OCTA en face images and B-scans were analyzed for lesions at baseline, 1 month, 3 months, and 6 months. Whenever detectable, lesion area on outer retina and choriocapillaris layers was measured. Results: Twelve eyes of 12 patients were included into the study. The most consistent OCTA sign at baseline was the presence of a vascular tuft in the outer retina (100%). The highest response was achieved at 3 months, with statistically significant decrease in lesion detection in the outer retina, in the choriocapillaris, and outer retinal lesion size. At 6 months, 58% of outer retinal lesions had disappeared. Conclusions: Brolucizumab IVI shows a good short-term efficacy for the treatment of type 3 neovascularizations. Further studies with greater number of patients and longer follow-up are warranted to confirm these findings.

Keywords: neovascular age-related macular degeneration; type 3 neovascularization; retinal angiomatous proliferation; brolucizumab; optical coherence tomography angiography; intravitreal injection

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1. Introduction

Neovascular age-related macular degeneration (nAMD) can be classified according to the location of the macular neovascularization (MNV). Donald Gass was the first to use the terms type 1 and type 2 neovascularization, corresponding to lesions developing beneath and above the retinal pigment epithelium (RPE), respectively [1]. Early type 3 MNV corresponds to an intraretinal neovascularization, also known as retinal angiomatous proliferation [2], which can, in turn, progress towards the formation of a retino-choroidal anastomosis and eventually a pigment epithelium detachment (PED) in the late phase of the disease [3]. While the location and origin of type 1 and 2 MNV have been established with little debate, the origins of type 3 lesions have not always been clear [2,4]. Currently, sufficient evidence exists to support an origin from the retina, with further downward extension towards the choroid as the lesion progresses [5]. Type 3 MNV is the second most common MNV type, representing 34% of cases in a study by Jung et al. [6], behind type 1 MNV (40%), while pure type 2 MNV is the rarest (9%) [6].

Although differences exist in terms of prognosis of each MNV type, the first-line treatment of nAMD as a whole consists of intravitreal injections (IVI) of anti-vascular endothelial growth factor (VEGF) drugs. Brolucizumab is a novel anti-VEGF first approved

Efficacy in Type III MNV (RAP)

Case series reporting the initial results of Brolucizumab intravitreal injections (IVI) on **type 3 MNVs** in 12 newly diagnosed patients

- High rate of **lesion regression** after treatment
- The **high rate of regression obtained with Brolucizumab**, compared with other anti-VEGFs could be attributable to **the high potency of the drug**
- Brolucizumab may allow for **complete VEGF and neovascular activity inhibition** and **stop the progression of the lesion** towards a stage where reversal is no longer possible

Table 2. Characteristics on optical coherence tomography (OCT) B-scan at baseline, at one month, three months, and six months after Brolucizumab treatment.

OCT B-Scan	Baseline	1 Month	3 Months	6 Months
Mean CRT ± SD (microns)	400 ± 64	342 ± 53	329 ± 18	289 ± 23
Dry macula, *n* (%)	0	9 (75%)	10 (83%)	9 (75%)
IRF, *n* (%)	5 (42%)	0	1 (8%)	1 (8%)
SRF, *n* (%)	3 25%)	2 (17%)	1 (8%)	1 (8%)
IRF + SRF, *n* (%)	2 (17%)	0	0	0
IRF + SRF + PED, *n* (%)	2 (17%)	1 (8%)	1 (8%)	1 (8%)

OCT = Optical coherence tomography, CRT = central retinal thickness, IRF = intraretinal fluid, SRF = subretinal fluid, PED = pigment epithelium detachment.

KEY TAKEAWAYS

- **Brolucizumab** (6 mg q12w/q8w) showed **superior retinal thickness reduction** to most comparators including Aflibercept, Ranibizumab and Faricimab in neovascular-AMD

- Intravitreal **Brolucizumab** for treatment-naive neovascular AMD was **effective in the short-term**, achieving significantly **improved BCVA**, good retinal **fluid resolution**

- These outcomes were confirmed in **different subtypes of macular neovascularizations (Type I, Type II, Type III, PCV)**

- In **Polypoidal Choroidal Vasculopathy:**
  - A **dry macula** was achieved in **73.3%** after 1 year
  - The polypoidal lesions **regressed completely** after 1 year in **93.3% of eyes**
- In **Type III MNVs:**
  - High rate of **lesion regression** after treatment
  - Brolucizumab may allow for **complete VEGF and neovascular activity inhibition** and **stop the progression of the lesion** towards a stage where reversal is no longer possible