Sponsor

Novartis

Generic Drug Name

Brolucizumab

Trial Indication(s)

Neovascular age-related macular degeneration (nAMD)

Protocol Number

CRTH258APT02

Protocol Title

Observational Study to Evaluate Fluid Resolution and Effectiveness of Brolucizumab for Neovascular Age-related Macular Degeneration (nAMD) in Portugal (BLUESKY-PT)

Clinical Trial Phase

Not applicable

Phase of Drug Development

Not applicable

Study Start/End Dates

Study Start Date: 10 May 2021 (First Patient First Visit)

Study Completion Date: 16 February 2024 (Last Patient Last Visit)

Reason for Termination

The study was terminated earlier since the obtained sample was not representative of the Portuguese population, and pointed to the high fragility in evaluating the data, making it difficult to carry out a statistical study and draw valid conclusions.

Study Design/Methodology

This study was a prospective, observational, non-interventional, multicenter, open-label, single arm study in patients being treated for nAMD with brolucizumab.

Patients were enrolled in the study upon signing an informed consent form (ICF). The index date visit was used to assess eligibility and collect baseline characteristics information. The study eye was defined as the first eye treated during the study. If both eyes were treated at baseline/index date, the eye with the worse visual acuity (VA) was chosen. The follow-up visits took place at a frequency defined per investigator's discretion. Patients that had not received an intravitreal anti-Vascular Endothelial Growth Factor (anti-VEGF) injection or visited an eye specialist for at least 6 months were discontinued from the observation.

Patients that started brolucizumab in the last 6 months prior to index date (ICF signature) were considered for the study. Retrospective data was collected since the first brolucizumab injection. Data was also collected for up to twelve months before baseline (first injection of brolucizumab).

Centers

Multiple centers in Portugal.

Objectives:

Primary objective(s)

Evaluate fluid resolution after initiation of brolucizumab.

Secondary objective(s)

1. Characterize nAMD patients who initiated treatment with brolucizumab with respect to baseline characteristics and patient history.
2. Evaluate anatomical parameters during the first 24 Months of treatment with brolucizumab.
3. Estimate VA change from baseline during the first 24 months of treatment with brolucizumab.
4. Estimate the number of anti-VEGF injections, number of non-injection visits and total number of visits during treatment with brolucizumab, as well as the percentage (%) of patients' eyes with anti-VEGF injection intervals ≤8 weeks (every 8 weeks) and ≥12 weeks (every 12 weeks) up to Month 12 of treatment with brolucizumab.
5. Estimate the percentage (%) of patients' eyes that switched to another anti-VEGF during the first 24 months of treatment with brolucizumab and characterize switchers with respect to their baseline characteristics at baseline and during the pre-switching period.
6. Estimate discontinuation rate in nAMD patients receiving brolucizumab during the first year (Month 1-12) of therapy and estimate the time to discontinuation (persistence).
7. Assess re-treatment criteria.
8. Estimate the number of Optical Coherence Tomography (OCT), the number of visits with/without OCT during the 1st two years of treatment with brolucizumab and assess their association to Choroidal Neovascularization (CNV) activity & VA.
9. Assess safety of brolucizumab during treatment: number and nature of adverse events (AEs), causes, severity, duration, treatment, resolution and outcome.
10. In naïve patients, explore the predictive value of age, baseline VA, baseline CNV activity [active, active (sub-retinal fluid [SRF] only), inactive], complete loading phase (yes/no), presence or not of intra-retinal fluid (IRF) and SRF at baseline, VA at the end of the loading phase (Month 3), CNV activity at the end of the loading phase, number of anti-VEGF injections (maintenance phase), comorbidities, geographic atrophy (yes/no; during the first months of treatment), subretinal fibrosis (yes/no; during the first two years of treatment), on the VA gains at Month 6, 9, 12 and 24 of treatment with brolucizumab.

Test Product (s), Dose(s), and Mode(s) of Administration

Patients received brolucizumab per their prescribed dosing regimen.

Statistical Methods

The statistical methods for this study, conducted using RStudio v4.2.2, are outlined in several steps:

As this was an exploratory study, most outcomes were analyzed descriptively. Treatment-naïve and switch patients were evaluated independently across different follow-up periods (e.g., months 3, 6, 9, 12, 18, 24).

Inferential statistics (e.g., paired t-tests or Wilcoxon tests) were applied only when specified and when sample sizes were sufficient (at least 10 patient eyes per timepoint). Normality was tested using the Shapiro-Wilk test and QQ-plots.

Survival analysis: Kaplan-Meier estimators were used to assess time-to-event data, specifically for fluid resolution, SRF, and IRF. Log-rank tests were applied to compare survival curves between patient groups.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion criteria:

1. Diagnosis of nAMD;
2. Male and female patients with ≥40 years of age at baseline or index date (for patients who had not started brolucizumab treatment at index date);
3. Receipt of at least one injection of brolucizumab during the recruitment period or in the last 6 months prior to index date (ICF signing date);
4. Signed written ICF.

Exclusion criteria:

1. Patients treated for retinal vascular occlusion (RVO), diabetic macular edema (DME), myopic choroidal neovascularization (mCNV), and having diagnoses of diabetes-related macular degeneration within 6 months prior to the baseline or index date (for patients who had not started brolucizumab treatment at index date);
2. Receipt of any anti-VEGF treatment other than brolucizumab in the study eye at baseline or index date (for patients who had not started brolucizumab treatment at index date);

3. Central subfield of the study eye affected by fibrosis or geographic atrophy or total area of fibrosis >50% of the total lesion in the study eye at baseline or index date (for patients who had not started brolucizumab treatment at index date);
4. Any active intraocular or periocular infection or active intraocular inflammation in either eye at baseline or index date (for patients who had not started brolucizumab treatment at index date);
5. Patients who had been on anti-VEGF treatment for longer than 3 years before baseline or index date (for patients who had not started brolucizumab treatment at index date);
6. Patients that had any contraindication and were not eligible for treatment with brolucizumab as according to the Summary of Product Characteristics (SmPC);
7. Any medical or psychological condition in the treating physician's opinion which may have prevented the patient from the 24 months study participation;
8. Patients who were participating in parallel in an interventional clinical trial;
9. Patients who were participating in parallel in any other non-interventional study (NIS) generating primary data for an anti-VEGF drug;
10. Retinal pigment epithelial rip/tear in the study eye at baseline or index date (for patients who had not started brolucizumab treatment at index date) or current vitreous hemorrhage or history of vitreous hemorrhage in the study eye within 4 weeks prior to baseline or index date (for patients who had not started brolucizumab treatment at index date);
11. Subretinal blood affecting the foveal center point and/or >50% of the lesion of the study eye at baseline or index date (for patients who had not started brolucizumab treatment at index date).

Participant Flow Table

A total of 81 participants were included in the study and analyzed at baseline. Of these, 46 were naïve patients and 35 were switch patients. Several dropouts were verified between follow-up visits, as described below.

Follow-up visit	Number of Naïve Patients Analyzed	Number of Switch Patients Analyzed
Month 3 (3M)	44	31
Month 6 (6M)	42	30
Month 12 (12M)	34	27
Month 24 (24M)	23	10

Follow-up visits	Naïve Patients Number of Dropouts	Switch Patients Number of Dropouts
Between Baseline and 3M	2	4
Between 3M and 6M	2	1
Between 6M and 12M	8	3
Between 12M and 24M	11	17

Baseline Characteristics

Refer to Secondary Outcome Results.

Primary Outcome Result(s)

SRF and/or IRF at month 12

	Naïve Patients	Switch patients
SRF and/or IRF at Month 12	**n = 29**	**n = 22**
Presence	15 (62.5%) 95%CI [42.7%;78.8%]	15 (75.0%) 95%CI [53.1%;88.8%]
Absence	9 (37.5%) 95%CI [21.2%;57.3%]	5 (25.0%) 95%CI [11.2%;46.9%]
Missing	5	2

Abbreviations: CI: confidence interval

Secondary Outcome Result(s)

1. Characterize nAMD patients who initiated treatment with brolucizumab.

Demographic characteristics and comorbidities of naïve and switch patients

	Naïve patients (n=46)	Switch patients (n=35)
Study eye		
Right	23 (50.0%) 95%CI [36.1%;63.9%]	18 (51.4%) 95%CI [35.6%;67.0%]
Left	23 (50.0%) 95%CI [36.1%;63.9%]	17 (48.6%) 95%CI [33.0%;64.4%]
Age at 1st brolucizumab injection (in years)		
Valid n (Missing)	46 (0)	35 (0)
Mean [95%CI]	79.33 [77.26;81.39]	79.53 [76.99;82.07]
Std. dev	7.15	7.67
Med [P25,P75]	80.22 [74.62;84.55]	80.76 [71.89;85.67]
Min / Max	61.79 / 90.78	65.08 / 91.51
Age at 1st brolucizumab injection (in years) classes		
<80 years	20 (43.5%) 95%CI [30.2%;57.8%]	15 (42.9%) 95%CI [28.0%;59.1%]
≥80 years	26 (56.5%) 95%CI [42.2%;69.8%]	20 (57.1%) 95%CI [40.9%;72.0%]
Gender		
Male	23 (50.0%) 95%CI [36.0%;63.9%]	10 (28.6%) 95%CI [16.0%;45.1%]

Female	23 (50.0%) 95%CI [36.0%;63.9%]	25 (71.4%) 95%CI [55.0%;83.7%]
Other	0 (0.0%) 95%CI [0.0%;7.7%]	0 (0.0%) 95%CI [0.0%;9.9%]
Weight (in kg)		
Valid n (Missing)	26 (20)	15 (20)
Mean [95%CI]	73.19 [69.05;77.33]	68.47 [63.93;73.00]
Std. dev	14.33	13.69
Med [P25,P75]	73.00 [63.00;80.75]	70.00 [57.50;76.50]
Min / Max	50.00 / 115.00	50.00 / 91.00
Smoker		
Never	25 (54.3%) 95%CI [40.2%;67.8%]	14 (40.0%) 95%CI [25.6%;56.4%]
Former Smoker	6 (13.0%) 95%CI [6.1%;25.7%]	4 (11.4%) 95%CI [4.5%;26.0%]
Smoker	2 (4.3%) 95%CI [1.2%;14.5%]	2 (5.7%) 95%CI [1.6%;18.6%]
Unknown	13 (28.3%) 95%CI [17.3%;42.5%]	15 (42.9%) 95%CI [28.0%;59.1%]
Driver?		
Yes	14 (30.4%) 95%CI [19.1%;44.8%]	6 (17.1%) 95%CI [8.1%;32.7%]
No (no driving license)	11 (23.9%) 95%CI [13.9%;37.9%]	7 (20.0%) 95%CI [10.0%;35.9%]
No (other)	5 (10.9%) 95%CI [4.7%;23.0%]	7 (20.0%) 95%CI [10.0%;35.9%]

No (due to VA)	2 (4.3%) 95%CI [1.2%;14.5%]	1 (2.9%) 95%CI [0.5%;14.5%]
Unknown	14 (30.4%) 95%CI [19.1%;44.8%]	14 (40.0%) 95%CI [25.6%;56.4%]
Insurance		
Private	10 (24.4%) 95%CI [13.8%;39.3%]	12 (34.3%) 95%CI [20.8%;50.8%]
Public	31 (75.6%) 95%CI [60.7%;86.2%]	23 (65.7%) 95%CI [49.2%;79.2%]
Missing	5	0
If Private, Insurance type:		
Out-of-pocket	2 (20.0%) 95%CI [5.7%;51.0%]	0 (0%) 95%CI [0%;24.2%]
Healthcare subsystem	7 (70.0%) 95%CI [39.7%;89.2%]	10 (83.3%) 95%CI [55.2%;95.3%]
Private insurance	1 (10.0%) 95%CI [1.8%;40.4%]	2 (16.7%) 95%CI [4.7%;44.8%]
Systemic comorbidities	39 (84.8%) 95%CI [71.8%;92.4%]	27 (77.1%) 95%CI [61.0%;87.9%]
Arterial hypertension	35 (76.1%) 95%CI [62.1%;86.1%]	18 (51.4%) 95%CI [35.6%;67.0%]
Dyslipidemia	26 (56.5%) 95%CI [42.2%;69.8%]	16 (45.7%) 95%CI [30.5%;61.8%]
Type 2 DM	12 (26.1%) 95%CI [15.6%;40.3%]	3 (8.6%) 95%CI [3.0%;22.4%]
Arrhythmia	5 (10.9%)	2 (5.7%)

	95%CI [4.7%;23.0%]	95%CI [1.6%;18.6%]
Acute Myocardial Infarction	4 (8.7%)	0 (0.0%)
	95%CI [3.4%;20.3%]	95%CI [0.0%;9.9%]
History of malignancy of any organ system	1 (2.2%)	3 (8.6%)
	95%CI [0.4%;11.3%]	95%CI [3.0%;22.4%]
Stroke/TIA	1 (2.2%)	1 (2.9%)
	95%CI [0.4%;11.3%]	95%CI [0.5%;14.5%]
Type 1 DM	1 (2.2%)	1 (2.9%)
	95%CI [0.4%;11.3%]	95%CI [0.5%;14.5%]
Autoimmune disease	0 (0%)	0 (0.0%)
	95%CI [0%;7.7%]	95%CI [0.0%;9.9%]
Other	25 (54.3%)	14 (40.0%)
	95%CI [40.2%;67.8%]	95%CI [25.6%;56.4%]
Depression	5 (20.0%)	4 (28.6%)
	95%CI [8.9%;39.1%]	95%CI [11.7%;54.6%]
Hyperuricemia	3 (12.0%)	1 (7.1%)
	95%CI [4.2%;30.0%]	95%CI [1.3%;31.5%]
Overweight	3 (12.0%)	0 (0%)
	95%CI [4.2%;30.0%]	95%CI [0%;21.5%]
Anxiety	2 (8.0%)	0 (0%)
	95%CI [2.2%;25.0%]	95%CI [0%;21.5%]
Benign prostate hyperplasia	2 (8.0%)	1 (7.1%)
	95%CI [2.2%;25.0%]	95%CI [1.3%;31.5%]
Osteoarticular pathology	2 (8.0%)	0 (0%)
	95%CI [2.2%;25.0%]	95%CI [0%;21.5%]
Acute aortic syndrome	1 (4.0%)	0 (0%)

	95%CI [0.7%;19.5%]	95%CI [0%;21.5%]
Aortic stenosis	1 (4.0%)	0 (0%)
	95%CI [0.7%;19.5%]	95%CI [0%;21.5%]
Arterial hypertension	1 (4.0%)	0 (0%)
	95%CI [0.7%;19.5%]	95%CI [0%;21.5%]
Atherosclerosis	1 (4.0%)	0 (0%)
	95%CI [0.7%;19.5%]	95%CI [0%;21.5%]
Arthralgia	1 (4.0%)	0 (0%)
	95%CI [0.7%;19.5%]	95%CI [0%;21.5%]
Auricular ventricular block	1 (4.0%)	0 (0%)
	95%CI [0.7%;19.5%]	95%CI [0%;21.5%]
Benign digestive system neoplasm	1 (4.0%)	0 (0%)
	95%CI [0.7%;19.5%]	95%CI [0%;21.5%]
Bronchitis	1 (4.0%)	0 (0%)
	95%CI [0.7%;19.5%]	95%CI [0%;21.5%]
Cardiomyopathy	1 (4.0%)	1 (7.1%)
	95%CI [0.7%;19.5%]	95%CI [1.3%;31.5%]
Cholecystitis/cholelithiasis	1 (4.0%)	0 (0%)
	95%CI [0.7%;19.5%]	95%CI [0%;21.5%]
COPD	1 (4.0%)	0 (0%)
	95%CI [0.7%;19.5%]	95%CI [0%;21.5%]
Dementia	1 (4.0%)	1 (7.1%)
	95%CI [0.7%;19.5%]	95%CI [1.3%;31.5%]
Dizziness	1 (4.0%)	0 (0%)
	95%CI [0.7%;19.5%]	95%CI [0%;21.5%]
Hypertriglyceridemia	1 (4.0%)	0 (0%)

	95%CI [0.7%;19.5%]	95%CI [0%;21.5%]
Hypoacusis	1 (4.0%)	0 (0%)
	95%CI [0.7%;19.5%]	95%CI [0%;21.5%]
Hypothyroidism	1 (4.0%)	2 (14.3%)
	95%CI [0.7%;19.5%]	95%CI [4.0%;39.9%]
Nephropathy	0 (0%)	1 (7.1%)
	95%CI [0%;13.3%]	95%CI [1.3%;31.5%]
Neurological changes	1 (4.0%)	0 (0%)
	95%CI [0.7%;19.5%]	95%CI [0%;21.5%]
Obesity	1 (4.0%)	1 (7.1%)
	95%CI [0.7%;19.5%]	95%CI [1.3%;31.5%]
Osteoporosis	1 (4.0%)	0 (0%)
	95%CI [0.7%;19.5%]	95%CI [0%;21.5%]
Peripheral vascular insufficiency	1 (4.0%)	0 (0%)
	95%CI [0.7%;19.5%]	95%CI [0%;21.5%]
Prostatic hypertrophy	1 (4.0%)	0 (0%)
	95%CI [0.7%;19.5%]	95%CI [0%;21.5%]
Pulmonary hypertension	1 (4.0%)	0 (0%)
	95%CI [0.7%;19.5%]	95%CI [0%;21.5%]
Thyroid pathology	1 (4.0%)	0 (0%)
	95%CI [0.7%;19.5%]	95%CI [0%;21.5%]
Urinary disease	1 (4.0%)	0 (0%)
	95%CI [0.7%;19.5%]	95%CI [0%;21.5%]
Urinary incontinence	1 (4.0%)	0 (0%)
	95%CI [0.7%;19.5%]	95%CI [0%;21.5%]
Valvular heart disease	1 (4.0%)	0 (0%)

	95%CI [0.7%;19.5%]	95%CI [0%;21.5%]
Atrial fibrillation	0 (0%)	1 (7.1%)
	95%CI [0%;13.3%]	95%CI [1.3%;31.5%]
Bilateral pseudophosphona	0 (0%)	1 (7.1%)
	95%CI [0%;13.3%]	95%CI [1.3%;31.5%]
Gastric pathology	0 (0%)	1 (7.1%)
	95%CI [0%;13.3%]	95%CI [1.3%;31.5%]
Gonarthrosis	0 (0%)	1 (7.1%)
	95%CI [0%;13.3%]	95%CI [1.3%;31.5%]
Intestinal diverticular disease	0 (0%)	1 (7.1%)
	95%CI [0%;13.3%]	95%CI [1.3%;31.5%]
Osteoporosis obesity	0 (0%)	1 (7.1%)
	95%CI [0%;13.3%]	95%CI [1.3%;31.5%]
Osteoarthrosis	0 (0%)	1 (7.1%)
	95%CI [0%;13.3%]	95%CI [1.3%;31.5%]
Schizophrenia	0 (0%)	1 (7.1%)
	95%CI [0%;13.3%]	95%CI [1.3%;31.5%]
Sleep disturbance	0 (0%)	1 (7.1%)
	95%CI [0%;13.3%]	95%CI [1.3%;31.5%]
Thalassemia minor	0 (0%)	1 (7.1%)
	95%CI [0%;13.3%]	95%CI [1.3%;31.5%]

Abbreviations: CI: confidence interval; Std. dev: standard deviation; Med: median; P25: percentile 25; P75: percentile 75; DM: diabetes mellitus; TIA: transient ischemic attack; COPD: chronic obstructive pulmonary disease.

Age-related Macular Degeneration (AMD) diagnosis

	Naïve patients (n=46)	Switch patients (n=35)
AMD		
Unilateral	18 (39.1%) 95%CI [26.4%;53.5%]	23 (65.7%) 95%CI [49.2%;79.2%]
Bilateral	28 (60.9%) 95%CI [46.5%;73.6%]	12 (34.3%) 95%CI [20.8%;50.8%]
Age at diagnosis (in years)		
Valid n (Missing)	41 (5)	30 (5)
Mean [95%CI]	78.59 [76.48;80.70]	77.73 [75.08;80.39]
Std. dev	7.29	8.01
Med [P25,P75]	80.05 [74.14;84.16]	79.34 [69.89;84.62]
Min / Max	61.77 / 90.75	64.53 / 89.94
Age at diagnosis (in years) classes		
<80 years	20 (48.8%) 95%CI [34.3%;63.5%]	16 (53.3%) 95%CI [36.1%;69.8%]
≥80 years	21 (51.2%) 95%CI [36.5%;65.7%]	14 (46.7%) 95%CI [30.2%;63.9%]
Missing	5	5
Time between diagnosis and first treatment (in months)		
Valid n (Missing)	41 (5)	30 (5)
Mean [95%CI]	4.68 [0.79;8.57]	17.70 [11.69;23.71]
Std. dev	13.45	18.13
Med [P25,P75]	0 [0;1.00]	10.50 [8.00;22.75]
Min / Max	0 / 61.00	3.00 / 96.00

Time between diagnosis and start of treatment with brolucizumab (in months)		
Valid n (Missing)	41 (5)	30 (5)
Mean [95%CI]	4.76 [0.88;8.63]	17.93 [12.01;23.84]
Std. dev	13.42	17.86
Med [P25,P75]	0.43 [0.20;1.38]	10.76 [8.33;22.85]
Min / Max	-4.44 [1] / 60.85	3.42 / 95.15
Mean lesion area (mm^2)		
Valid n (Missing)	0 (46)	2 (33)
Mean [95%CI]	NA [NA;NA]	15.00 [9.85;20.15]
Std. dev	NA	15.56
Med [P25,P75]	NA [NA;NA]	15.00 [9.50;20.50]
Min / Max	NA / NA	4.00 / 26.00
CNV Classification (based on angiographic criteria)		
Occult	0 (0.0%) 95%CI [0.0%;7.9%]	0 (0.0%) 95%CI [0.0%;9.9%]
Minimally classic	0 (0.0%) 95%CI [0.0%;7.9%]	0 (0.0%) 95%CI [0.0%;9.9%]
Predominantly classic	0 (0.0%) 95%CI [0.0%;7.9%]	0 (0.0%) 95%CI [0.0%;9.9%]
Other/Not applicable	45 (100.0%) 95%CI [92.0%;100.0%]	35 (100.0%) 95%CI [90.0%;100.0%]
Missing	1	0
CNV Classification (OCT)		
Type I	14 (31.1%)	13 (37.1%)

	95%CI [20.0%;45.7%]	95%CI [23.0%;53.7%]
Type II	10 (22.2%)	6 (17.1%)
	95%CI [13.0%;36.3%]	95%CI [8.1%;32.7%]
Type III	1 (2.2%)	4 (11.4%)
	95%CI [0.4%;11.6%]	95%CI [4.5%;26.0%]
PCV	1 (2.2%)	1 (2.9%)
	95%CI [0.4%;11.6%]	95%CI [0.5%;14.5%]
RAP	0 (0%)	0 (0%)
	95%CI [0.0%;7.9%]	95%CI [0.0%;9.9%]
Other/Not applicable	19 (42.2%)	11 (31.4%)
	95%CI [29.0%;56.7%]	95%CI [19.0%;48.0%]
Missing	1	0

Abbreviations: CI: confidence interval; Std. dev: standard deviation; Med: median; P25: percentile 25; P75: percentile 75; PCV: polypoidal choroidal vasculopathy; RAP: retinal angiomatous proliferation

[1] One patient had a diagnosis date posterior to the date of treatment initiation.

Characterization of nAMD treatment switchers patients that have initiated treatment with brolucizumab according to treatment history

Previous anti-VEGF	**n=35**
Aflibercept	13 (37.1%) 95%CI [23.0%;53.7%]
Ranibizumab	12 (34.3%) 95%CI [21.0%;50.8%]
Ranibizumab + Aflibercept	5 (14.3%) 95%CI [6.3%;29.4%]
Aflibercept + Bevacizumab	3 (8.6%) 95%CI [3.0%;22.4%]
Bevacizumab	2 (5.7%) 95%CI [1.6%;18.6%]
Ranibizumab + Bevacizumab	0 (0%) 95%CI [0.0%;9.9%]
Ranibizumab + Aflibercept + Bevacizumab	0 (0%) 95%CI [0.0%;9.9%]
Total # of previous injections	
By last anti-VEGF	
Ranibizumab	
Valid n (Missing)	9 (2)
Mean [95%CI]	6.22 [5.17;7.28]
Std. dev	1.79
Med [P25,P75]	7.00 [5.00;7.00]
Min / Max	3.00 / 8.00

Aflibercept	
Valid n (Missing)	15 (4)
Mean [95%CI]	8.47 [6.49;10.44]
Std. dev	4.39
Med [P25,P75]	8.00 [5.00;10.00]
Min / Max	3.00 / 17.00
Bevacizumab	
Valid n (Missing)	5 (0)
Mean [95%CI]	10.60 [7.65;13.55]
Std. dev	3.36
Med [P25,P75]	10.00 [8.00;13.00]
Min / Max	7.00 / 15.00
By BCVA at diagnosis (ETDRS)	
≤35	
Valid n (Missing)	4 (0)
Mean [95%CI]	12.25 [6.63;17.87]
Std. dev	5.74
Med [P25,P75]	14.00 [10.75;15.50]
Min / Max	4.00 / 17.00
36-69	
Valid n (Missing)	4 (0)
Mean [95%CI]	7.00 [4.60;9.40]
Std. dev	2.45
Med [P25,P75]	7.00 [6.25;7.75]

Min / Max	4.00 / 10.00
≥70	
Valid n (Missing)	7 (1)
Mean [95%CI]	8.29 [6.26;10.31]
Std. dev	2.93
Med [P25,P75]	7.00 [7.00;9.00]
Min / Max	5.00 / 14.00
Missing	19
Total # of previous injections over last 24 months	
By last anti-VEGF	
Ranibizumab	
Valid n (Missing)	9 (2)
Mean [95%CI]	5.22 [3.27;7.18]
Std. dev	3.31
Med [P25,P75]	7.00 [3.00;7.00]
Min / Max	0 / 8.00
Aflibercept	
Valid n (Missing)	15 (4)
Mean [95%CI]	5.73 [3.57;7.89]
Std. dev	4.80
Med [P25,P75]	4.00 [3.00;9.00]
Min / Max	0 / 15.00
Bevacizumab	
Valid n (Missing)	5 (0)

Mean [95%CI]	4.60 [2.00;7.20]
Std. dev	2.97
Med [P25,P75]	5.00 [4.00;6.00]
Min / Max	0 / 8.00
By BCVA at diagnosis (ETDRS)	
≤35	
Valid n (Missing)	4 (0)
Mean [95%CI]	3.25 [0.80;5.70]
Std. dev	2.50
Med [P25,P75]	3.50 [2.25;4.50]
Min / Max	0 / 6.00
36-69	
Valid n (Missing)	4 (0)
Mean [95%CI]	2.75 [-0.59;6.09]
Std. dev	3.40
Med [P25,P75]	2.00 [0;4.75]
Min / Max	0 / 7.00
≥70	
Valid n (Missing)	7 (1)
Mean [95%CI]	7.29 [4.30;10.27]
Std. dev	4.31
Med [P25,P75]	7.00 [6.00;9.00]
Min / Max	0 / 14.00
Missing	19

Total # of previous injections over last 12 months	
By last anti-VEGF	
Ranibizumab	
Valid n (Missing)	9 (2)
Mean [95%CI]	5.11 [3.21;7.01]
Std. dev	3.22
Med [P25,P75]	7.00 [3.00;7.00]
Min / Max	0 / 8.00
Aflibercept	
Valid n (Missing)	15 (4)
Mean [95%CI]	5.07 [3.72;6.41]
Std. dev	2.99
Med [P25,P75]	5.00 [3.00;7.00]
Min / Max	0 / 11.00
Bevacizumab	
Valid n (Missing)	4 (1)
Mean [95%CI]	4.25 [2.75;5.75]
Std. dev	1.71
Med [P25,P75]	4.50 [3.50;5.25]
Min / Max	2.00 / 6.00
By BCVA at diagnosis (ETDRS)	
≤35	
Valid n (Missing)	4 (0)
Mean [95%CI]	5.00 [2.47;7.53]

Std. dev	2.58
Med [P25,P75]	5.00 [3.50;6.50]
Min / Max	2.00 / 8.00
36-69	
Valid n (Missing)	4 (0)
Mean [95%CI]	3.50 [0.45;6.55]
Std. dev	3.11
Med [P25,P75]	3.50 [1.50;5.50]
Min / Max	0 / 7.00
≥70	
Valid n (Missing)	7 (1)
Mean [95%CI]	5.57 [2.95;8.19]
Std. dev	3.78
Med [P25,P75]	7.00 [3.00;7.50]
Min / Max	0 / 11.00
Missing	19
Total # of previous injections over last 6 months	
By last anti-VEGF	
Ranibizumab	
Valid n (Missing)	9 (2)
Mean [95%CI]	3.33 [2.40;4.27]
Std. dev	1.58
Med [P25,P75]	3.00 [2.00;4.00]
Min / Max	1.00 / 6.00

Aflibercept	
Valid n (Missing)	15 (4)
Mean [95%CI]	3.27 [2.48;4.05]
Std. dev	1.75
Med [P25,P75]	3.00 [2.00;4.50]
Min / Max	1.00 / 6.00
Bevacizumab	
Valid n (Missing)	5 (0)
Mean [95%CI]	1.80 [0.23;3.37]
Std. dev	1.79
Med [P25,P75]	2.00 [0;3.00]
Min / Max	0 / 4.00
Total # of previous injections over last 3 months	
By last anti-VEGF	
Ranibizumab	
Valid n (Missing)	9 (2)
Mean [95%CI]	2.33 [1.92;2.75]
Std. dev	0.71
Med [P25,P75]	2.00 [2.00;3.00]
Min / Max	1.00 / 3.00
Aflibercept	
Valid n (Missing)	15 (4)
Mean [95%CI]	1.53 [1.12;1.94]
Std. dev	0.92

Med [P25,P75]	1.00 [1.00;2.00]
Min / Max	0 / 3.00
Bevacizumab	
Valid n (Missing)	5 (0)
Mean [95%CI]	0.40 [-0.08;0.88]
Std. dev	0.55
Med [P25,P75]	0 [0;1.00]
Min / Max	0 / 1.00
By BCVA at diagnosis (ETDRS)	
≤35	
Valid n (Missing)	4 (0)
Mean [95%CI]	0.75 [0.26;1.24]
Std. dev	0.50
Med [P25,P75]	1.00 [0.75;1.00]
Min / Max	0 / 1.00
36-69	
Valid n (Missing)	4 (0)
Mean [95%CI]	1.75 [0.28;3.22]
Std. dev	1.50
Med [P25,P75]	2.00 [0.75;3.00]
Min / Max	0 / 3.00
≥70	
Valid n (Missing)	7 (1)
Mean [95%CI]	1.86 [1.12;2.60]

Std. dev	1.07
Med [P25,P75]	2.00 [1.50;2.50]
Min / Max	0 / 3.00
Missing	19
Last anti-VEGF	
Aflibercept	19 (54.3%) 95%CI [38.2%;69.5%]
Ranibizumab	11 (31.4%) 95%CI [18.6%;48.0%]
Bevacizumab	5 (14.3%) 95%CI [6.3%;29.4%]
Reason for switch	
Anatomical	22 (71.0%) 95%CI [53.4%;83.9%]
Functional	5 (16.1%) 95%CI [7.1%;32.6%]
Burden	4 (12.9%) 95%CI [5.1%;28.9%]
Missing	4
BCVA at diagnosis (ETDRS)	
≤35	4 (25.0%) 95%CI [10.2%;49.5%]
36-69	4 (25.0%) 95%CI [10.2%;49.5%]

≥70	8 (50.0%) 95%CI [28.0%;72.0%]
Missing	19
Time between 1st brolucizumab injection and last injection of other anti-VEGF (months)	
Valid n (Missing)	32 (3)
Mean [95%CI]	2.34 [1.72;2.96]
Std. dev	1.88
Med [P25,P75]	1.89 [1.38;2.41]
Min / Max	0.89 / 10.91

Abbreviations: CI: confidence interval; Std. dev: standard deviation; Med: median; P25: percentile 25; P75: percentile 75; BCVA: Best Corrected VA; ETDRS: Early Treatment Diabetic Retinopathy Study.

Baseline (first visit) data of naïve and switch patients

	Naïve patients (n=46)	**Switch patients (n=35)**
Year of baseline visit		
2021	10 (21.7%) 95%CI [12.01%;35.6%]	13 (37.1%) 95%CI [23.0%;53.7%]
2022	35 (76.1%) 95%CI [62.0%;86.1%]	22 (62.9%) 95%CI [46.0%;76.8%]
2023	1 (2.2%) 95%CI [0.4%;11.3%]	0 (0%) 95%CI [0.0%;9.9%]
Ocular condition		
Left Eye	7 (15.2%) 95%CI [7.6%;28.2%]	4 (11.4%) 95%CI [4.5%;26.0%]

Right Eye	13 (28.3%) 95%CI [17.3%;42.5%]	6 (17.1%) 95%CI [8.1%;32.7%]
Both Eyes	20 (43.5%) 95%CI [30.2%;57.8%]	13 (37.1%) 95%CI [23.2%;53.7%]
None	6 (13.0%) 95%CI [6.1%;25.7%]	12 (34.3%) 95%CI [20.8%;50.8%]
Left Eye		
Cataract	15 (32.6%) 95%CI [20.9%;47.0%]	11 (31.4%) 95%CI [18.6%;48.0%]
Refractive errors	3 (6.5%) 95%CI [2.2%;17.5%]	1 (2.9%) 95%CI [0.5%;14.5%]
Glaucoma	2 (4.3%) 95%CI [1.2%;14.5%]	1 (2.9%) 95%CI [0.5%;14.5%]
Vitreous detachment	1 (2.2%) 95%CI [0.38%;11.3%]	0 (0.0%) 95%CI [0.0%;9.9%]
Strabismus	0 (0.0%) 95%CI [0.0%;7.7%]	0 (0.0%) 95%CI [0.0%;9.9%]
Orbit pathology	0 (0.0%) 95%CI [0.0%;7.7%]	0 (0.0%) 95%CI [0.0%;9.9%]
Endophthalmitis	0 (0.0%) 95%CI [0.0%;7.7%]	0 (0.0%) 95%CI [0.0%;9.9%]
Uveitis	0 (0.0%) 95%CI [0.0%;7.7%]	0 (0.0%) 95%CI [0.0%;9.9%]
Dry eye	0 (0.0%) 95%CI [0.0%;7.7%]	0 (0.0%) 95%CI [0.0%;9.9%]
Inflammation of the anterior chamber	0 (0.0%)	0 (0.0%)

	95%CI [0.0%;7.7%]	95%CI [0.0%;9.9%]
Other eye inflammation	0 (0.0%) 95%CI [0.0%;7.7%]	0 (0.0%) 95%CI [0.0%;9.9%]
Retinal vascular occlusion	0 (0.0%) 95%CI [0.0%;7.7%]	0 (0.0%) 95%CI [0.0%;9.9%]
Retinal detachment	0 (0.0%) 95%CI [0.0%;7.7%]	0 (0.0%) 95%CI [0.0%;9.9%]
Other	13 (28.3%) 95%CI [17.3%;42.5%]	9 (25.7%) 95%CI [14.2%;42.1%]
Right Eye		
Cataract	15 (32.6%) 95%CI [20.9%;47.0%]	13 (37.1%) 95%CI [23.2%;53.7%]
Refractive errors	4 (8.7%) 95%CI [3.4%;20.3%]	1 (2.9%) 95%CI [0.5%;14.5%]
Glaucoma	3 (6.5%) 95%CI [2.2%;17.5%]	1 (2.9%) 95%CI [0.5%;14.5%]
Vitreous detachment	1 (2.2%) 95%CI [0.38%;11.3%]	0 (0.0%) 95%CI [0.0%;9.9%]
Strabismus	0 (0.0%) 95%CI [0.0%;7.7%]	0 (0.0%) 95%CI [0.0%;9.9%]
Orbit pathology	0 (0.0%) 95%CI [0.0%;7.7%]	0 (0.0%) 95%CI [0.0%;9.9%]
Endophthalmitis	0 (0.0%) 95%CI [0.0%;7.7%]	0 (0.0%) 95%CI [0.0%;9.9%]
Uveitis	0 (0.0%) 95%CI [0.0%;7.7%]	0 (0.0%) 95%CI [0.0%;9.9%]

Dry eye	0 (0.0%) 95%CI [0.0%;7.7%]	0 (0.0%) 95%CI [0.0%;9.9%]
Inflammation of the anterior chamber	0 (0.0%) 95%CI [0.0%;7.7%]	0 (0.0%) 95%CI [0.0%;9.9%]
Other eye inflammation	0 (0.0%) 95%CI [0.0%;7.7%]	0 (0.0%) 95%CI [0.0%;9.9%]
Retinal vascular occlusion	0 (0.0%) 95%CI [0.0%;7.7%]	0 (0.0%) 95%CI [0.0%;9.9%]
Retinal detachment	0 (0.0%) 95%CI [0.0%;7.7%]	0 (0.0%) 95%CI [0.0%;9.9%]
Other	18 (39.1%) 95%CI [26.4%;53.5%]	8 (22.9%) 95%CI [12.1%;39.0%]
IOI in previous 12 months before start of brolucizumab treatment[1]		
Yes	0 (0.0%) 95%CI [0%;12.9%]	0 (0.0%) 95%CI [0.0%;16.1%]
No	2 (7.7%) 95%CI [2.1%;24.1%]	5 (25.0%) 95%CI [11.0%;46.9%]
Unknown	24 (92.3%) 95%CI [76.0%;97.9%]	15 (75.0%) 95%CI [53.0%;88.8%]
Missing	20	15
Endophthalmitis in previous 12 months before start of brolucizumab treatment[1]		
Yes	0 (0.0%) 95%CI [0%;12.9%]	0 (0.0%) 95%CI [0.0%;16.1%]
No	3 (11.5%)	4 (20.0%)

	95%CI [4.0%;29.0%]	95%CI [8.1%;41.6%]
Unknown	23 (88.5%)	16 (80.0%)
	95%CI [71.0%;96.0%]	95%CI [58.0%;91.9%]
Missing	20	15
Intraocular Pressure (mmHg)		
Valid n (Missing)	38 (8)	28 (7)
Mean [95%CI]	14.21 [13.27;15.15]	14.25 [13.29;15.21]
Std. dev	3.25	2.89
Med [P25,P75]	14.00 [12.00;16.00]	14.50 [12.00;16.00]
Min / Max	9.00 / 25.00	9.00 / 19.00
FA		
	0 (0.0%)	2 (5.7%)
Yes	95%CI [0.0%;7.7%]	95%CI [1.6%;18.6%]
	46 (100.0%)	33 (94.3%)
No	95%CI [92.3%;100.0%]	95%CI [81.4%;98.4%]
Time from FA until 1st visit		
Valid n (Missing)	0 (46)	2 (33)
Mean [95%CI]	NA [NA;NA]	160.50 [131.22;189.78]
Std. dev	NA	88.39
Med [P25,P75]	NA [NA;NA]	160.50 [129.25;191.75]
Min / Max	NA / NA	98.00 / 223.00
Activity in FA?		
	0 (NA%)	1 (50.0%)
Yes	95%CI [NA%;NA%]	95%CI [9.5%;90.5%]
	0 (NA%)	1 (50.0%)
No	95%CI [NA%;NA%]	95%CI [9.5%;90.5%]

Missing	46	33
OCT		
Yes	44 (95.7%) 95%CI [85.0%;98.8%]	35 (100.0%) 95%CI [90.0%;100.0%]
No	2 (4.3%) 95%CI [1.2%;14.5%]	0 (0.0%) 95%CI [0.0%;9.9%]
VA Scale		
ETDRS	15 (34.1%) 95%CI [22.0%;48.9%]	17 (48.6%) 95%CI [33.0%;64.4%]
Snellen	0 (0.0%) 95%CI [0%;8.0%]	0 (0.0%) 95%CI [0.0%;9.9%]
LogMAR	1 (2.3%) 95%CI [0.4%;11.8%]	0 (0.0%) 95%CI [0.0%;9.9%]
Decimal	25 (56.8%) 95%CI [42.0%;70.3%]	16 (45.7%) 95%CI [30.0%;61.8%]
Not determined	3 (6.8%) 95%CI [2.3%;18.2%]	2 (5.7%) 95%CI [1.6%;18.6%]
Missing	2	0
VA (ETDRS) [1]		
≤35	8 (20.0%) 95%CI [10.5%;34.8%]	3 (9.1%) 95%CI [3.1%;23.6%]
36-69	27 (67.5%) 95%CI [52.0%;79.9%]	15 (45.5%) 95%CI [29.8%;62.0%]
≥70	5 (12.5%) 95%CI [5.5%;26.1%]	15 (45.5%) 95%CI [29.8%;62.0%]
NA	6	2

CST (µm)		
Valid n (Missing)	44 (2)	31 (4)
Mean [95%CI]	420.00 [374.60;465.40]	315.71 [268.61;362.81]
Std. dev	157.12	142.18
Med [P25,P75]	385.50 [302.50;518.75]	283.00 [242.50;366.50]
Min / Max	94.00 / 791.00	140.00 / 892.00
SRF		
Present	30 (68.2%) 95%CI [53.4%;80.0%]	22 (62.9%) 95%CI [46.3%;76.8%]
Absent	14 (31.8%) 95%CI [20.0%;46.6%]	13 (37.1%) 95%CI [23.2%;53.7%]
Missing	2	0
IRF		
Present	26 (59.1%) 95%CI [44.4%;72.3%]	16 (45.7%) 95%CI [30.5%;61.8%]
Absent	18 (40.9%) 95%CI [27.7%;55.6%]	19 (54.3%) 95%CI [38.2%;69.5%]
Missing	2	0
SRF and/or IRF		
Present	40 (90.9%) 95%CI [78.8%;96.4%]	27 (77.1%) 95%CI [61.0%;87.9%]
Absent	4 (9.1%) 95%CI [3.6%;21.2%]	8 (22.9%) 95%CI [12.1%;39.0%]
Missing	2	0
Sub-RPE fluid		
Present	27 (61.4%)	23 (65.7%)

	95%CI [46.6%;74.3%]	95%CI [49.2%;79.2%]
Absent	17 (38.6%)	12 (34.3%)
	95%CI [25.7%;53.4%]	95%CI [20.8%;50.8%]
Missing	2	0
Geographic atrophy		
Yes	11 (23.9%)	1 (2.9%)
	95%CI [13.9%;37.9%]	95%CI [0.5%;14.5%]
No	32 (69.6%)	32 (91.4%)
	95%CI [55.2%;80.9%]	95%CI [77.6%;97.0%]
Unknown/inconclusive	3 (6.5%)	2 (5.7%)
	95%CI [2.2%;17.5%]	95%CI [1.6%;18.6%]
Subretinal fibrosis		
Yes	6 (13.0%)	6 (17.1%)
	95%CI [6.1%;25.7%]	95%CI [8.1%;32.7%]
No	36 (78.3%)	26 (74.3%)
	95%CI [64.4%;87.7%]	95%CI [57.9%;85.8%]
Unknown/inconclusive	4 (8.7%)	3 (8.6%)
	95%CI [3.4%;20.3%]	95%CI [3.0%;22.4%]

Abbreviations: CI: confidence interval; Std. dev: standard deviation; Med: median; P25: percentile 25; P75: percentile 75; IOI: intraocular inflammation; FA: fluorescein angiography; OCT: optical coherence tomography; CST: central subfield thickness; ETDRS: Early Treatment Diabetic Retinopathy Study.
[1]ETDRS letters were estimated in cases were Decimal or LogMar scales were provided.

2. Anatomical parameters during treatment with brolucizumab

SRF at baseline, month 3, 6, 12, 18 and 24

	Naïve Patients	Switch patients
SRF baseline	**n = 46**	**n = 35**
Present	30 (68.2%) 95%CI [53.4%;80.0%]	22 (62.9%) 95%CI [46.3%;76.8%]
Absent	14 (31.8%) 95%CI [20.0%;46.6%]	13 (37.1%) 95%CI [23.2%;53.7%]
Missing	2	0
SRF at M3	**n = 36**	**n = 28**
Increased	2 (8.3%) 95%CI [2.3%;25.8%]	1 (4.3%) 95%CI [0.8%;21.0%]
Decreased	2 (8.3%) 95%CI [2.3%;25.8%]	0 (0%) 95%CI [0%;14.3%]
Maintained	6 (25.0%) 95%CI [12.0%;44.9%]	7 (30.4%) 95%CI [15.6%;50.9%]
Absent	14 (58.3%) 95%CI [38.8%;75.5%]	15 (65.2%) 95%CI [44.9%;81.2%]
Missing	12	5
SRF at M6	**n = 25**	**n = 23**
Increased	3 (15.0%) 95%CI [5.2%;36.0%]	6 (28.6%) 95%CI [14.0%;50.0%]
Decreased	0 (0%)	0 (0%)

	95%CI [0.0%;16.1%]	95%CI [0%;15.5%]
Maintained	4 (20.0%) 95%CI [8.1%;41.6%]	5 (23.8%) 95%CI [11.0%;45.1%]
Absent	13 (65.0%) 95%CI [43.0%;81.9%]	10 (47.6%) 95%CI [28.0%;67.6%]
Missing	5	2
SRF at M9	**n = 21**	**n = 20**
Increased	0 (0%) 95%CI [0%;17.6%]	2 (11.1%) 95%CI [3.1%;32.8%]
Decreased	1 (5.6%) 95%CI [1.0%;25.8%]	1 (5.6%) 95%CI [1.0%;25.8%]
Maintained	8 (44.4%) 95%CI [24.6%;66.3%]	4 (22.2%) 95%CI [9.0%;45.2%]
Absent	9 (50.0%) 95%CI [29.0%;71.0%]	11 (61.1%) 95%CI [38.6%;79.7%]
Missing	3	2
SRF at M12	**n = 29**	**n = 22**
Increased	0 (0%) 95%CI [0%;13.8%]	4 (20.0%) 95%CI [8.1%;41.6%]
Decreased	2 (8.3%) 95%CI [2.3%;25.8%]	1 (5.0%) 95%CI [0.9%;23.6%]
Maintained	10 (41.7%) 95%CI [24.5%;61.2%]	7 (35.0%) 95%CI [18.1%;56.7%]
Absent	12 (50.0%)	8 (40.0%)

	95%CI [31.4%;68.6%]	95%CI [21.9%;61.3%]
Absence of SRF and IRF	9 (37.5%) 95%CI [21.2%;57.3%]	5 (25.0%) 95%CI [11.2%;46.9%]
Missing	5	2
SRF at M18	**n = 16**	**n = 19**
Increased	1 (8.3%) 95%CI [1.5%;35.4%]	1 (5.9%) 95%CI [1.0%;27.0%]
Decreased	0 (0%) 95%CI [0%;24.2%]	0 (0%) 95%CI [0.0%;18.4%]
Maintained	7 (58.3%) 95%CI [32.0%;80.7%]	8 (47.1%) 95%CI 26.0%;69.0%]
Absent	4 (33.3%) 95%CI [14.0%;60.9%]	8 (47.1%) 95%CI [26.0%;69.0%]
Missing	4	2
SRF at M24	**n = 6**	**n = 3**
Increased	2 (40.0%) 95%CI [12.0%;76.9%]	0 (0%) 95%CI [0%;56.1%]
Decreased	0 (0%) 95%CI [3.1e-15%;43.4%]	0 (0%) 95%CI [0%;56.1%]
Maintained	2 (40.0%) 95%CI [12.0%;76.9%]	2 (66.7%) 95%CI [21.0%;93.9%]
Absent	1 (20.0%) 95%CI [3.6%;62.4%]	1 (33.3%) 95%CI [6.1%;79.2%]
Missing	1	0

Abbreviations: CI: confidence interval.

Time to absence of SRF during the first two years of brolucizumab treatment

	N at start	Nr. events	Mean	SE	Median time of survival	95%CI LL	95%CI UL
Naïve	29	22	255.214	62.671	84	42	133
Switch	22	19	143.215	42.014	84	39	122

Abbreviations: SE: standard error; LL: lower limit; UL: upper limit

SRF, in patients with presence of SRF at baseline at months 3, 6, 9, 12, 18 and 24

	Naïve Patients	Switch patients
SRF at M3	**n = 21**	**n = 19**
Increased	2 (11.1%) 95%CI [3.1%;32.8%]	1 (6.2%) 95%CI [1.1%;28.3%]
Decreased	2 (11.1%) 95%CI [3.1%;32.8%]	0 (0%) 95%CI [0%;19.4%]
Maintained	4 (22.2%) 95%CI [9.0%;45.2%]	6 (37.5%) 95%CI [18.5%;61.4%]
Absent	10 (55.6%) 95%CI [33.7%;75.4%]	9 (56.2%) 95%CI [33.2%;76.9%]
Missing	3	3
SRF at M6	**n = 17**	**n = 16**
Increased	3 (20.0%) 95%CI [7.0%;45.2%]	4 (26.7%) 95%CI [11.0%;52.0%]
Decreased	0 (0%)	0 (0%)

	95%CI [0%;20.4%]	95%CI [0%;20.4%]
Maintained	3 (20.0%)	5 (33.3%)
	95%CI [7.0%;45.2%]	95%CI [15.0%;58.3%]
Absent	9 (60.0%)	6 (40.0%)
	95%CI [36.0%;80.2%]	95%CI [20.0%;64.3%]
Missing	2	1
SRF at M9	**n = 14**	**n = 14**
Increased	0 (0%)	1 (7.7%)
	95%CI [0%;24.2%]	95%CI [1.4%;33.3%]
Decreased	1 (8.3%)	1 (7.7%)
	95%CI [1.5%;35.4%]	95%CI [1.4%;33.3%]
Maintained	6 (50.0%)	3 (23.1%)
	95%CI [25.0%;74.6%]	95%CI [8.2%;50.3%]
Absent	5 (41.7%)	8 (61.5%)
	95%CI [19.0%;68.0%]	95%CI [36.0%;82.3%]
Missing	2	1
SRF at M12	**n = 21**	**n = 14**
Increased	0 (0%)	2 (15.4%)
	95%CI [0%;17.6%]	95%CI [4.3%;42.2%]
Decreased	2 (11.1%)	0 (0%)
	95%CI [3.1%;32.8%]	95%CI [0%;22.8%]
Maintained	7 (38.9%)	5 (38.5%)
	95%CI [20.3%;61.4%]	95%CI [17.7%;64.5%]

Absent	9 (50.0%) 95%CI [29.0%;71.0%]	6 (46.2%) 95%CI [23.2%;70.9%]
Missing	3	1
SRF at M18	**n = 13**	**n = 11**
Increased	1 (9.1%) 95%CI [1.6%;37.7%]	1 (10.0%) 95%CI [1.8%;40.4%]
Decreased	0 (0%) 95%CI [0%;25.9%]	0 (0%) 95%CI [0.0%;27.8%]
Maintained	6 (54.5%) 95%CI [28.0%;78.7%]	5 (50.0%) 95%CI [24.0%;76.3%]
Absent	4 (36.4%) 95%CI [15.0%;64.6%]	4 (40.0%) 95%CI [17.0%;68.7%]
Missing	2	1
SRF at M24	**n = 4**	**n = 3**
Increased	2 (50.0%) 95%CI [15.0%;85.0%]	0 (0%) 95%CI [0%;56.1%]
Decreased	0 (0%) 95%CI [0%;49.0%]	0 (0%) 95%CI [0%;56.1%]
Maintained	1 (25.0%) 95%CI [4.6%;69.9%]	2 (66.7%) 95%CI [20.8%;93.9%]
Absent	1 (25.0%) 95%CI [4.6%;69.9%]	1 (33.3%) 95%CI [6.1%;79.2%]

Abbreviations: CI: confidence interval.

Stable SRF in patients with absence of SRF at baseline, at months 3, 6, 9, 12, 18 and 24

		Naïve Patients	Switch patients
SRF at M3		**n = 11**	n = 9
	Stable	2 (33.3%) 95%CI [9.7%;70.0%]	1 (14.3%) 95%CI [2.6%;51.3%]
	Missing	5	2
SRF at M6		**n = 7**	**n = 7**
	Stable	1 (20.0%) 95%CI [3.6%;62.4%]	0 (0%) 95%CI [0%;39.0%
	Missing	2	1
SRF at M9		**n = 7**	**n = 6**
	Stable	2 (33.3%) 95%CI [9.7%;70.0%]	1 (20.0%) 95%CI [3.6%;62.4%]
	Missing	1	1
SRF at M12		**n = 8**	**n = 8**
	Stable	3 (50.0%) 95%CI [18.8%;81.2%]	2 (28.6%) 95%CI [8.2%;64.1%]
	Missing	2	1
SRF at M18		**n = 3**	**n = 8**
	Stable	1 (100.0%) 95%CI [2.1e+01%;100.0%]	1 (100.0%) 95%CI [2.1e+01%;100.0%]
	Missing	2	1
SRF at M24		**n = 2**	**n = 0**

Stable	1 (100.0%) 95%CI [20.7%;100.0%]	0 (NA%) 95%CI [NA%;NA%]
Missing	1	0

Abbreviations: CI: confidence interval.

Time to absence of IRF during the first two years of brolucizumab treatment

	N at start	Nr. events	Mean	SE	Median time of survival	95%CI LL	95%CI UL
Naïve	25	19	225.1120	49.39381	94	44	NA
Switch	16	13	192.0972	57.88531	84	39	309

Abbreviations: SE: standard error; LL: lower limit; UL: upper limit

IRF at baseline, month 3, 6, 9, 12, 18 and 24

	Naïve Patients	Switch patients
IRF at baseline	**n = 46**	**n = 35**
Present	26 (59.1%) 95%CI [44.4%;72.3%]	16 (45.7%) 95%CI [30.5%;61.8%]
Absent	18 (40.9%) 95%CI [27.7%;55.6%]	19 (54.3%) 95%CI [38.2%;69.5%]
Missing	2	0
IRF at M3	**n = 36**	**n = 28**
Increased	3 (12.5%) 95%CI [4.3%;31.0%]	0 (0%) 95%CI [0%;14.3%]

Decreased	2 (8.3%) 95%CI [2.3%;25.8%]	1 (4.3%) 95%CI [0.8%;21.0%]
Maintained	5 (20.8%) 95%CI [9.2%;40.5%]	8 (34.8%) 95%CI [18.8%;55.1%]
Absent	14 (58.3%) 95%CI [38.8%;75.5%]	14 (60.9%) 95%CI [40.8%;77.8%]
Missing	12	5
IRF at M6	**n = 25**	**n = 23**
Increased	2 (9.5%) 95%CI [2.7%;28.9%]	3 (14.3%) 95%CI [5.0%;34.6%]
Decreased	2 (9.5%) 95%CI [2.7%;28.9%]	0 (0%) 95%CI [0%;15.5%]
Maintained	4 (19.0%) 95%CI [7.7%;40.0%]	6 (28.6%) 95%CI [13.8%;50.0%]
Absent	13 (61.9%) 95%CI [40.9%;79.2%]	12 (57.1%) 95%CI [36.5%;75.5%]
Missing	4	2
IRF at M9	**n = 21**	**n = 20**
Increased	0 (0%) 95%CI [0%;17.6%]	0 (0%) 95%CI [0%;17.6%]
Decreased	0 (0%) 95%CI [0%;17.6%]	1 (5.6%) 95%CI [1.0%;25.8%]
Maintained	5 (27.8%)	3 (16.7%)

	95%CI [12.5%;50.9%]	95%CI [5.8%;39.2%]
Absent	13 (72.2%)	14 (77.8%)
	95%CI [49.1%;87.5%]	95%CI [54.8%;91.0%]
Missing	3	2
IRF at M12	**n = 29**	**n = 22**
Increased	3 (12.5%)	4 (20.0%)
	95%CI [4.3e+00%;31.0%]	95%CI [8.1e+00%;41.6%]
Decreased	1 (4.2%)	0 (0%)
	95%CI [7.4e-01%;20.2%]	95%CI [1.2e-15%;16.1%]
Maintained	9 (37.5%)	7 (35.0%)
	95%CI [2.1e+01%;57.3%]	95%CI [1.8e+01%;56.7%]
Absent	11 (45.8%)	9 (45.0%)
	95%CI [2.8e+01%;64.9%]	95%CI [2.6e+01%;65.8%]
Missing	5	2
IRF at M18	**n = 16**	**n = 19**
Increased	0 (0%)	1 (5.9%)
	95%CI [0%;24.2%]	95%CI [1.0e+00%;27.0%]
Decreased	1 (8.3%)	0 (0%)
	95%CI [1.5e+00%;35.4%]	95%CI [1.1e-15%;18.4%]
Maintained	5 (41.7%)	7 (41.2%)
	95%CI [1.9e+01%;68.0%]	95%CI [2.2e+01%;64.0%]
Absent	6 (50.0%)	9 (52.9%)
	95%CI [2.5e+01%;74.6%]	95%CI [3.1e+01%;73.8%]

Missing	4	2
IRF at M24	**n = 6**	**n = 3**
Increased	1 (20.0%) 95%CI [3.6e+00%;62.4%]	0 (0%) 95%CI [0%;56.1%]
Decreased	0 (0%) 95%CI [3.1e-15%;43.4%]	1 (33.3%) 95%CI [6.1e+00%;79.2%]
Maintained	2 (40.0%) 95%CI [1.2e+01%;76.9%]	2 (66.7%) 95%CI [2.1e+01%;93.9%]
Absent	2 (40.0%) 95%CI [1.2e+01%;76.9%]	0 (0%) 95%CI [0%;56.1%]
Missing	1	0

Abbreviations: CI: confidence interval.

IRF in patients with presence of IRF at baseline, at months 3, 6, 9, 12, 18 and 24

	Naïve Patients	**Switch patients**
IRF at M3	**n = 19**	**n = 14**
Increased	3 (23.1%) 95%CI [8.2%;50.3%]	0 (0%) 95%CI [0%;24.2%]
Decreased	2 (15.4%) 95%CI [4.3%;42.2%]	1 (8.3%) 95%CI [1.5%;35.4%]
Maintained	3 (23.1%) 95%CI [8.2%;50.3%]	4 (33.3%) 95%CI [13.8%;60.9%]

Absent	5 (38.5%) 95%CI [17.7%;64.5%]	7 (58.3%) 95%CI [32.0%;80.7%]
Missing	6	2
IRF at M6	**n = 13**	**n = 11**
Increased	2 (20.0%) 95%CI [5.7%;51.0%]	3 (30.0%) 95%CI [11.0%;60.3%]
Decreased	1 (10.0%) 95%CI [1.8%;40.4%]	0 (0%) 95%CI [0.0%;27.8%]
Maintained	3 (30.0%) 95%CI [11.0%;60.3%]	4 (40.0%) 95%CI [17.0%;68.7%]
Absent	4 (40.0%) 95%CI [17.0%;68.7%]	3 (30.0%) 95%CI [11.0%;60.3%]
Missing	3	1
IRF at M9	**n = 10**	**n = 11**
Increased	0 (0%) 95%CI [0%;32.4%]	0 (0%) 95%CI [0.0%;27.8%]
Decreased	0 (0%) 95%CI [0%;32.4%]	1 (10.0%) 95%CI [1.8%;40.4%]
Maintained	4 (50.0%) 95%CI [22.0%;78.5%]	3 (30.0%) 95%CI [11.0%;60.3%]
Absent	4 (50.0%) 95%CI [22.0%;78.5%]	6 (60.0%) 95%CI [31.0%;83.2%]
Missing	2	1

IRF at M12	**n = 16**	**n = 12**
Increased	3 (23.1%) 95%CI [8.2%;50.3%]	3 (27.3%) 95%CI [9.7%;56.6%]
Decreased	1 (7.7%) 95%CI [1.4%;33.3%]	0 (0%) 95%CI [0%;25.9%]
Maintained	5 (38.5%) 95%CI [17.7%;64.5%]	4 (36.4%) 95%CI [15.2%;64.6%]
Absent	4 (30.8%) 95%CI [12.7%;57.6%]	4 (36.4%) 95%CI [15.2%;64.6%]
Missing	3	1
IRF at M18	**n = 8**	**n = 11**
Increased	0 (0%) 95%CI [0%;39.0%]	0 (0%) 95%CI [0%;29.9%]
Decreased	1 (16.7%) 95%CI [3.0%;56.4%]	0 (0%) 95%CI [0%;29.9%]
Maintained	4 (66.7%) 95%CI [30.0%;90.3%]	5 (55.6%) 95%CI [26.7%;81.1%]
Absent	1 (16.7%) 95%CI [3.0%;56.4%]	4 (44.4%) 95%CI [18.9%;73.3%]
Missing	2	2
IRF at M24	**n = 3**	**n = 2**
Increased	0 (0%) 95%CI [0%;56.1%]	0 (0%) 95%CI [0%;65.8%]

Decreased	0 (0%) 95%CI [0%;56.1%]	1 (50.0%) 95%CI [9.5%;90.5%]
Maintained	2 (66.7%) 95%CI [20.8%;93.9%]	1 (50.0%) 95%CI [9.5%;90.5%]
Absent	1 (33.3%) 95%CI [6.1%;79.2%]	0 (0%) 95%CI [0%;65.8%]

Abbreviations: CI: confidence interval.

Stable IRF in patients with absence of IRF at baseline, at months 3, 6, 9, 12, 18 and 24

	Naïve Patients	Switch patients
IRF at M3	**n = 13**	**n = 12**
Stable	2 (18.2%) 95%CI [5.1%;47.7%]	4 (36.4%) 95%CI [15.2%;64.6%]
Missing	2	3
IRF at M6	**n = 11**	**n = 12**
Stable	1 (10.0%) 95%CI [1.8e+00%;40.4%]	2 (18.2%) 95%CI [5.1e+00%;47.7%]
Missing	1	1
IRF at M9	**n = 11**	**n = 9**
Stable	1 (10.0%) 95%CI [1.8%;40.4%]	0 (0%) 95%CI [0%;32.4%]
Missing	1	1
IRF at M12	**n = 13**	**n = 10**

	Stable	4 (36.4%) 95%CI [15.2%;64.6%]	3 (33.3%) 95%CI [12.1%;64.6%]
	Missing	2	1
IRF at M18		**n = 8**	**n = 8**
	Stable	1 (16.7%) 95%CI [3.0%;56.4%]	2 (25.0%) 95%CI [7.1%;59.1%]
	Missing	2	0
IRF at M24		**n = 3**	**n = 1**
	Stable	0 (0%) 95%CI [0%;65.8%]	1 (100.0%) 95%CI [20.7%;100.0%]
	Missing	1	0

Abbreviations: CI: confidence interval.

Time to absence of subRPE during the first two years of brolucizumab treatment

	N at start	Nr. events	Mean	SE	Median time of survival	95%CI LL	95% CI UL
Naïve	25	17	327.4927	65.81619	120	91	NA
Switch	23	13	391.4783	69.91144	270	107	NA

Abbreviations: SE: standard error; LL: lower limit; UL: upper limit.

Sub-RPE at baseline, month 3, 6, 9, 12, 18 and 24

	Naïve Patients	Switch patients
Sub-RPE at Baseline		
Present	27 (61.4%) 95%CI [46.6%;74.3%]	23 (65.7%) 95%CI [49.2%;79.2%]
Absent	17 (38.6%) 95%CI [25.7%;53.4%]	12 (34.3%) 95%CI [20.8%;50.8%]
Missing	2	0
Sub-RPE at M3	**n = 36**	**n = 28**
Increased	2 (8.3%) 95%CI [2.3%;25.8%]	2 (8.7%) 95%CI [2.4%;26.8%]
Decreased	1 (4.2%) 95%CI [0.7%;20.2%]	1 (4.3%) 95%CI [0.8%;21.0%]
Maintained	8 (33.3%) 95%CI [18.0%;53.3%]	11 (47.8%) 95%CI [29.2%;67.0%]
Absent	13 (54.2%) 95%CI [35.1%;72.1%]	9 (39.1%) 95%CI [22.2%;59.2%]
Missing	12	5
Sub-RPE at M6	**n = 25**	**n = 23**
Increased	2 (10.0%) 95%CI [2.8%;30.1%]	1 (4.8%) 95%CI [0.8%;22.7%]
Decreased	1 (5.0%) 95%CI [0.9%;23.6%]	1 (4.8%) 95%CI [0.8%;22.7%]

Maintained	7 (35.0%) 95%CI [18.1%;56.7%]	11 (52.4%) 95%CI [32.4%;71.7%]
Absent	10 (50.0%) 95%CI [29.9%;70.1%]	8 (38.1%) 95%CI [20.8%;59.1%]
Missing	5	2
Sub-RPE at M9	**n = 21**	**n = 20**
Increased	0 (0%) 95%CI [0%;17.6%]	2 (11.1%) 95%CI [3.1%;32.8%]
Decreased	0 (0%) 95%CI [0%;17.6%]	1 (5.6%) 95%CI [1.0%;25.8%]
Maintained	7 (38.9%) 95%CI [20.3%;61.4%]	8 (44.4%) 95%CI [24.6%;66.3%]
Absent	11 (61.1%) 95%CI [38.6%;79.7%]	7 (38.9%) 95%CI [20.3%;61.4%]
Missing	3	2
Sub-RPE at M12	**n = 29**	**n = 22**
Increased	0 (0%) 95%CI [0%;13.8%]	1 (5.0%) 95%CI [0.9%;23.6%]
Decreased	2 (8.3%) 95%CI [2.3%;25.8%]	0 (0%) 95%CI [0.0%;16.1%]
Maintained	10 (41.7%) 95%CI [24.0%;61.2%]	14 (70.0%) 95%CI [48.0%;85.5%]
Absent	12 (50.0%)	5 (25.0%)

	95%CI [31.0%;68.6%]	95%CI [11.0%;46.9%]
Missing	5	2
Sub-RPE at M18	**n = 16**	**n = 19**
Increased	1 (8.3%) 95%CI [1.5%;35.4%]	2 (11.8%) 95%CI [3.3%;34.3%]
Decreased	0 (0%) 95%CI [0%;24.2%]	0 (0%) 95%CI [0.0%;18.4%]
Maintained	6 (50.0%) 95%CI [25.0%;74.6%]	10 (58.8%) 95%CI [36.0%;78.4%]
Absent	5 (41.7%) 95%CI [19.0%;68.0%]	5 (29.4%) 95%CI [13.0%;53.1%]
Missing	4	2
Sub-RPE at M24	**n = 6**	**n = 3**
Increased	0 (0%) 95%CI [0.0%;43.4%]	0 (0%) 95%CI [0%;56.1%]
Decreased	1 (20.0%) 95%CI [3.6%;62.4%]	0 (0%) 95%CI [0%;56.1%]
Maintained	1 (20.0%) 95%CI [3.6%;62.4%]	3 (100.0%) 95%CI [44.0%;100.0%]
Absent	3 (60.0%) 95%CI [23.0%;88.2%]	0 (0%) 95%CI [0%;56.1%]
Missing	1	0

Abbreviations: CI: confidence interval.

Sub-RPE in patients with presence of sub-RPE at baseline, at month 3, 6, 9, 12, 18 and 24

	Naïve Patients	Switch patients
Sub-RPE at M3	**n = 22**	**n = 19**
Increased	2 (11.8%) 95%CI [3.3%;34.3%]	2 (12.5%) 95%CI [3.5%;36.0%]
Decreased	1 (5.9%) 95%CI [1.0%;27.0%]	1 (6.2%) 95%CI [1.1%;28.3%]
Maintained	7 (41.2%) 95%CI [21.6%;64.0%]	11 (68.8%) 95%CI [44.4%;85.8%]
Absent	7 (41.2%) 95%CI [21.6%;64.0%]	2 (12.5%) 95%CI [3.5%;36.0%]
Missing	5	3
Sub-RPE at M6	**n = 19**	**n = 16**
Increased	2 (11.8%) 95%CI [3.3%;34.3%]	1 (6.7%) 95%CI [1.2%;29.8%]
Decreased	1 (5.9%) 95%CI [1.0%;27.0%]	1 (6.7%) 95%CI [1.2%;29.8%]
Maintained	7 (41.2%) 95%CI [21.6%;64.0%]	11 (73.3%) 95%CI [48.0%;89.1%]
Absent	7 (41.2%) 95%CI [21.6%;64.0%]	2 (13.3%) 95%CI [3.7%;37.9%]
Missing	2	1
Sub-RPE at M9	**n = 15**	**n = 14**

Increased	0 (0%) 95%CI [0%;22.8%]	1 (8.3%) 95%CI [1.5%;35.4%]
Decreased	0 (0%) 95%CI [0%;22.8%]	1 (8.3%) 95%CI [1.5%;35.4%]
Maintained	6 (46.2%) 95%CI [23.0%;70.9%]	8 (66.7%) 95%CI [39.0%;86.2%]
Absent	7 (53.8%) 95%CI [29.0%;76.8%]	2 (16.7%) 95%CI [4.7%;44.8%]
Missing	2	2
Sub-RPE at M12	**n = 23**	**n = 16**
Increased	0 (0%) 95%CI [0%;15.5%]	0 (0%) 95%CI [0%;20.4%]
Decreased	2 (9.5%) 95%CI [2.7%;28.9%]	0 (0%) 95%CI [0%;20.4%]
Maintained	9 (42.9%) 95%CI [24.0%;63.5%]	14 (93.3%) 95%CI [70.0%;98.8%]
Absent	10 (47.6%) 95%CI [28.0%;67.6%]	1 (6.7%) 95%CI [1.2%;29.8%]
Missing	2	1
Sub-RPE at M18	**n = 11**	**n = 16**
Increased	1 (10.0%) 95%CI [1.8%;40.4%]	2 (14.3%) 95%CI [4.0%;39.9%]
Decreased	0 (0%)	0 (0%)

	95%CI [0.0%;27.8%]	95%CI [0%;21.5%]
Maintained	6 (60.0%) 95%CI [31.0%;83.2%]	10 (71.4%) 95%CI [45.0%;88.3%]
Absent	3 (30.0%) 95%CI [11.0%;60.3%]	2 (14.3%) 95%CI [4.0%;39.9%]
Missing	1	2
Sub-RPE at M24	**n = 4**	**n = 3**
Increased	0 (0%) 95%CI [0%;56.1%]	0 (0%) 95%CI [0%;56.1%]
Decreased	1 (33.3%) 95%CI [6.1%;79.2%]	0 (0%) 95%CI [0%;56.1%]
Maintained	1 (33.3%) 95%CI [6.1%;79.2%]	3 (100.0%) 95%CI [43.9%;100.0%]
Absent	1 (33.3%) 95%CI [6.1%;79.2%]	0 (0%) 95%CI [0%;56.1%]
Missing	1	0

Abbreviations: CI: confidence interval.

Stable sub-RPE in patients with absence of sub-RPE at baseline, at month 3, 6, 9, 12, 18 and 24

	Naïve Patients	Switch patients
Sub-RPE at M3	**n = 10**	**n = 9**
Stable	1 (14.3%) 95%CI [2.6%;51.3%]	0 (0%) 95%CI [0%;35.4%]
Missing	3	2
Sub-RPE at M6	**n = 5**	**n = 7**
Stable	0 (0%) 95%CI [0%;56.1%]	0 (0%) 95%CI [0%;39.0%]
Missing	2	1
Sub-RPE at M9	**n = 6**	**n = 6**
Stable	1 (20.0%) 95%CI [3.6%;62.4%]	0 (0%) 95%CI [0%;39.0%]
Missing	1	0
Sub-RPE at M12	**n = 6**	**n = 6**
Stable	1 (33.3%) 95%CI [6.1%;79.2%]	0 (0%) 95%CI [0.0%;43.4%]
Missing	3	1
Sub-RPE at M18	**n = 5**	**n = 3**
Stable	0 (0%) 95%CI [0%;65.8%]	0 (0%) 95%CI [0%;56.1%]
Missing	3	0
Sub-RPE at M24	**n = 2**	**n = 0**

Stable	0 (0%) 95%CI [0%;65.8%]	0 (NA%) 95%CI [NA%;NA%]
Missing	0	0

Abbreviations: CI: confidence interval.

SRF+IRF+sub-RPE at baseline, months 3, 6, 9, 12, 18 and 24

	Naïve Patients	Switch patients
SRF+IRF+sub-RPE at Baseline		
Presence	10 (22.7%) 95%CI [12.8%;37.0%]	8 (22.9%) 95%CI [12.1%;39.0%]
Absence	34 (77.3%) 95%CI [63.0%;87.2%]	27 (77.1%) 95%CI [61.0%;87.9%]
Missing	2	0
SRF+IRF+sub-RPE at M3	**n = 36**	**n = 28**
Presence	5 (20.8%) 95%CI [9.2%;40.5%]	6 (26.1%) 95%CI [12.5%;46.5%]
Absence	19 (79.2%) 95%CI [59.5%;90.8%]	17 (73.9%) 95%CI [53.5%;87.5%]
Missing	12	5
SRF+IRF+sub-RPE at M6	**n = 25**	**n = 23**
Presence	3 (15.0%) 95%CI [5.2%;36.0%]	6 (28.6%) 95%CI [13.8%;50.0%]
Absence	17 (85.0%)	15 (71.4%)

	95%CI [64.0%;94.8%]	95%CI [50.0%;86.2%]
Missing	5	2
SRF+IRF+sub-RPE at M9	**n = 21**	**n = 20**
Presence	5 (27.8%) 95%CI [12.5%;50.9%]	2 (11.1%) 95%CI [3.1%;32.8%]
Absence	13 (72.2%) 95%CI [49.1%;87.5%]	16 (88.9%) 95%CI [67.2%;96.9%]
Missing	3	2
SRF+IRF+sub-RPE at M12	**n = 29**	**n = 22**
Presence	10 (41.7%) 95%CI [24.5%;61.2%]	7 (35.0%) 95%CI [18.1%;56.7%]
Absence	14 (58.3%) 95%CI [38.8%;75.5%]	13 (65.0%) 95%CI [43.3%;81.9%]
Missing	5	2
SRF+IRF+sub-RPE at M18	**n = 16**	**n = 19**
Presence	5 (41.7%) 95%CI [19.3%;68.0%]	5 (29.4%) 95%CI [13.3%;53.1%]
Absence	7 (58.3%) 95%CI [32.0%;80.7%]	12 (70.6%) 95%CI [46.9%;86.7%]
Missing	4	2
SRF+IRF+sub-RPE at M24	**n = 6**	**n = 3**
Presence	1 (20.0%) 95%CI [3.6%;62.4%]	2 (66.7%) 95%CI [20.8%;93.9%]

Absence	4 (80.0%) 95%CI [37.6%;96.4%]	1 (33.3%) 95%CI [6.1%;79.2%]
Missing	1	0

Abbreviations: CI: confidence interval.

SRF+IRF+sub-RPE from those with presence at baseline, at months 3, 6, 9, 12, 18 and 24

	Naïve Patients	Switch patients
SRF+IRF+sub-RPE at M3	**n = 32**	**n = 27**
Presence	5 (20.8%) 95%CI [9.2%;40.5%]	6 (27.3%) 95%CI [13.2%;48.2%]
Absence	19 (79.2%) 95%CI [59.5%;90.8%]	16 (72.7%) 95%CI [51.8%;86.8%]
Missing	8	5
SRF+IRF+sub-RPE at M6	**n = 24**	**n = 22**
Presence	3 (15.0%) 95%CI [5.2%;36.0%]	6 (30.0%) 95%CI [14.5%;51.9%]
Absence	17 (85.0%) 95%CI [64.0%;94.8%]	14 (70.0%) 95%CI [48.1%;85.5%]
Missing	4	2
SRF+IRF+sub-RPE at M9	**n = 21**	**n = 19**
Presence	5 (27.8%) 95%CI [12.5%;50.9%]	2 (11.8%) 95%CI [3.3%;34.3%]
Absence	13 (72.2%)	15 (88.2%)

	95%CI [49.1%;87.5%]	95%CI [65.7%;96.7%]
Missing	3	2
SRF+IRF+sub-RPE at M12	**n = 29**	**n = 22**
Presence	10 (41.7%) 95%CI [24.5%;61.2%]	7 (35.0%) 95%CI [18.1%;56.7%]
Absence	14 (58.3%) 95%CI [38.8%;75.5%]	13 (65.0%) 95%CI [43.3%;81.9%]
Missing	5	2
SRF+IRF+sub-RPE at M18	**n = 16**	**n = 19**
Presence	5 (41.7%) 95%CI [19.3%;68.0%]	5 (29.4%) 95%CI [13.3%;53.1%]
Absence	7 (58.3%) 95%CI [32.0%;80.7%]	12 (70.6%) 95%CI [46.9%;86.7%]
Missing	4	2
SRF+IRF+sub-RPE at M24	**n = 6**	**n = 3**
Presence	1 (20.0%) 95%CI [3.6%;62.4%]	2 (66.7%) 95%CI [20.8%;93.9%]
Absence	4 (80.0%) 95%CI [37.6%;96.4%]	1 (33.3%) 95%CI [6.1%;79.2%]
Missing	1	0

Abbreviations: CI: confidence interval.

SRF and/or IRF at baseline, month 3, 6, 9, 18 and 24

	Naïve Patients	Switch patients
SRF and/or IRF baseline	**n = 46**	**n = 35**
Presence	40 (90.9%) 95%CI [78.8%;96.4%]	27 (77.1%) 95%CI [61.0%;87.9%]
Absence	4 (9.1%) 95%CI [3.6%;21.2%]	8 (22.9%) 95%CI [12.1%;39.0%]
Missing	2	0
SRF and/or IRF at M3	**n = 36**	**n = 28**
Presence	13 (54.2%) 95%CI [35.1%;72.1%]	11 (47.8%) 95%CI [29.2%;67.0%]
Absence	11 (45.8%) 95%CI [27.9%;64.9%]	12 (52.2%) 95%CI [33.0%;70.8%]
Missing	12	5
SRF and/or IRF at M6	**n = 25**	**n = 23**
Presence	12 (57.1%) 95%CI [36.5%;75.5%]	13 (61.9%) 95%CI [40.9%;79.2%]
Absence	9 (42.9%) 95%CI [24.5%;63.5%]	8 (38.1%) 95%CI [20.8%;59.1%]
Missing	4	2
SRF and/or IRF at M9	**n = 21**	**n = 20**
Presence	9 (50.0%) 95%CI [29.0%;71.0%]	9 (50.0%) 95%CI [29.0%;71.0%]

Absence	9 (50.0%) 95%CI [29.0%;71.0%]	9 (50.0%) 95%CI [29.0%;71.0%]
Missing	3	2
SRF and/or IRF at M18	**n = 16**	**n = 19**
Presence	9 (75.0%) 95%CI [46.8%;91.1%]	11 (64.7%) 95%CI [41.3%;82.7%]
Absence	3 (25.0%) 95%CI [8.9%;53.2%]	6 (35.3%) 95%CI [17.3%;58.7%]
Missing	4	2
SRF and/or IRF at M24	**n = 6**	**n = 3**
Presence	4 (80.0%) 95%CI [37.6%;96.4%]	3 (100.0%) 95%CI [43.9%;100.0%]
Absence	1 (20.0%) 95%CI [3.6%;62.4%]	0 (0%) 95%CI [0%;56.1%]
Missing	1	0

Abbreviations: CI: confidence interval.

CST change from baseline vs month 3, 6, 9, 12, 18 and 24

	Naïve Patients			Switch patients		
		Test statistic	P-value[2]		Test statistic	P-value[2]
CST change from baseline (in µm) at M3	**n = 36**			**n = 28**		
Valid n (Missing)	17 (19)			14 (14)		
Mean [95%CI]	-144.29 [-191.49;-97.09]	W = 151	**<0.001**	-23.50 [-38.93;-8.07]	t = 2.111	0.258
Std. dev	144.49			41.66		
Med [P25,P75]	-92.00 [-167.00;-44.00]			-22.50 [-32.75;-10.00]		
Min / Max	-470.00 / 11.00			-112.00 / 70.00		
Reduced CST at M3 vs baseline	**n = 36**			**n = 28**		
Maintained/Increased	1 (5.9%) 95%CI [1.0%;27.0%]	NA	NA	2 (14.3%) 95%CI [4.0%;39.9%]	NA	NA
Reduced	16 (94.1%) 95%CI [73.0%;99.0%]			12 (85.7%) 95%CI [60.1%;96.0%]		
Missing	19			14		
CST change from baseline (in µm) at M6	**n = 25**			**n = 23**		
Valid n (Missing)	16 (9)			14 (9)		
Mean [95%CI]	-96.69 [-165.16;-28.22]	t = 2.14	**0.043**	-23.21 [-67.28;20.85]	W = 62.5	0.557
Std. dev	174.67			107.82		
Med [P25,P75]	-63.00 [-151.00;-15.00]			-6.50 [-30.75;9.75]		

Min / Max	-476.00 / 251.00			-358.00 / 97.00		
Reduced CST at M6 vs baseline	**n = 25**			**n = 23**		
Maintained/Increased	3 (18.8%) 95%CI [6.6%;43.0%]	NA	NA	5 (35.7%) 95%CI [16.3%;61.2%]	NA	NA
Reduced	13 (81.2%) 95%CI [57.0%;93.4%]			9 (64.3%) 95%CI [38.8%;83.7%]		
Missing	9			9		
CST change from baseline (in µm) at M9	**n = 21**			**n = 20**		
Valid n (Missing)	12 (9)			13 (7)		
Mean [95%CI]	-96.75 [-126.50;-67.00]	t = 4.818	**<0.001**	-22.23 [-42.12;-2.35]	t = 1.767	0.258
Std. dev	69.57			45.37		
Med [P25,P75]	-84.50 [-125.75;-44.25]			-30.00 [-56.00;-9.00]		
Min / Max	-255.00 / -15.00			-84.00 / 92.00		
Reduced CST at M9 vs baseline	**n = 21**			**n = 20**		
Maintained/Increased	0 (0%) 95%CI [0%;24.2%]	NA	NA	3 (23.1%) 95%CI [8.2%;50.3%]	NA	NA
Reduced	12 (100.0%) 95%CI [75.8%;100.0%]			10 (76.9%) 95%CI [49.7%;91.8%]		
Missing	9			7		

CST change from baseline (in µm) at M12	**n = 29**			**n = 22**		
Valid n (Missing)	14 (15)			13 (9)		
Mean [95%CI]	-132.29 [-181.53;-83.04]	W = 104	**<0.001**	-22.85 [-58.89;13.20]	W = 54.5	0.557
Std. dev	135.31			86.26		
Med [P25,P75]	-82.50 [-189.75;-41.50]			-5.00 [-32.00;22.00]		
Min / Max	-410.00 / 5.00			-262.00 / 99.00		
Reduced CST at M12 vs baseline	**n = 29**			**n = 22**		
Maintained/Increased	1 (7.1%) 95%CI [1.3%;31.5%]	NA	NA	5 (38.5%) 95%CI [17.7%;64.5%]	NA	NA
Reduced	13 (92.9%) 95%CI [68.5%;98.7%]			8 (61.5%) 95%CI [35.5%;82.3%]		
Missing	15			9		
CST change from baseline (in µm) at M18	**n = 16**			**n = 19**		
Valid n (Missing)	7 (9)			10 (9)		
Mean [95%CI]	-117.71 [-179.37;-56.06]	W = 18	**0.020**	-47.80 [-115.32;19.72]	W = 34	0.557
Std. dev	125.83			150.17		
Med [P25,P75]	-94.00 [-111.00;-60.00]			-6.50 [-64.50;19.25]		
Min / Max	-387.00 / -1.00			-436.00 / 90.00		
Reduced CST at M18 vs baseline	**n = 16**			**n = 19**		

Maintained/Increased	0 (0%) 95%CI [0%;35.4%]	NA	NA	4 (40.0%) 95%CI [16.8%;68.7%]	NA	NA
Reduced	7 (100.0%) 95%CI [64.6%;100.0%]			6 (60.0%) 95%CI [31.3%;83.2%]		
Missing	9			9		
CST change from baseline (in µm) at M24[1]	**n = 6**			**n = 3**		
Valid n (Missing)	4 (2)			1 (2)		
Mean [95%CI]	-176.25 [-329.26;-23.24]	NA	NA	-26.00 [NA;NA]	NA	NA
Std. dev	191.23			NA		
Med [P25,P75]	-170.00 [-308.50;-37.75]			-26.00 [-26.00;-26.00]		
Min / Max	-388.00 / 23.00			-26.00 / -26.00		
Reduced CST at M24 vs baseline[1]	**n = 6**			**n = 3**		
Maintained/Increased	1 (25.0%) 95%CI [4.6%;69.9%]	NA	NA	0 (0%) 95%CI [0%;79.3%]	NA	NA
Reduced	3 (75.0%) 95%CI [30.1%;95.4%]			1 (100.0%) 95%CI [20.7%;100.0%]		
Missing	2			2		

Abbreviations: CST: central subfield thickness; CI: confidence interval; Std. dev: standard deviation; Med: median; P25: percentile 25; P75: percentile 75.

[1]Both subgroups a small sample size (lower than 10 patients). Therefore, statistical tests were not performed.

[2]P-values were adjusted using the Benjamini-Hochberg correction for multiple comparisons

Clinician-graded SRF and/or macular atrophy at baseline, month 3, 6, 9, 12

	Naïve Patients	Switch patients
Clinician-graded subretinal fibrosis and/or macular atrophy (Baseline)	**n = 46**	**n = 35**
Yes	14 (30.4%) 95%CI [19.1%;44.8%]	7 (20.0%) 95%CI [10.0%;35.9%]
No	29 (63.0%) 95%CI [48.6%;75.5%]	25 (71.4%) 95%CI [54.9%;83.7%]
Unknown/inconclusive	3 (6.5%) 95%CI [2.2%;17.5%]	3 (8.6%) 95%CI [3.0%;22.4%]
Clinician-graded subretinal fibrosis (Baseline)	**n = 46**	**n = 35**
Yes	6 (13.0%) 95%CI [6.1%;25.7%]	6 (17.1%) 95%CI [8.1%;32.7%]
No	36 (78.3%) 95%CI [64.4%;87.7%]	26 (74.3%) 95%CI [57.9%;85.8%]
Unknown/inconclusive	4 (8.7%) 95%CI [3.4%;20.3%]	3 (8.6%) 95%CI [3.0%;22.4%]
Clinician-graded macular atrophy (Baseline)	**n = 46**	**n = 35**
Yes	11 (23.9%) 95%CI [13.9%;37.9%]	1 (2.9%) 95%CI [0.5%;14.5%]
No	32 (69.6%) 95%CI [55.2%;80.9%]	32 (91.4%) 95%CI [77.6%;97.0%]
Unknown/inconclusive	3 (6.5%) 95%CI [2.2%;17.5%]	2 (5.7%) 95%CI [1.6%;18.6%]

Clinician-graded subretinal fibrosis and/or macular atrophy (M3)	**n = 36**	**n = 28**
Yes	7 (20.6%) 95%CI [10.3%;36.8%]	5 (21.7%) 95%CI [9.7%;41.9%]
No	10 (29.4%) 95%CI [16.8%;46.2%]	11 (47.8%) 95%CI [29.2%;67.0%]
Unknown/inconclusive	17 (50.0%) 95%CI [34.1%;65.9%]	7 (30.4%) 95%CI [15.6%;50.9%]
Missing	2	5
Clinician-graded subretinal fibrosis (M3)	**n = 36**	**n = 28**
Yes	6 (17.6%) 95%CI [8.3%;33.5%]	3 (13.0%) 95%CI [4.5%;32.1%]
No	11 (32.4%) 95%CI [19.1%;49.2%]	13 (56.5%) 95%CI [36.8%;74.4%]
Unknown/inconclusive	17 (50.0%) 95%CI [34.1%;65.9%]	7 (30.4%) 95%CI [15.6%;50.9%]
Missing	2	5
Clinician-graded macular atrophy (M3)	**n = 36**	**n = 28**
Yes	2 (5.9%) 95%CI [1.6%;19.1%]	3 (13.0%) 95%CI [4.5%;32.1%]
No	16 (47.1%) 95%CI [31.5%;63.3%]	14 (60.9%) 95%CI [40.8%;77.8%]
Unknown/inconclusive	16 (47.1%) 95%CI [31.5%;63.3%]	6 (26.1%) 95%CI [12.5%;46.5%]

Missing	2	5
Clinician-graded subretinal fibrosis and/or macular atrophy (M6)	**n = 25**	**n = 23**
Yes	5 (20.8%) 95%CI [9.2%;40.5%]	4 (19.0%) 95%CI [7.7%;40.0%]
No	10 (41.7%) 95%CI [24.5%;61.2%]	13 (61.9%) 95%CI [40.9%;79.2%]
Unknown/inconclusive	9 (37.5%) 95%CI [21.2%;57.3%]	4 (19.0%) 95%CI [7.7%;40.0%]
Missing	1	2
Clinician-graded subretinal fibrosis (M6)	**n = 25**	**n = 23**
Yes	4 (16.7%) 95%CI [6.7%;35.9%]	3 (14.3%) 95%CI [5.0%;34.6%]
No	11 (45.8%) 95%CI [27.9%;64.9%]	14 (66.7%) 95%CI [45.4%;82.8%]
Unknown/inconclusive	9 (37.5%) 95%CI [21.2%;57.3%]	4 (19.0%) 95%CI [7.7%;40.0%]
Missing	1	2
Clinician-graded macular atrophy (M6)	**n = 25**	**n = 23**
Yes	2 (8.3%) 95%CI [2.3%;25.8%]	1 (4.8%) 95%CI [0.8%;22.7%]
No	13 (54.2%) 95%CI [35.1%;72.1%]	16 (76.2%) 95%CI [54.9%;89.4%]
Unknown/inconclusive	9 (37.5%)	4 (19.0%)

	95%CI [21.2%;57.3%]	95%CI [7.7%;40.0%]
Missing	1	2
Clinician-graded subretinal fibrosis and/or macular atrophy (M9)	**n = 21**	**n = 20**
Yes	4 (21.1%) 95%CI [8.5%;43.3%]	3 (16.7%) 95%CI [5.8%;39.2%]
No	8 (42.1%) 95%CI [23.1%;63.7%]	13 (72.2%) 95%CI [49.1%;87.5%]
Unknown/inconclusive	7 (36.8%) 95%CI [19.1%;59.0%]	2 (11.1%) 95%CI [3.1%;32.8%]
Missing	2	2
Clinician-graded subretinal fibrosis (M9)	**n = 21**	**n = 20**
Yes	2 (10.5%) 95%CI [2.9%;31.4%]	2 (11.1%) 95%CI [3.1%;32.8%]
No	8 (42.1%) 95%CI [23.1%;63.7%]	14 (77.8%) 95%CI [54.8%;91.0%]
Unknown/inconclusive	9 (47.4%) 95%CI [27.3%;68.3%]	2 (11.1%) 95%CI [3.1%;32.8%]
Missing	2	2
Clinician-graded macular atrophy (M9)	**n = 21**	**n = 20**
Yes	2 (10.5%) 95%CI [2.9%;31.4%]	1 (5.6%) 95%CI [1.0%;25.8%]
No	10 (52.6%) 95%CI [31.7%;72.7%]	15 (83.3%) 95%CI [60.8%;94.2%]

Unknown/inconclusive	7 (36.8%) 95%CI [19.1%;59.0%]	2 (11.1%) 95%CI [3.1%;32.8%]
Missing	2	2
Clinician-graded subretinal fibrosis and/or macular atrophy (M12)	**n = 29**	**n = 22**
Yes	6 (23.1%) 95%CI [11.0%;42.1%]	7 (35.0%) 95%CI [18.1%;56.7%]
No	9 (34.6%) 95%CI [19.4%;53.8%]	10 (50.0%) 95%CI [29.9%;70.1%]
Unknown/inconclusive	11 (42.3%) 95%CI [25.5%;61.1%]	3 (15.0%) 95%CI [5.2%;36.0%]
Missing	3	2
Clinician-graded subretinal fibrosis (M12)	**n = 29**	**n = 22**
Yes	4 (15.4%) 95%CI [6.2%;33.5%]	5 (25.0%) 95%CI [11.2%;46.9%]
No	10 (38.5%) 95%CI [22.4%;57.5%]	12 (60.0%) 95%CI [38.7%;78.1%]
Unknown/inconclusive	12 (46.2%) 95%CI [28.8%;64.5%]	3 (15.0%) 95%CI [5.2%;36.0%]
Missing	3	2
Clinician-graded macular atrophy (M12)	**n = 29**	**n = 22**
Yes	3 (11.5%) 95%CI [4.0%;29.0%]	3 (15.0%) 95%CI [5.2%;36.0%]
No	12 (46.2%)	14 (70.0%)

	95%CI [28.8%;64.5%]	95%CI [48.1%;85.5%]
Unknown/inconclusive	11 (42.3%) 95%CI [25.5%;61.1%]	3 (15.0%) 95%CI [5.2%;36.0%]
Missing	3	2
Clinician-graded subretinal fibrosis and/or macular atrophy (M18)	**n = 16**	**n = 19**
Yes	1 (6.2%) 95%CI [1.1%;28.3%]	5 (29.4%) 95%CI [13.3%;53.1%]
No	6 (37.5%) 95%CI [18.5%;61.4%]	7 (41.2%) 95%CI [21.6%;64.0%]
Unknown/inconclusive	9 (56.2%) 95%CI [33.2%;76.9%]	5 (29.4%) 95%CI [13.3%;53.1%]
Missing	0	2
Clinician-graded subretinal fibrosis (M18)	**n = 16**	**n = 19**
Yes	0 (0%) 95%CI [0%;19.4%]	4 (23.5%) 95%CI [9.6%;47.3%]
No	7 (43.8%) 95%CI [23.1%;66.8%]	8 (47.1%) 95%CI [26.2%;69.0%]
Unknown/inconclusive	9 (56.2%) 95%CI [33.2%;76.9%]	5 (29.4%) 95%CI [13.3%;53.1%]
Missing	0	2
Clinician-graded macular atrophy (M18)	**n = 16**	**n = 19**
Yes	1 (6.2%) 95%CI [1.1%;28.3%]	2 (11.8%) 95%CI [3.3%;34.3%]

No	6 (37.5%) 95%CI [18.5%;61.4%]	10 (58.8%) 95%CI [36.0%;78.4%]
Unknown/inconclusive	9 (56.2%) 95%CI [33.2%;76.9%]	5 (29.4%) 95%CI [13.3%;53.1%]
Missing	0	2
Clinician-graded subretinal fibrosis and/or macular atrophy (M24)	**n = 6**	**n = 3**
Yes	1 (16.7%) 95%CI [3.0%;56.4%]	1 (33.3%) 95%CI [6.1%;79.2%]
No	3 (50.0%) 95%CI [18.8%;81.2%]	0 (0%) 95%CI [0%;56.1%]
Unknown/inconclusive	2 (33.3%) 95%CI [9.7%;70.0%]	2 (66.7%) 95%CI [20.8%;93.9%]
Clinician-graded subretinal fibrosis (M24)	**n = 6**	**n = 3**
Yes	1 (16.7%) 95%CI [3.0%;56.4%]	1 (33.3%) 95%CI [6.1%;79.2%]
No	3 (50.0%) 95%CI [18.8%;81.2%]	0 (0%) 95%CI [0%;56.1%]
Unknown/inconclusive	2 (33.3%) 95%CI [9.7%;70.0%]	2 (66.7%) 95%CI [20.8%;93.9%]
Clinician-graded macular atrophy (M24)	**n = 6**	**n = 3**
Yes	1 (16.7%) 95%CI [3.0%;56.4%]	0 (0%) 95%CI [0%;56.1%]
No	3 (50.0%)	0 (0%)

Unknown/inconclusive	95%CI [18.8%;81.2%] 2 (33.3%) 95%CI [9.7%;70.0%]	95%CI [0%;56.1%] 3 (100.0%) 95%CI [43.9%;100.0%]

Abbreviations: CI: confidence interval.

Association between CST variability at Months 1-12 (quartiles) and VA change (in ETDRS letters) from baseline to months 3, 6, 9, 12

	Naïve Patients				Switch patients			
	CST (Q1) (n=8)	**CST (Q2) (n=5)**	**CST (Q3) (n=2)**	**CST (Q4) (n=2)**	**CST (Q1) (n=0)**	**CST (Q2) (n=3)**	**CST (Q3) (n=5)**	**CST (Q4) (n=6)**
VA change in 3M from baseline								
≤-15	0 (0%) 95%CI [0%;56.1%]	0 (0%) 95%CI [0%;49.0%]	0 (0%) 95%CI [0%;65.8%]	0 (0%) 95%CI [0%;79.3%]	0 (NA%) 95%CI [NA%;NA%]	0 (0%) 95%CI [0%;65.8%]	0 (0%) 95%CI [0%;56.1%]	0 (0%) 95%CI [0.0%;43.4%]
]-15,-10]	0 (0%) 95%CI [0%;56.1%]	0 (0%) 95%CI [0%;49.0%]	0 (0%) 95%CI [0%;65.8%]	0 (0%) 95%CI [0%;79.3%]	0 (NA%) 95%CI [NA%;NA%]	0 (0%) 95%CI [0%;65.8%]	0 (0%) 95%CI [0%;56.1%]	0 (0%) 95%CI [0.0%;43.4%]
]-10,-5]	0 (0%) 95%CI [0%;56.1%]	0 (0%) 95%CI [0%;49.0%]	0 (0%) 95%CI [0%;65.8%]	1 (100.0%) 95%CI [21.0%;100.0%]	0 (NA%) 95%CI [NA%;NA%]	0 (0%) 95%CI [0%;65.8%]	0 (0%) 95%CI [0%;56.1%]	0 (0%) 95%CI [0.0%;43.4%]
]-5,5[	1 (33.3%) 95%CI [6.1%;79.2%]	4 (100.0%) 95%CI [51.0%;100.0%]	1 (50.0%) 95%CI [9.5%;90.5%]	0 (0%) 95%CI [0%;79.3%]	0 (NA%) 95%CI [NA%;NA%]	1 (50.0%) 95%CI [9.5%;90.5%]	2 (66.7%) 95%CI [21.0%;93.9%]	2 (40.0%) 95%CI [12.0%;76.9%]
[5,10[	0 (0%) 95%CI [0%;56.1%]	0 (0%) 95%CI [0%;49.0%]	0 (0%) 95%CI [0%;65.8%]	0 (0%) 95%CI [0%;79.3%]	0 (NA%) 95%CI [NA%;NA%]	1 (50.0%) 95%CI [9.5%;90.5%]	1 (33.3%) 95%CI [6.1%;79.2%]	1 (20.0%) 95%CI [3.6%;62.4%]

[10,15[	0 (0%) 95%CI [0%;56.1%]	0 (0%) 95%CI [0%;49.0%]	1 (50.0%) 95%CI [9.5%;90.5%]	0 (0%) 95%CI [0%;79.3%]	0 (NA%) 95%CI [NA%;NA%]	0 (0%) 95%CI [0%;65.8%]	0 (0%) 95%CI [0%;56.1%]	0 (0%) 95%CI [0.0%;43.4%]
≥15	2 (66.7%) 95%CI [21.0%;93.9%]	0 (0%) 95%CI [0%;49.0%]	0 (0%) 95%CI [0%;65.8%]	0 (0%) 95%CI [0%;79.3%]	0 (NA%) 95%CI [NA%;NA%]	0 (0%) 95%CI [0%;65.8%]	0 (0%) 95%CI [0%;56.1%]	2 (40.0%) 95%CI [12.0%;76.9%]
Missing	5	1	0	1	0	1	2	1
VA change in 6M from baseline	**n=7**	**n=4**	**n=2**	**n=3**	**n=2**	**n=2**	**n=5**	**n=5**
≤-15	0 (0%) 95%CI [0%;49.0%]	0 (0%) 95%CI [0%;56.1%]	0 (0%) 95%CI [0%;65.8%]	0 (0%) 95%CI [0%;65.8%]	0 (0%) 95%CI [0%;79.3%]	0 (0%) 95%CI [0%;79.3%]	0 (0%) 95%CI [0%;56.1%]	0 (0%) 95%CI [0%;56.1%]
]-15,-10]	0 (0%) 95%CI [0%;49.0%]	0 (0%) 95%CI [0%;56.1%]	0 (0%) 95%CI [0%;65.8%]	0 (0%) 95%CI [0%;65.8%]	0 (0%) 95%CI [0%;79.3%]	0 (0%) 95%CI [0%;79.3%]	0 (0%) 95%CI [0%;56.1%]	0 (0%) 95%CI [0%;56.1%]
]-10,-5]	0 (0%) 95%CI [0%;49.0%]	0 (0%) 95%CI [0%;56.1%]	0 (0%) 95%CI [0%;65.8%]	1 (50.0%) 95%CI [9.5%;90.5%]	0 (0%) 95%CI [0%;79.3%]	0 (0%) 95%CI [0%;79.3%]	0 (0%) 95%CI [0%;56.1%]	0 (0%) 95%CI [0%;56.1%]
]-5,5[	2 (50.0%) 95%CI [15.0%;85.0%]	1 (33.3%) 95%CI [6.1%;79.2%]	1 (50.0%) 95%CI [9.5%;90.5%]	1 (50.0%) 95%CI [9.5%;90.5%]	1 (100.0%) 95%CI [20.7%;100.0%]	1 (100.0%) 95%CI [20.7%;100.0%]	2 (66.7%) 95%CI [20.8%;93.9%]	1 (33.3%) 95%CI [6.1%;79.2%]
[5,10[	0 (0%) 95%CI [0%;49.0%]	1 (33.3%) 95%CI [6.1%;79.2%]	0 (0%) 95%CI [0%;65.8%]	0 (0%) 95%CI [0%;65.8%]	0 (0%) 95%CI [0%;79.3%]	0 (0%) 95%CI [0%;79.3%]	0 (0%) 95%CI [0%;56.1%]	1 (33.3%) 95%CI [6.1%;79.2%]
[10,15[	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (33.3%)

	95%CI [0%;49.0%]	95%CI [0%;56.1%]	95%CI [0%;65.8%]	95%CI [0%;65.8%]	95%CI [0%;79.3%]	95%CI [0%;79.3%]	95%CI [0%;56.1%]	95%CI [6.1%;79.2%]
	2 (50.0%)	1 (33.3%)	1 (50.0%)	0 (0%)	0 (0%)	0 (0%)	1 (33.3%)	0 (0%)
≥15	95%CI [15.0%;85.0%]	95%CI [6.1%;79.2%]	95%CI [9.5%;90.5%]	95%CI [0%;65.8%]	95%CI [0%;79.3%]	95%CI [0%;79.3%]	95%CI [6.1%;79.2%]	95%CI [0%;56.1%]
Missing	3	1	0	1	1	1	2	2
VA change in 9M from baseline	**n=6**	**n=3**	**n=2**	**n=1**	**n=1**	**n=3**	**n=4**	**n=5**
	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
≤-15	95%CI [0%;79.3%]	95%CI [0%;79.3%]	95%CI [0%;79.3%]	95%CI [0%;79.3%]	95%CI [0%;79.3%]	95%CI [0%;65.8%]	95%CI [0%;65.8%]	95%CI [0%;49.0%]
	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
]-15,-10]	95%CI [0%;79.3%]	95%CI [0%;79.3%]	95%CI [0%;79.3%]	95%CI [0%;79.3%]	95%CI [0%;79.3%]	95%CI [0%;65.8%]	95%CI [0%;65.8%]	95%CI [0%;49.0%]
	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (50.0%)	0 (0%)	0 (0%)
]-10,-5]	95%CI [0%;79.3%]	95%CI [0%;79.3%]	95%CI [0%;79.3%]	95%CI [0%;79.3%]	95%CI [0%;79.3%]	95%CI [9.5%;90.5%]	95%CI [0%;65.8%]	95%CI [0%;49.0%]
	0 (0%)	1 (100.0%)	0 (0%)	0 (0%)	1 (100.0%)	0 (0%)	2 (100.0%)	3 (75.0%)
]-5,5[	95%CI [0%;79.3%]	95%CI [20.7%;100.0%]	95%CI [0%;79.3%]	95%CI [0%;79.3%]	95%CI [20.7%;100.0%]	95%CI [0%;65.8%]	95%CI [34.2%;100.0%]	95%CI [30.1%;95.4%]
	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (50.0%)	0 (0%)	1 (25.0%)
[5,10[	95%CI [0%;79.3%]	95%CI [0%;79.3%]	95%CI [0%;79.3%]	95%CI [0%;79.3%]	95%CI [0%;79.3%]	95%CI [9.5%;90.5%]	95%CI [0%;65.8%]	95%CI [4.6%;69.9%]
	0 (0%)	0 (0%)	1 (100.0%)	1 (100.0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
[10,15[	95%CI [0%;79.3%]	95%CI [0%;79.3%]	95%CI [20.7%;100.0%]	95%CI [20.7%;100.0%]	95%CI [0%;79.3%]	95%CI [0%;65.8%]	95%CI [0%;65.8%]	95%CI [0%;49.0%]
≥15	1 (100.0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

	95%CI [20.7%;100.0 %]	95%CI [0%;79.3%]	95%CI [0%;79.3%]	95%CI [0%;79.3%]	95%CI [0%;79.3%]	95%CI [0%;65.8%]	95%CI [0%;65.8%]	95%CI [0%;49.0%]
Missing	5	2	1	0	0	1	2	1
VA change in 12M from baseline	**n=6**	**n=5**	**n=2**	**n=1**	**n=1**	**n=2**	**n=5**	**n=5**
	0 (0%)	1 (25.0%)	0 (0%)	0 (0%)	0 (NA%)	0 (0%)	0 (0%)	1 (33.3%)
≤-15	95%CI [0%;65.8%]	95%CI [4.6%;69.9%]	95%CI [0%;65.8%]	95%CI [0%;79.3%]	95%CI [NA%;NA%]	95%CI [0%;65.8%]	95%CI [0%;49.0%]	95%CI [6.1%;79.2%]
	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (NA%)	0 (0%)	0 (0%)	0 (0%)
]-15,-10]	95%CI [0%;65.8%]	95%CI [0%;49.0%]	95%CI [0%;65.8%]	95%CI [0%;79.3%]	95%CI [NA%;NA%]	95%CI [0%;65.8%]	95%CI [0%;49.0%]	95%CI [0%;56.1%]
	0 (0%)	0 (0%)	0 (0%)	1 (100.0%)	0 (NA%)	0 (0%)	0 (0%)	1 (33.3%)
]-10,-5]	95%CI [0%;65.8%]	95%CI [0%;49.0%]	95%CI [0%;65.8%]	95%CI [20.7%;100.0%]	95%CI [NA%;NA%]	95%CI [0%;65.8%]	95%CI [0%;49.0%]	95%CI [6.1%;79.2%]
	1 (50.0%)	2 (50.0%)	0 (0%)	0 (0%)	0 (NA%)	2 (100.0%)	2 (50.0%)	1 (33.3%)
]-5,5[	95%CI [9.5%;90.5%]	95%CI [15.0%;85.0%]	95%CI [0%;65.8%]	95%CI [0%;79.3%]	95%CI [NA%;NA%]	95%CI [34.2%;100.0%]	95%CI [15.0%;85.0%]	95%CI [6.1%;79.2%]
	0 (0%)	1 (25.0%)	0 (0%)	0 (0%)	0 (NA%)	0 (0%)	1 (25.0%)	0 (0%)
[5,10[	95%CI [0%;65.8%]	95%CI [4.6%;69.9%]	95%CI [0%;65.8%]	95%CI [0%;79.3%]	95%CI [NA%;NA%]	95%CI [0%;65.8%]	95%CI [4.6%;69.9%]	95%CI [0%;56.1%]
	0 (0%)	0 (0%)	2 (100.0%)	0 (0%)	0 (NA%)	0 (0%)	0 (0%)	0 (0%)
[10,15[	95%CI [0%;65.8%]	95%CI [0%;49.0%]	95%CI [34.2%;100.0%]	95%CI [0%;79.3%]	95%CI [NA%;NA%]	95%CI [0%;65.8%]	95%CI [0%;49.0%]	95%CI [0%;56.1%]
	1 (50.0%)	0 (0%)	0 (0%)	0 (0%)	0 (NA%)	0 (0%)	1 (25.0%)	0 (0%)
≥15	95%CI [9.5%;90.5%]	95%CI [0%;49.0%]	95%CI [0%;65.8%]	95%CI [0%;79.3%]	95%CI [NA%;NA%]	95%CI [0%;65.8%]	95%CI [4.6%;69.9%]	95%CI [0%;56.1%]

Missing	4	1	0	0	1	0	1	2

Abbreviations: ETDRS: Early Treatment Diabetic Retinopathy Study; CI: confidence interval.

Association between CST variability at months 1-12 (quartiles) and number of injections during the first year (month 1-12) of treatment with brolucizumab

	CST variation			
	CST (Q1) (n=8)	**CST (Q2) (n=6)**	**CST (Q3) (n=6)**	**CST (Q4) (n=7)**
Month 1-3				
Valid n (Missing)	8 (0)	6 (0)	6 (0)	7 (0)
Mean [95%CI]	1.38 [1.02;1.73]	1.33 [0.92;1.75]	1.33 [0.92;1.75]	1.00 [0.26;1.74]
Std. dev	0.52	0.52	0.52	1.00
Med [P25,P75]	1.00 [1.00;2.00]	1.00 [1.00;1.75]	1.00 [1.00;1.75]	1.00 [0;2.00]
Min / Max	1.00 / 2.00	1.00 / 2.00	1.00 / 2.00	0 / 2.00
Month 1-6				
Valid n (Missing)	8 (0)	6 (0)	6 (0)	7 (0)
Mean [95%CI]	2.50 [1.98;3.02]	2.67 [2.01;3.32]	2.50 [1.83;3.17]	2.29 [1.26;3.31]
Std. dev	0.76	0.82	0.84	1.38
Med [P25,P75]	3.00 [2.00;3.00]	2.50 [2.00;3.00]	2.00 [2.00;2.75]	2.00 [1.00;3.50]
Min / Max	1.00 / 3.00	2.00 / 4.00	2.00 / 4.00	1.00 / 4.00
Month 1-9				
Valid n (Missing)	8 (0)	6 (0)	6 (0)	7 (0)
Mean [95%CI]	5.12 [4.11;6.14]	5.17 [3.99;6.34]	5.00 [4.12;5.88]	4.00 [2.72;5.28]
Std. dev	1.46	1.47	1.10	1.73
Med [P25,P75]	5.00 [4.75;5.25]	4.50 [4.00;6.50]	5.00 [4.25;5.00]	3.00 [3.00;5.00]
Min / Max	3.00 / 8.00	4.00 / 7.00	4.00 / 7.00	2.00 / 7.00

Month 1-12				
Valid n (Missing)	8 (0)	6 (0)	6 (0)	7 (0)
Mean [95%CI]	5.12 [4.11;6.14]	5.17 [3.99;6.34]	5.00 [4.12;5.88]	4.00 [2.72;5.28]
Std. dev	1.46	1.47	1.10	1.73
Med [P25,P75]	5.00 [4.75;5.25]	4.50 [4.00;6.50]	5.00 [4.25;5.00]	3.00 [3.00;5.00]
Min / Max	3.00 / 8.00	4.00 / 7.00	4.00 / 7.00	2.00 / 7.00

Abbreviations: CI: confidence interval; Std. dev: standard deviation; Med: median; P25: percentile 25; P75: percentile 75.

Time to first reactivation (in days) of CNV since the first grading of inactivity during the study period

	Naïve Patients (n=22)	**Switch patients (n=23)**
Time to 1st reactivation (in days) of CNV since the 1st grading of inactivity during the study period		
Valid n (Missing)	13 (9)	13 (10)
Mean [95%CI]	147.85 [107.67;188.02]	130.15 [94.47;165.84]
Std. dev	96.15	87.32
Med [P25,P75]	141.00 [67.00;191.00]	133.00 [45.00;189.00]
Min / Max	28.00 / 378.00	14.00 / 273.00

Abbreviations: CI: confidence interval; Std. dev: standard deviation; Med: median; P25: percentile 25; P75: percentile 75.

Number of visits with CNV inactive during the maintenance phase (M4-M12) in association to VA change from baseline to month 12

	Naïve Patients (n=9)						
VA change from baseline to Month 12	**≤-15 (n=1)**	**]-15,-10] (n=0)**	**]-10,-5] (n=1)**	**]-5,5[(n=3)**	**[5,10[(n=1)**	**[10,15[(n=2)**	**≥15 (n=1)**
Nr. of visits with CNV inactive during the maintenance phase (M4-M12)							
Valid n (Missing)	1 (0)	0 (0)	1 (0)	3 (0)	1 (0)	2 (0)	0 (1)
Mean [95%CI]	3.00 [NA;NA]	NA [NA;NA]	5.00 [NA;NA]	2.33 [1.68;2.99]	4.00 [NA;NA]	3.50 [0.56;6.44]	NA [NA;NA]
Std. dev	NA	NA	NA	0.58	NA	2.12	NA
Med [P25,P75]	3.00 [3.00;3.00]	NA [NA;NA]	5.00 [5.00;5.00]	2.00 [2.00;2.50]	4.00 [4.00;4.00]	3.50 [2.75;4.25]	NA [NA;NA]
Min / Max	3.00 / 3.00	NA / NA	5.00 / 5.00	2.00 / 3.00	4.00 / 4.00	2.00 / 5.00	NA / NA
	Switch patients (n=9)						
VA change from baseline to Month 12	**≤-15 (n=1)**	**]-15,-10] (n=0)**	**]-10,-5] (n=1)**	**]-5,5[(n=5)**	**[5,10[(n=1)**	**[10,15[(n=0)**	**≥15 (n=1)**
Nr. of visits with CNV inactive during the maintenance phase (M4-M12)							
Valid n (Missing)	1 (0)	0 (0)	1 (0)	4 (1)	0 (1)	0 (0)	0 (1)
Mean [95%CI]	2.00 [NA;NA]	NA [NA;NA]	4.00 [NA;NA]	2.25 [1.41;3.09]	NA [NA;NA]	NA [NA;NA]	NA [NA;NA]
Std. dev	NA	NA	NA	0.96	NA	NA	NA
Med [P25,P75]	2.00 [2.00;2.00]	NA [NA;NA]	4.00 [4.00;4.00]	2.50 [1.75;3.00]	NA [NA;NA]	NA [NA;NA]	NA [NA;NA]
Min / Max	2.00 / 2.00	NA / NA	4.00 / 4.00	1.00 / 3.00	NA / NA	NA / NA	NA / NA

Abbreviations: CI: confidence interval; Std. dev: standard deviation; Med: median; P25: percentile 25; P75: percentile 75.

Number of visits with CNV inactive during the maintenance phase (M4-M24) in association to VA change from baseline to month 24

	Naïve Patients (n=4)						
VA change from baseline to Month 24	**≤-15 (n=1)**	**]-15,-10] (n=0)**	**]-10,-5] (n=0)**	**]-5,5[(n=1)**	**[5,10[(n=1)**	**[10,15[(n=0)**	**≥15 (n=2)**
Nr. of visits with CNV inactive during the maintenance phase (M4-M24)							
Valid n (Missing)	0 (0)	0 (0)	0 (0)	0 (1)	1 (0)	0 (0)	1 (1)
Mean [95%CI]	NA [NA;NA]	NA [NA;NA]	NA [NA;NA]	NA [NA;NA]	8.00 [NA;NA]	NA [NA;NA]	2.00 [NA;NA]
Std. dev	NA	NA	NA	NA	NA	NA	NA
Med [P25,P75]	NA [NA;NA]	NA [NA;NA]	NA [NA;NA]	NA [NA;NA]	8.00 [8.00;8.00]	NA [NA;NA]	2.00 [2.00;2.00]
Min / Max	NA / NA	NA / NA	NA / NA	NA / NA	8.00 / 8.00	NA / NA	2.00 / 2.00
	Switch patients (n=1)						
VA change from baseline to Month 24	**≤-15 (n=1)**	**]-15,-10] (n=0)**	**]-10,-5] (n=0)**	**]-5,5[(n=0)**	**[5,10[(n=0)**	**[10,15[(n=0)**	**≥15 (n=0)**
Nr. of visits with CNV inactive during the maintenance phase (M4-M24)							
Valid n (Missing)	1 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Mean [95%CI]	6.00 [NA;NA]	NA [NA;NA]	NA [NA;NA]	NA [NA;NA]	NA [NA;NA]	NA [NA;NA]	NA [NA;NA]
Std. dev	NA	NA	NA	NA	NA	NA	NA
Med [P25,P75]	6.00 [6.00;6.00]	NA [NA;NA]	NA [NA;NA]	NA [NA;NA]	NA [NA;NA]	NA [NA;NA]	NA [NA;NA]
Min / Max	6.00 / 6.00	NA / NA	NA / NA	NA / NA	NA / NA	NA / NA	NA / NA

Abbreviations: CI: confidence interval; Std. dev: standard deviation; Med: median; P25: percentile 25; P75: percentile 75.

VA change from baseline (in ETDRS letters) to months 3, 6, 9, 12, 18 and 24 (in ETDRS letters)

	Naïve Patients	Switch patients
VA change from baseline to M3 (in ETDRS letters)*	**n = 36**	**n = 28**
≤-15	0 (0%) 95%CI [0.0%;27.8%]	0 (0%) 95%CI [0%;25.9%]
]-15,-10]	0 (0%) 95%CI [0.0%;27.8%]	0 (0%) 95%CI [0%;25.9%]
]-10,-5]	1 (10.0%) 95%CI [1.8%;40.4%]	0 (0%) 95%CI [0%;25.9%]
]-5,5[	6 (60.0%) 95%CI [31.0%;83.2%]	5 (45.5%) 95%CI [21.0%;72.0%]
[5,10[	0 (0%) 95%CI [0.0%;27.8%]	4 (36.4%) 95%CI [15.0%;64.6%]
[10,15[	1 (10.0%) 95%CI [1.8%;40.4%]	0 (0%) 95%CI [0%;25.9%]
≥15	2 (20.0%) 95%CI [5.7%;51.0%]	2 (18.2%) 95%CI [5.1%;47.7%]
Missing	26	17
VA change from baseline to M6 (in ETDRS letters)*	**n = 25**	**n = 23**
≤-15	0 (0%) 95%CI [0%;25.9%]	0 (0%) 95%CI [0.0%;27.8%]
]-15,-10]	0 (0%) 95%CI [0%;25.9%]	0 (0%) 95%CI [0.0%;27.8%]

]-10,-5]	1 (9.1%) 95%CI [1.6%;37.7%]	0 (0%) 95%CI [0.0%;27.8%]
]-5,5[	5 (45.5%) 95%CI [21.0%;72.0%]	6 (60.0%) 95%CI [31.0%;83.2%]
[5,10[	1 (9.1%) 95%CI [1.6%;37.7%]	2 (20.0%) 95%CI [5.7%;51.0%]
[10,15[	0 (0%) 95%CI [0%;25.9%]	1 (10.0%) 95%CI [1.8%;40.4%]
≥15	4 (36.4%) 95%CI [15.0%;64.6%]	1 (10.0%) 95%CI [1.8%;40.4%]
Missing	14	13
VA change from baseline to M9 (in ETDRS letters)*	**n = 21**	**n = 20**
≤-15	0 (0%) 95%CI [0%;49.0%]	0 (0%) 95%CI [0%;24.2%]
]-15,-10]	0 (0%) 95%CI [0%;49.0%]	1 (8.3%) 95%CI [1.5%;35.4%]
]-10,-5]	0 (0%) 95%CI [0%;49.0%]	1 (8.3%) 95%CI [1.5%;35.4%]
]-5,5[	1 (25.0%) 95%CI [4.6%;69.9%]	7 (58.3%) 95%CI [32.0%;80.7%]
[5,10[	0 (0%) 95%CI [0%;49.0%]	3 (25.0%) 95%CI [8.9%;53.2%]
[10,15[	2 (50.0%)	0 (0%)

	95%CI [15.0%;85.0%]	95%CI [0%;24.2%]
≥15	1 (25.0%) 95%CI [4.6%;69.9%]	0 (0%) 95%CI [0%;24.2%]
Missing	17	8
VA change from baseline to M12 (in ETDRS letters)*	**n = 29**	**n = 22**
≤-15	1 (11.1%) 95%CI [2.0%;43.5%]	1 (11.1%) 95%CI [2.0%;43.5%]
]-15,-10]	0 (0%) 95%CI [0%;29.9%]	0 (0%) 95%CI [0%;29.9%]
]-10,-5]	1 (11.1%) 95%CI [2.0%;43.5%]	1 (11.1%) 95%CI [2.0%;43.5%]
]-5,5[	3 (33.3%) 95%CI [12.1%;64.6%]	5 (55.6%) 95%CI [26.7%;81.1%]
[5,10[	1 (11.1%) 95%CI [2.0%;43.5%]	1 (11.1%) 95%CI [2.0%;43.5%]
[10,15[	2 (22.2%) 95%CI [6.3%;54.7%]	0 (0%) 95%CI [0%;29.9%]
≥15	1 (11.1%) 95%CI [2.0%;43.5%]	1 (11.1%) 95%CI [2.0%;43.5%]
Missing	20	13
VA change from baseline to M18 (in ETDRS letters)*	**n = 16**	**n = 19**
≤-15	1 (20.0%) 95%CI [3.6e+00%;62.4%]	2 (28.6%) 95%CI [8.2%;64.1%]

]-15,-10]	0 (0%) 95%CI 0.0%;43.4%]	0 (0%) 95%CI [0%;35.4%]
]-10,-5]	0 (0%) 95%CI 0.0%;43.4%]	0 (0%) 95%CI [0%;35.4%]
]-5,5[	3 (60.0%) 95%CI [23.0%;88.2%]	3 (42.9%) 95%CI [16.0%;75.0%]
[5,10[	0 (0%) 95%CI 0.0%;43.4%]	1 (14.3%) 95%CI [2.6%;51.3%]
[10,15[	0 (0%) 95%CI 0.0%;43.4%]	0 (0%) 95%CI [0%;35.4%]
≥15	1 (20.0%) 95%CI [3.6%;62.4%]	1 (14.3%) 95%CI [2.6%;51.3%]
Missing	11	12
VA change from baseline to M24 (in ETDRS letters)*	**n = 6**	**n = 3**
≤-15	0 (0%) 95%CI [0%;49.0%]	1 (100.0%) 95%CI [20.7%;100.0%]
]-15,-10]	0 (0%) 95%CI [0%;49.0%]	0 (0%) 95%CI [0%;79.3%]
]-10,-5]	0 (0%) 95%CI [0%;49.0%]	0 (0%) 95%CI [0%;79.3%]
]-5,5[	1 (25.0%) 95%CI [4.6%;69.9%]	0 (0%) 95%CI [0%;79.3%]
[5,10[	1 (25.0%)	0 (0%)

	95%CI [4.6%;69.9%]	95%CI [0%;79.3%]
[10,15[	0 (0%) 95%CI [0%;49.0%]	0 (0%) 95%CI [0%;79.3%]
≥15	2 (50.0%) 95%CI [15.0%;85.0%]	0 (0%) 95%CI [0%;79.3%]
Missing	4	2

Abbreviations: ETDRS: Early Treatment Diabetic Retinopathy Study; CI: confidence interval.
*Paired comparisons were not performed due to the small number of patients with data regarding VA change throughout the study period.

3. Drug utilization and re-treatment criteria

Follow-up visits: Injection and Re-treatment criteria[1]

	Naïve Patients	Switch patients
Nr. brolucizumab injections		
1-3 months		
Valid n (Missing)	44 (0)	31 (0)
Mean [95%CI]	1.36 [1.14;1.59]	1.42 [1.18;1.66]
Std. dev	0.78	0.72
Med [P25,P75]	1.50 [1.00;2.00]	1.00 [1.00;2.00]
Min / Max	0 / 3.00	0 / 4.00
3-6 months		
Valid n (Missing)	42 (0)	30 (0)
Mean [95%CI]	1.90 [1.57;2.24]	1.90 [1.68;2.12]
Std. dev	1.16	0.66
Med [P25,P75]	2.00 [1.00;2.75]	2.00 [2.00;2.00]
Min / Max	0 / 5.00	0 / 3.00
6-12 months		
Valid n (Missing)	34 (0)	27 (0)
Mean [95%CI]	2.97 [2.52;3.42]	3.26 [2.74;3.78]
Std. dev	1.55	1.56
Med [P25,P75]	3.00 [2.00;4.00]	3.00 [2.00;4.00]
Min / Max	0 / 6.00	0 / 6.00

1-12 months		
Valid n (Missing)	34 (0)	27 (0)
Mean [95%CI]	4.74 [4.13;5.34]	4.85 [4.21;5.49]
Std. dev	2.08	1.94
Med [P25,P75]	5.00 [3.25;6.00]	5.00 [3.50;6.00]
Min / Max	0 / 9.00	1.00 / 8.00
13-24 months		
Valid n (Missing)	23 (0)	10 (0)
Mean [95%CI]	2.52 [2.00;3.04]	4.10 [3.65;4.55]
Std. dev	1.81	1.37
Med [P25,P75]	2.00 [1.00;3.50]	4.50 [3.25;5.00]
Min / Max	0 / 6.00	2.00 / 6.00
≥3 injections by Month 3		
<3 injections	43 (97.7%) 95%CI [88.2%;99.6%]	30 (96.8%) 95%CI [83.8%;99.4%]
≥3 injections	1 (2.3%) 95%CI [0.4%;11.8%]	1 (3.2%) 95%CI [0.6%;16.2%]
Missing	2	4
Non-injection visits		
1-3 months		
Valid n (Missing)	44 (0)	31 (0)
Mean [95%CI]	1.36 [1.14;1.59]	1.42 [1.18;1.66]
Std. dev	0.78	0.72

Med [P25,P75]	1.50 [1.00;2.00]	1.00 [1.00;2.00]
Min / Max	0 / 3.00	0 / 4.00
3-6 months		
Valid n (Missing)	42 (0)	30 (0)
Mean [95%CI]	1.00 [0.66;1.34]	0.67 [0.37;0.96]
Std. dev	1.17	0.88
Med [P25,P75]	1.00 [0;1.00]	0 [0;1.00]
Min / Max	0 / 5.00	0 / 3.00
6-12 months		
Valid n (Missing)	34 (0)	27 (0)
Mean [95%CI]	1.59 [1.13;2.04]	1.63 [1.12;2.14]
Std. dev	1.58	1.55
Med [P25,P75]	1.00 [0;2.75]	1.00 [0;3.00]
Min / Max	0 / 5.00	0 / 4.00
1-12 months		
Valid n (Missing)	34 (0)	27 (0)
Mean [95%CI]	2.47 [1.81;3.13]	2.22 [1.60;2.85]
Std. dev	2.29	1.89
Med [P25,P75]	2.00 [1.00;4.00]	1.00 [1.00;4.00]
Min / Max	0 / 10.00	0 / 5.00
13-24 months		
Valid n (Missing)	23 (0)	10 (0)
Mean [95%CI]	1.22 [0.81;1.63]	1.60 [0.92;2.28]

Std. dev	1.41	2.07
Med [P25,P75]	1.00 [0;2.00]	1.00 [0;2.00]
Min / Max	0 / 5.00	0 / 6.00
Injection (3M), re-treatment criteria	**Naïve Patients (n=36)**	**Switch patients (n=28)**
VA	1 (2.8%) 95%CI [0.5%;14.2%]	0 (0%) 95%CI [0%;12.1%]
Anatomic parameters	3 (8.3%) 95%CI [2.9%;21.8%]	6 (21.4%) 95%CI [10.2%;39.5%]
Both	0 (0%) 95%CI [0%;9.6%]	0 (0%) 95%CI [0%;12.1%]
Posology requirement	28 (77.8%) 95%CI [61.9%;88.3%]	20 (71.4%) 95%CI [52.9%;84.7%]
Others	4 (11.1%) 95%CI [4.4%;25.3%]	2 (7.1%) 95%CI [2.0%;22.6%]
FA (3M)		
Yes	0 (0%) 95%CI [0%;9.6%]	0 (0%) 95%CI [0%;12.1%]
No	36 (100.0%) 95%CI [90.4%;100.0%]	28 (100.0%) 95%CI [87.9%;100.0%]
Injection (6M), re-treatment criteria	**Naïve Patients (n=25)**	**Switch patients (n=23)**
VA	0 (0%) 95%CI [0%;13.3%]	1 (4.3%) 95%CI [0.8%;21.0%]
Anatomic parameters	1 (4.0%)	5 (21.7%)

	95%CI [0.7%;19.5%]	95%CI [9.7%;41.9%]
Both	0 (0%) 95%CI [0%;13.3%]	1 (4.3%) 95%CI [0.8%;21.0%]
Posology requirement	21 (84.0%) 95%CI [65.3%;93.6%]	14 (60.9%) 95%CI [40.8%;77.8%]
Others	3 (12.0%) 95%CI [4.2%;30.0%]	2 (8.7%) 95%CI [2.4%;26.8%]
FA (6M)		
Yes	0 (0%) 95%CI [0%;13.3%]	0 (0%) 95%CI [0%;14.3%]
No	25 (100.0%) 95%CI [86.7%;100.0%]	23 (100.0%) 95%CI [85.7%;100.0%]
Injection (9M), re-treatment criteria	**Naïve Patients (n=21)**	**Switch patients (n=20)**
VA	0 (0%) 95%CI [0%;15.5%]	0 (0%) 95%CI [0.0%;16.1%]
Anatomic parameters	1 (4.8%) 95%CI [0.9%;22.7%]	6 (30.0%) 95%CI [15.0%;51.9%]
Both	0 (0%) 95%CI [0%;15.5%]	1 (5.0%) 95%CI [0.9%;23.6%]
Posology requirement	17 (81.0%) 95%CI [60.0%;92.3%]	11 (55.0%) 95%CI [34.0%;74.2%]
Others	3 (14.3%) 95%CI [5.0%;34.6%]	2 (10.0%) 95%CI [2.8%;30.1%]

FA (9M)		
Yes	0 (0%) 95%CI [0%;15.5%]	0 (0%) 95%CI [0.0%;16.1%]
No	21 (100.0%) 95%CI [85.0%;100.0%]	20 (100.0%) 95%CI [84.0%;100.0%]
Injection (12M), re-treatment criteria	**Naïve Patients (n=29)**	**Switch patients (n=22)**
VA	0 (0%) 95%CI [0%;11.7%]	0 (0%) 95%CI [0%;14.9%]
Anatomic parameters	2 (6.9%) 95%CI [1.9%;22.0%]	6 (27.3%) 95%CI [13.2%;48.2%]
Both	0 (0%) 95%CI [0%;11.7%]	0 (0%) 95%CI [0%;14.9%]
Posology requirement	22 (75.9%) 95%CI [57.9%;87.8%]	13 (59.1%) 95%CI [38.7%;76.7%]
Others	5 (17.2%) 95%CI [7.6%;34.5%]	3 (13.6%) 95%CI [4.7%;33.3%]
FA (12M)		
Yes	0 (0%) 95%CI [0%;11.7%]	0 (0%) 95%CI [0%;14.9%]
No	29 (100.0%) 95%CI [88.3%;100.0%]	22 (100.0%) 95%CI [85.1%;100.0%]
Injection (18M), re-treatment criteria	**Naïve Patients (n=16)**	**Switch patients (n=19)**
VA	0 (0%)	0 (0%)

	95%CI [0%;19.4%]	95%CI [0%;16.8%]
Anatomic parameters	2 (12.5%) 95%CI [3.5%;36.0%]	3 (15.8%) 95%CI [5.5%;37.6%]
Both	0 (0%) 95%CI [0%;19.4%]	0 (0%) 95%CI [0%;16.8%]
Posology requirement	13 (81.2%) 95%CI [57.0%;93.4%]	15 (78.9%) 95%CI [56.7%;91.5%]
Others	1 (6.2%) 95%CI [1.1%;28.3%]	1 (5.3%) 95%CI [0.9%;24.6%]
FA (18M)		
Yes	0 (0%) 95%CI [0%;19.4%]	0 (0%) 95%CI [0%;16.8%]
No	16 (100.0%) 95%CI [80.6%;100.0%]	19 (100.0%) 95%CI [83.2%;100.0%]
Injection (24M), re-treatment criteria	**Naïve Patients (n=6)**	**Switch patients (n=3)**
VA	0 (0%) 95%CI [0%;39.0%]	0 (0%) 95%CI [0%;56.1%]
Anatomic parameters	1 (16.7%) 95%CI [3.0%;56.4%]	1 (33.3%) 95%CI [6.1%;79.2%]
Both	0 (0%) 95%CI [0%;39.0%]	0 (0%) 95%CI [0%;56.1%]
Posology requirement	5 (83.3%) 95%CI [43.6%;97.0%]	1 (33.3%) 95%CI [6.1%;79.2%]

Others	0 (0%) 95%CI [0%;39.0%]	1 (33.3%) 95%CI [6.1%;79.2%]
FA (24M)		
Yes	0 (0%) 95%CI [0%;39.0%]	0 (0%) 95%CI [0%;56.1%]
No	6 (100.0%) 95%CI [61.0%;100.0%]	3 (100.0%) 95%CI [43.9%;100.0%]

Abbreviations: CI: confidence interval; Std. dev: standard deviation; Med: median; P25: percentile 25; P75: percentile 75; FA: fluorescein angiography.
[1]Dropouts before the end of each interval were not considered

Follow-up visits: Injection (number and time between)

	Naïve patients (n=46)	Switch patients (n=35)
Total number of visits		
1-3 months		
Valid n (Missing)	42 (4)	31 (4)
Mean [95%CI]	2.10 [1.80;2.39]	1.90 [1.58;2.23]
Std. dev	1.01	0.98
Med [P25,P75]	2.00 [1.00;3.00]	2.00 [1.00;2.00]
Min / Max	1.00 / 6.00	1.00 / 5.00
3-6 months		
Valid n (Missing)	39 (7)	30 (5)
Mean [95%CI]	3.13 [2.62;3.64]	2.57 [2.27;2.86]
Std. dev	1.76	0.90

Med [P25,P75]	3.00 [2.00;4.00]	2.50 [2.00;3.00]
Min / Max	1.00 / 9.00	1.00 / 5.00
4-12 months		
Valid n (Missing)	34 (12)	27 (8)
Mean [95%CI]	5.68 [4.93;6.43]	5.81 [5.26;6.37]
Std. dev	2.59	1.69
Med [P25,P75]	5.00 [4.00;6.00]	6.00 [4.50;7.00]
Min / Max	1.00 / 13.00	3.00 / 9.00
6-12 months		
Valid n (Missing)	33 (13)	27 (8)
Mean [95%CI]	4.70 [4.18;5.21]	4.89 [4.37;5.40]
Std. dev	1.78	1.55
Med [P25,P75]	4.00 [4.00;6.00]	5.00 [4.00;6.00]
Min / Max	2.00 / 9.00	2.00 / 7.00
1-12 months		
Valid n (Missing)	34 (12)	27 (8)
Mean [95%CI]	7.21 [6.33;8.08]	7.07 [6.39;7.76]
Std. dev	3.03	2.06
Med [P25,P75]	7.00 [6.00;8.00]	7.00 [6.00;8.00]
Min / Max	2.00 / 17.00	3.00 / 12.00
13-24 months		
Valid n (Missing)	22 (24)	10 (25)
Mean [95%CI]	3.91 [3.30;4.51]	5.70 [4.93;6.47]

Std. dev	2.09	2.31
Med [P25,P75]	4.00 [2.25;5.00]	5.50 [4.00;7.00]
Min / Max	1.00 / 9.00	2.00 / 9.00
Time between visits (days)		
Valid n (Missing)	337 (46)	276 (35)
Mean [95%CI]	55.42 [51.73;59.11]	55.13 [51.89;58.37]
Std. dev	36.84	29.13
Med [P25,P75]	50.00 [32.00;73.00]	50.00 [31.75;76.25]
Min / Max	2.00 / 393.00	7.00 / 157.00
Time between two consecutive injections (days)		
Valid n (Missing)	204 (42)	171 (31)
Mean [95%CI]	73.07 [66.85;79.29]	74.15 [69.59;78.71]
Std. dev	49.80	33.07
Med [P25,P75]	66.00 [44.50;90.00]	72.00 [49.00;88.00]
Min / Max	2.00 / 581.00	13.00 / 203.00
Distribution of injection intervals during Month 1-6	**n = 106**	**n = 78**
<4 weeks	2 (3.2%)	1 (2.3%)
	95%CI [0.9%;10.9%]	95%CI [0.4%;12.1%]
[4,6[weeks	17 (27.0%)	4 (9.3%)
	95%CI [17.6%;39.0%]	95%CI [3.7%;21.6%]
[6,8[weeks	11 (17.5%)	9 (20.9%)
	95%CI [10.0%;28.6%]	95%CI [11.4%;35.2%]
[8,10[weeks	10 (15.9%)	10 (23.3%)

	95%CI [8.9%;26.8%]	95%CI [13.2%;37.7%]
[10,12[weeks	10 (15.9%)	3 (7.0%)
	95%CI [8.9%;26.8%]	95%CI [2.4%;18.6%]
≥12 weeks	13 (20.6%)	16 (37.2%)
	95%CI [12.5%;32.2%]	95%CI [24.4%;52.1%]
Missing	43	35
Distribution of injection intervals during Month 1-12	**n = 181**	**n = 146**
<4 weeks	2 (1.5%)	1 (0.9%)
	95%CI [0.4%;5.2%]	95%CI [0.2%;4.9%]
[4,6[weeks	24 (17.5%)	10 (9.0%)
	95%CI [12.1%;24.7%]	95%CI [5.0%;15.8%]
[6,8[weeks	17 (12.4%)	22 (19.8%)
	95%CI [7.9%;19.0%]	95%CI [13.5%;28.2%]
[8,10[weeks	29 (21.2%)	23 (20.7%)
	95%CI [15.2%;28.7%]	95%CI [14.2%;29.2%]
[10,12[weeks	23 (16.8%)	11 (9.9%)
	95%CI [11.5%;23.9%]	95%CI [5.6%;16.9%]
≥12 weeks	42 (30.7%)	44 (39.6%)
	95%CI [23.6%;38.8%]	95%CI [31.0%;48.9%]
Missing	44	35
Distribution of injection intervals during Month 13-24	**n = 92**	**n = 92**
<4 weeks	0 (0%)	0 (0%)
	95%CI [0%;6.2%]	95%CI [0%;5.3%]

[4,6[weeks	7 (12.1%) 95%CI [6.0%;22.9%]	8 (11.6%) 95%CI [6.0%;21.2%]
[6,8[weeks	1 (1.7%) 95%CI [0.3%;9.1%]	13 (18.8%) 95%CI [11.4%;29.6%]
[8,10[weeks	8 (13.8%) 95%CI [7.2%;24.9%]	9 (13.0%) 95%CI [7.0%;23.0%]
[10,12[weeks	12 (20.7%) 95%CI [12.3%;32.8%]	11 (15.9%) 95%CI [9.1%;26.3%]
≥12 weeks	30 (51.7%) 95%CI [39.2%;64.1%]	28 (40.6%) 95%CI [29.8%;52.4%]
Missing	34	23

Abbreviations: CI: confidence interval; Std. dev: standard deviation; Med: median; P25: percentile 25; P75: percentile 75.

4. Discontinuation in nAMD patients receiving brolucizumab

Discontinuation rate in nAMD patients receiving brolucizumab

	Naïve Patients (n=46)	Switch patients (n=35)
Patient eyes that discontinue therapy of treatment with brolucizumab		
Yes	23 (50.0%) 95%CI [36.1%;63.9%]	25 (71.4%) 95%CI [54.9%;83.7%]
No	23 (50.0%) 95%CI [36.1%;63.9%]	10 (28.6%) 95%CI [16.3%;45.1%]
Reasons for brolucizumab treatment discontinuation		
Lack of effectiveness	2 (8.7%) 95%CI [2.4%;26.8%]	2 (8.0%) 95%CI [2.2%;25.0%]
Lost to follow-up	6 (26.1%) 95%CI [12.5%;46.5%]	5 (20.0%) 95%CI [8.9%;39.1%]
AE	1 (4.3%) 95%CI [0.8%;21.0%]	4 (16.0%) 95%CI [6.4%;34.7%]
Informed consent withdrawal	0 (0%) 95%CI [0%;14.3%]	0 (0%) 95%CI [0%;13.3%]
Death	0 (0%) 95%CI [0%;14.3%]	0 (0%) 95%CI [0%;13.3%]
Other	14 (60.9%) 95%CI [40.8%;77.8%]	14 (56.0%) 95%CI [37.1%;73.3%]

Period of discontinuation		
Discontinue therapy during the 1st year (Month 1-12) of treatment with brolucizumab	12 (52.2%) 95%CI [33.0%;70.8%]	8 (32.0%) 95%CI [17.2%;51.6%]
Discontinue therapy during the 2nd year (Month 13-24) of treatment with brolucizumab	11 (47.8%) 95%CI [29.2%;67.0%]	17 (68.0%) 95%CI [48.4%;82.8%]
Persistence, time between the treatment initiation and the dropout		
Valid n (Missing)	23 (0)	25 (0)
Mean [95%CI]	11.83 [10.00;13.67]	14.48 [12.15;16.80]
Std. dev	6.36	7.02
Med [P25,P75]	10.58 [7.36;16.62]	16.46 [10.45;20.73]
Min / Max	0.46 / 23.00	2.14 / 22.77
Nr of injections of brolucizumab during treatment, until dropout		
Valid n (Missing)	23 (0)	25 (0)
Mean [95%CI]	3.91 [2.78;5.04]	4.92 [3.52;6.32]
Std. dev	2.76	3.58
Med [P25,P75]	3.00 [2.00;5.50]	4.00 [2.00;7.00]
Min / Max	0 / 10.00	0 / 13.00
Switch to another anti-VEGF		
Yes	10 (43.5%) 95%CI [25.6%;63.2%]	14 (56.0%) 95%CI [37.1%;73.3%]
No	13 (56.5%) 95%CI [36.8%;74.4%]	11 (44.0%) 95%CI [26.7%;62.9%]

At dropout: FA		
Yes	0 (0%) 95%CI [0%;14.3%]	0 (0%) 95%CI [0%;13.3%]
No	23 (100.0%) 95%CI [85.7%;100.0%]	25 (100.0%) 95%CI [86.7%;100.0%]
At dropout: OCT		
Yes	16 (69.6%) 95%CI [49.1%;84.4%]	18 (72.0%) 95%CI [52.4%;85.7%]
No	7 (30.4%) 95%CI [15.6%;50.9%]	7 (28.0%) 95%CI [14.3%;47.6%]
At dropout: VA (ETDRS)*		
≤35	2 (25.0%) 95%CI [7.1%;59.1%]	1 (10.0%) 95%CI [1.8%;40.4%]
36-69	2 (25.0%) 95%CI [7.1%;59.1%]	4 (40.0%) 95%CI [16.8%;68.7%]
≥70	4 (50.0%) 95%CI [21.5%;78.5%]	5 (50.0%) 95%CI [23.7%;76.3%]
Missing	15	15
At dropout: CST (in µm)		
Valid n (Missing)	16 (7)	17 (8)
Mean [95%CI]	280.88 [240.35;321.40]	281.47 [242.78;320.16]
Std. dev	99.17	98.70
Med [P25,P75]	276.00 [227.25;333.75]	269.00 [213.00;305.00]

Min / Max	46.00 / 473.00	176.00 / 585.00
At dropout: IRF		
Present	1 (33.3%) 95%CI [6.1%;79.2%]	1 (50.0%) 95%CI [9.5%;90.5%]
Absent	2 (66.7%) 95%CI [20.8%;93.9%]	1 (50.0%) 95%CI [9.5%;90.5%]
Missing	20	23
At dropout: SRF		
Present	3 (100.0%) 95%CI [43.9%;100.0%]	1 (100.0%) 95%CI [20.7%;100.0%]
Absent	0 (0%) 95%CI [0%;56.1%]	0 (0%) 95%CI [0%;79.3%]
Missing	20	24
At dropout: Sub-RPE fluid		
Present	1 (100.0%) 95%CI [20.7%;100.0%]	2 (100.0%) 95%CI [34.2%;100.0%]
Absent	0 (0%) 95%CI [0%;79.3%]	0 (0%) 95%CI [0%;65.8%]
Missing	22	23
At dropout: Geographic atrophy		
Yes	3 (13.6%) 95%CI [4.7%;33.3%]	3 (15.0%) 95%CI [5.2%;36.0%]

No	11 (50.0%) 95%CI [30.7%;69.3%]	14 (70.0%) 95%CI [48.1%;85.5%]
Unknown/inconclusive	8 (36.4%) 95%CI [19.7%;57.0%]	3 (15.0%) 95%CI [5.2%;36.0%]
Missing	1	5
At dropout: Subretinal fibrosis		
Yes	6 (27.3%) 95%CI [13.2%;48.2%]	4 (20.0%) 95%CI [8.1%;41.6%]
No	8 (36.4%) 95%CI [19.7%;57.0%]	13 (65.0%) 95%CI [43.3%;81.9%]
Unknown/inconclusive	8 (36.4%) 95%CI [19.7%;57.0%]	3 (15.0%) 95%CI [5.2%;36.0%]
Missing	1	5

Abbreviations: CI: confidence interval; Std. dev: standard deviation; Med: median; P25: percentile 25; P75: percentile 75; CST: central subfield thickness.

5. Characterization of nAMD switchers.

Due to the existence of dropouts, it was not possible to calculate a proportion of patients that switched to another anti-VEGF therapy. Thus, a survival analysis was performed.

Switch to another anti-VEGF during the first 6, 9, 12, 18 and 24 months of treatment with brolucizumab

	Naïve Patients (n = 46)					Switch patients (n = 35)				
Patient eyes that switch to another anti-VEGF[1]	**N at risk**	**N events**	**Survival rate**	**95%CI**	**Probability of switching**	**N at risk**	**N events**	**Survival rate**	**95%CI**	**Probability of switching**
First 6M	41	0	1.000	[1.000;1.000]	0.000	30	4	0.884	[0.783;0.998]	0.116
First 9M	37	0	1.000	[1.000;1.000]	0.000	30	4	0.884	[0.783;0.998]	0.116
First 12M	32	2	0.944	[0.872;1.000]	0.056	27	6	0.823	[0.704;0.962]	0.177
First 18M	19	6	0.810	[0.682;0.963]	0.190	17	8	0.758	[0.625;0.920]	0.242
First 24M	2	9	0.567	[0.353;0.910]	0.433	3	14	0.385	[0.209;0.709]	0.615

Abbreviations: CI: confidence interval.

[1]Kaplan-Meier estimator was used due to the existence of dropouts during the study period.

Characterization of nAMD switchers: demographics and comorbidities

	Naïve patients (n=9)	Switch patients (n=14)
Study eye		
Right	1 (11.1%) 95%CI [2.0%;43.5%]	10 (71.4%) 95%CI [45.4%;88.3%]
Left	8 (88.9%) 95%CI [56.5%;98.0%]	4 (28.6%) 95%CI [11.7%;54.6%]
Age at 1st brolucizumab injection (in years)		
Valid n (Missing)	9 (0)	14 (0)
Mean [95%CI]	80.45 [76.58;84.32]	78.82 [75.37;82.27]
Std. dev	5.92	6.59
Med [P25,P75]	80.42 [76.99;84.66]	79.36 [73.05;83.14]
Min / Max	70.78 / 89.17	69.74 / 88.44
Age at 1st brolucizumab injection (in years) classes		
<80 years	3 (33.3%) 95%CI [12.1%;64.6%]	8 (57.1%) 95%CI [32.6%;78.6%]
≥80 years	6 (66.7%) 95%CI [35.4%;87.9%]	6 (42.9%) 95%CI [21.4%;67.4%]
Gender		
Male	5 (55.6%) 95%CI [26.7%;81.1%]	2 (14.3%) 95%CI [4.0%;39.9%]
Female	4 (44.4%) 95%CI [18.9%;73.3%]	12 (85.7%) 95%CI [60.1%;96.0%]

Other	0 (0%) 95%CI [0%;29.9%]	0 (0%) 95%CI [0%;21.5%]
Weight (in kg)		
Valid n (Missing)	2 (7)	1 (13)
Mean [95%CI]	62.00 [55.53;68.47]	73.00 [NA;NA]
Std. dev	9.90	NA
Med [P25,P75]	62.00 [58.50;65.50]	73.00 [73.00;73.00]
Min / Max	55.00 / 69.00	73.00 / 73.00
Smoker		
Never	2 (22.2%) 95%CI [6.3%;54.7%]	1 (7.1%) 95%CI [1.3%;31.5%]
Former Smoker	1 (11.1%) 95%CI [2.0%;43.5%]	1 (7.1%) 95%CI [1.3%;31.5%]
Smoker	0 (0%) 95%CI [0%;29.9%]	0 (0%) 95%CI [0%;21.5%]
Unknown	6 (66.7%) 95%CI [35.4%;87.9%]	12 (85.7%) 95%CI [60.1%;96.0%]
Driver?		
yes	1 (11.1%) 95%CI [2.0%;43.5%]	0 (0%) 95%CI [0%;21.5%]
No (due to VA)	0 (0%) 95%CI [0%;29.9%]	0 (0%) 95%CI [0%;21.5%]
No (no driving license)	1 (11.1%)	1 (7.1%)

	95%CI [2.0%;43.5%]	95%CI [1.3%;31.5%]
No (other)	1 (11.1%)	1 (7.1%)
	95%CI [2.0%;43.5%]	95%CI [1.3%;31.5%]
Unknown	6 (66.7%)	12 (85.7%)
	95%CI [35.4%;87.9%]	95%CI [60.1%;96.0%]
Insurance		
Private	0 (0%)	1 (7.1%)
	95%CI [0%;29.9%]	95%CI [1.3%;31.5%]
Public	9 (100.0%)	13 (92.9%)
	95%CI [70.1%;100.0%]	95%CI [68.5%;98.7%]
Missing	0	0
If Private, Insurance type:		
Out-of-pocket	0 (NA%)	0 (0%)
	95%CI [NA%;NA%]	95%CI [0%;79.3%]
Healthcare subsystem	0 (NA%)	1 (100.0%)
	95%CI [NA%;NA%]	95%CI [20.7%;100.0%]
Private insurance	0 (NA%)	0 (0%)
	95%CI [NA%;NA%]	95%CI [0%;79.3%]
Systemic comorbidities	7 (77.8%)	9 (64.3%)
	95%CI [45.3%;93.7%]	95%CI [38.8%;83.7%]
Arterial hypertension	6 (66.7%)	7 (50.0%)
	95%CI [35.4%;87.9%]	95%CI [26.8%;73.2%]
Dyslipidemia	6 (66.7%)	7 (50.0%)

	95%CI [35.4%;87.9%]	95%CI [26.8%;73.2%]
Arrhythmia	1 (11.1%)	1 (7.1%)
	95%CI [2.0%;43.5%]	95%CI [1.3%;31.5%]
Type 1 DM	1 (11.1%)	0 (0%)
	95%CI [2.0%;43.5%]	95%CI [0%;21.5%]
Type 2 DM	1 (11.1%)	0 (0%)
	95%CI [2.0%;43.5%]	95%CI [0%;21.5%]
Acute Myocardial Infarction	1 (11.1%)	0 (0%)
	95%CI [2.0%;43.5%]	95%CI [0%;21.5%]
History of malignancy of any organ system	0 (0%)	1 (7.1%)
	95%CI [0%;29.9%]	95%CI [1.3%;31.5%]
Stroke/TIA	0 (0%)	0 (0%)
	95%CI [0%;29.9%]	95%CI [0%;21.5%]
Autoimmune disease	0 (0%)	0 (0%)
	95%CI [0%;29.9%]	95%CI [0%;21.5%]
Other	5 (55.6%)	5 (35.7%)
	95%CI [26.7%;81.1%]	95%CI [16.3%;61.2%]

Abbreviations: CI: confidence interval; Std. dev: standard deviation; Med: median; P25: percentile 25; P75: percentile 75; TIA: transient ischemic attack; DM: diabetes mellitus.

Characterization of nAMD switchers: AMD diagnosis

	Naïve patients (n=9)	Switch patients (n=14)
AMD		
Unilateral	6 (66.7%) 95%CI [35.4%;87.9%]	10 (71.4%) 95%CI [45.4%;88.3%]
Bilateral	3 (33.3%) 95%CI [12.1%;64.6%]	4 (28.6%) 95%CI [11.7%;54.6%]
Age at diagnosis (in years)		
Valid n (Missing)	7 (2)	11 (3)
Mean [95%CI]	80.41 [76.99;83.82]	76.08 [72.42;79.74]
Std. dev	5.23	6.99
Med [P25,P75]	80.41 [78.65;84.31]	77.67 [69.82;79.88]
Min / Max	70.77 / 85.76	67.24 / 87.94
Age at diagnosis (in years) classes		
<80 years	2 (28.6%) 95%CI [8.2%;64.1%]	8 (72.7%) 95%CI [43.4%;90.3%]
≥80 years	5 (71.4%) 95%CI [35.9%;91.8%]	3 (27.3%) 95%CI [9.7%;56.6%]
Missing	2	3
Time between diagnosis and first treatment (in months)		
Valid n (Missing)	7 (2)	11 (3)
Mean [95%CI]	8.86 [-6.17;23.88]	26.73 [12.92;40.54]
Std. dev	23.00	26.36

Med [P25,P75]	0 [0;0.50]	17.00 [9.50;33.00]
Min / Max	0 / 61.00	6.00 / 96.00
Time between diagnosis and start of treatment with brolucizumab (in months)		
Valid n (Missing)	7 (2)	11 (3)
Mean [95%CI]	9.05 [-5.88;23.98]	26.80 [13.20;40.40]
Std. dev	22.85	25.97
Med [P25,P75]	0.16 [0.10;1.07]	17.48 [9.86;32.79]
Min / Max	0 / 60.85	6.05 / 95.15
Mean lesion area (in mm^2)		
Valid n (Missing)	0 (9)	0 (14)
Mean [95%CI]	NA [NA;NA]	NA [NA;NA]
Std. dev	NA	NA
Med [P25,P75]	NA [NA;NA]	NA [NA;NA]
Min / Max	NA / NA	NA / NA
CNV Classification (based on angiographic criteria)		
Occult	0 (0%) 95%CI [0%;29.9%]	0 (0%) 95%CI [0%;21.5%]
Minimally classic	0 (0%) 95%CI [0%;29.9%]	0 (0%) 95%CI [0%;21.5%]
Predominantly classic	0 (0%) 95%CI [0%;29.9%]	0 (0%) 95%CI [0%;21.5%]
Other/Not applicable	9 (100.0%) 95%CI [70.1%;100.0%]	14 (100.0%) 95%CI [78.5%;100.0%]

Missing	0	0
CNV Classification (OCT)		
Type I	1 (11.1%) 95%CI [2.0%;43.5%]	2 (14.3%) 95%CI [4.0%;39.9%]
Type II	0 (0%) 95%CI [0%;29.9%]	1 (7.1%) 95%CI [1.3%;31.5%]
Type III	0 (0%) 95%CI [0%;29.9%]	0 (0%) 95%CI [0%;21.5%]
PCV	0 (0%) 95%CI [0%;29.9%]	0 (0%) 95%CI [0%;21.5%]
RAP	0 (0%) 95%CI [0%;29.9%]	0 (0%) 95%CI [0%;21.5%]
Other/Not applicable	8 (88.9%) 95%CI [56.5%;98.0%]	11 (78.6%) 95%CI [52.4%;92.4%]
Missing	0	0

Abbreviations: CI: confidence interval; Std. dev: standard deviation; Med: median; P25: percentile 25; P75: percentile 75; PCV: polypoidal choroidal vasculopathy; RAP: retinal angimatous proliferation.

Characterization of nAMD switchers: Baseline (first visit)

	Naïve Patients (n=9)	Switch patients (n=14)
Ocular condition		
Left Eye	0 (0%) 95%CI [0%;29.9%]	1 (7.1%) 95%CI [1.3%;31.5%]
Right Eye	3 (33.3%) 95%CI [12.1%;64.6%]	2 (14.3%) 95%CI [4.0%;39.9%]
Both Eyes	4 (44.4%) 95%CI [18.9%;73.3%]	1 (7.1%) 95%CI [1.3%;31.5%]
None	2 (22.2%) 95%CI [6.3%;54.7%]	10 (71.4%) 95%CI [45.4%;88.3%]
Left Eye		
Cataract	2 (22.2%) 95%CI [6.3%;54.7%]	2 (14.3%) 95%CI [4.0%;39.9%]
Glaucoma	2 (22.2%) 95%CI [6.3%;54.7%]	0 (0%) 95%CI [0%;21.5%]
Strabismus	0 (0%) 95%CI [0%;29.9%]	0 (0%) 95%CI [0%;21.5%]
Refractive errors	0 (0%) 95%CI [0%;29.9%]	0 (0%) 95%CI [0%;21.5%]
Orbit pathology	0 (0%) 95%CI [0%;29.9%]	0 (0%) 95%CI [0%;21.5%]
Endophthalmitis	0 (0%)	0 (0%)

	95%CI [0%;29.9%]	95%CI [0%;21.5%]
Uveitis	0 (0%)	0 (0%)
	95%CI [0%;29.9%]	95%CI [0%;21.5%]
Dry eye	0 (0%)	0 (0%)
	95%CI [0%;29.9%]	95%CI [0%;21.5%]
Inflammation of the anterior chamber	0 (0%)	0 (0%)
	95%CI [0%;29.9%]	95%CI [0%;21.5%]
Other eye inflammation	0 (0%)	0 (0%)
	95%CI [0%;29.9%]	95%CI [0%;21.5%]
Retinal vascular occlusion	0 (0%)	0 (0%)
	95%CI [0%;29.9%]	95%CI [0%;21.5%]
Vitreous detachment	0 (0%)	0 (0%)
	95%CI [0%;29.9%]	95%CI [0%;21.5%]
Retinal detachment	0 (0%)	0 (0%)
	95%CI [0%;29.9%]	95%CI [0%;21.5%]
Other	0 (0%)	0 (0%)
	95%CI [0%;29.9%]	95%CI [0%;21.5%]
Right Eye		
Cataract	2 (22.2%)	3 (21.4%)
	95%CI [6.3%;54.7%]	95%CI [7.6%;47.6%]
Glaucoma	3 (33.3%)	0 (0%)
	95%CI [12.1%;64.6%]	95%CI [0%;21.5%]
Strabismus	0 (0%)	0 (0%)

	95%CI [0%;29.9%]	95%CI [0%;21.5%]
Refractive errors	0 (0%)	0 (0%)
	95%CI [0%;29.9%]	95%CI [0%;21.5%]
Orbit pathology	0 (0%)	0 (0%)
	95%CI [0%;29.9%]	95%CI [0%;21.5%]
Endophthalmitis	0 (0%)	0 (0%)
	95%CI [0%;29.9%]	95%CI [0%;21.5%]
Uveitis	0 (0%)	0 (0%)
	95%CI [0%;29.9%]	95%CI [0%;21.5%]
Dry eye	0 (0%)	0 (0%)
	95%CI [0%;29.9%]	95%CI [0%;21.5%]
Inflammation of the anterior chamber	0 (0%)	0 (0%)
	95%CI [0%;29.9%]	95%CI [0%;21.5%]
Other eye inflammation	0 (0%)	0 (0%)
	95%CI [0%;29.9%]	95%CI [0%;21.5%]
Retinal vascular occlusion	0 (0%)	0 (0%)
	95%CI [0%;29.9%]	95%CI [0%;21.5%]
Vitreous detachment	0 (0%)	0 (0%)
	95%CI [0%;29.9%]	95%CI [0%;21.5%]
Retinal detachment	0 (0%)	0 (0%)
	95%CI [0%;29.9%]	95%CI [0%;21.5%]
Other	3 (33.3%)	0 (0%)
	95%CI [12.1%;64.6%]	95%CI [0%;21.5%]

IOI in previous 12 months before start of brolucizumab treatment		
Yes	0 (0%) 95%CI [0%;32.4%]	0 (0%) 95%CI [0%;24.2%]
No	0 (0%) 95%CI [0%;32.4%]	0 (0%) 95%CI [0%;24.2%]
Unknown	8 (100.0%) 95%CI [67.6%;100.0%]	12 (100.0%) 95%CI [75.8%;100.0%]
Missing	1	2
Endophthalmitis in previous 12 months before start of brolucizumab treatment		
Yes	0 (0%) 95%CI [0%;32.4%]	0 (0%) 95%CI [0%;24.2%]
No	0 (0%) 95%CI [0%;32.4%]	0 (0%) 95%CI [0%;24.2%]
Unknown	8 (100.0%) 95%CI [67.6%;100.0%]	12 (100.0%) 95%CI [75.8%;100.0%]
Missing	1	2
Intraocular Pressure (in mmHg)		
Valid n (Missing)	8 (1)	10 (4)
Mean [95%CI]	15.00 [12.00;18.00]	14.50 [12.66;16.34]
Std. dev	4.60	3.50
Med [P25,P75]	14.50 [13.50;15.25]	14.50 [12.25;17.75]
Min / Max	9.00 / 25.00	9.00 / 19.00

FA		
Yes	0 (0%) 95%CI [0%;29.9%]	0 (0%) 95%CI [0%;21.5%]
No	9 (100.0%) 95%CI [70.1%;100.0%]	14 (100.0%) 95%CI [78.5%;100.0%]
Time from FA until 1st visit		
Valid n (Missing)	0 (9)	0 (14)
Mean [95%CI]	NA [NA;NA]	NA [NA;NA]
Std. dev	NA	NA
Med [P25,P75]	NA [NA;NA]	NA [NA;NA]
Min / Max	NA / NA	NA / NA
Activity in FA?		
Yes	0 (NA%) 95%CI [NA%;NA%]	0 (NA%) 95%CI [NA%;NA%]
No	0 (NA%) 95%CI [NA%;NA%]	0 (NA%) 95%CI [NA%;NA%]
Missing	9	14
OCT		
Yes	9 (100.0%) 95%CI [70.1%;100.0%]	14 (100.0%) 95%CI [78.5%;100.0%]
No	0 (0%) 95%CI [0%;29.9%]	0 (0%) 95%CI [0%;21.5%]
VA Scale		

ETDRS	3 (42.9%) 95%CI [15.8%;75.0%]	10 (71.4%) 95%CI [45.4%;88.3%]
Snellen	0 (0%) 95%CI [0%;35.4%]	0 (0%) 95%CI [0%;21.5%]
LogMAR	0 (0%) 95%CI [0%;35.4%]	0 (0%) 95%CI [0%;21.5%]
Decimal	4 (57.1%) 95%CI [25.0%;84.2%]	3 (21.4%) 95%CI [7.6%;47.6%]
Not determined	0 (0%) 95%CI [0%;35.4%]	1 (7.1%) 95%CI [1.3%;31.5%]
Missing	2	0
VA (ETDRS)		
≤35	0 (0%) 95%CI [0%;35.4%]	0 (0%) 95%CI [0%;22.8%]
36-69	1 (14.3%) 95%CI [2.6%;51.3%]	6 (46.2%) 95%CI [23.2%;70.9%]
≥70	6 (85.7%) 95%CI [48.7%;97.4%]	7 (53.8%) 95%CI [29.1%;76.8%]
NA	2	1
CST (in µm)		
Valid n (Missing)	8 (1)	11 (3)
Mean [95%CI]	428.38 [362.28;494.47]	298.82 [262.17;335.46]
Std. dev	101.16	69.96

Med [P25,P75]	410.50 [350.75;486.00]	270.00 [263.00;337.50]
Min / Max	308.00 / 579.00	211.00 / 443.00
IRF		
Present	5 (55.6%) 95%CI [26.7%;81.1%]	5 (35.7%) 95%CI [16.3%;61.2%]
Absent	4 (44.4%) 95%CI [18.9%;73.3%]	9 (64.3%) 95%CI [38.8%;83.7%]
Missing	0	0
SRF		
Present	4 (44.4%) 95%CI [18.9%;73.3%]	6 (42.9%) 95%CI [21.4%;67.4%]
Absent	5 (55.6%) 95%CI [26.7%;81.1%]	8 (57.1%) 95%CI [32.6%;78.6%]
Missing	0	0
SRF and/or IRF		
Present	7 (77.8%) 95%CI [45.3%;93.7%]	9 (64.3%) 95%CI [38.8%;83.7%]
Absent	2 (22.2%) 95%CI [6.3%;54.7%]	5 (35.7%) 95%CI [16.3%;61.2%]
Missing	0	0
Sub-RPE fluid		
Present	6 (66.7%) 95%CI [35.4%;87.9%]	7 (50.0%) 95%CI [26.8%;73.2%]

Absent	3 (33.3%) 95%CI [12.1%;64.6%]	7 (50.0%) 95%CI [26.8%;73.2%]
Missing	0	0
Geographic atrophy		
Yes	1 (11.1%) 95%CI [2.0%;43.5%]	0 (0%) 95%CI [0%;21.5%]
No	8 (88.9%) 95%CI [56.5%;98.0%]	12 (85.7%) 95%CI [60.1%;96.0%]
Unknown/inconclusive	0 (0%) 95%CI [0%;29.9%]	2 (14.3%) 95%CI [4.0%;39.9%]
Subretinal fibrosis		
Yes	3 (33.3%) 95%CI [12.1%;64.6%]	1 (7.1%) 95%CI [1.3%;31.5%]
No	6 (66.7%) 95%CI [35.4%;87.9%]	11 (78.6%) 95%CI [52.4%;92.4%]
Unknown/inconclusive	0 (0%) 95%CI [0%;29.9%]	2 (14.3%) 95%CI [4.0%;39.9%]

Abbreviations: CI: confidence interval; Std. dev: standard deviation; Med: median; P25: percentile 25; P75: percentile 75; CST: central subfield thickness; FA: fluorescein angiography; ETDRS: Early Treatment Diabetic Retinopathy Study; IOI: intraocular inflammation.

[1]No statistical tests were performed due to the small sample size

Characterization of nAMD switchers: VA change from baseline

	Naïve Patients (n=9)	Switch patients (n=14)
VA change from baseline to time of switch (in ETDRS letters)[1]		
≤-15	0 (0%) 95%CI [0%;79.3%]	0 (0%) 95%CI [0%;39.0%]
]-15,-10]	0 (0%) 95%CI [0%;79.3%]	0 (0%) 95%CI [0%;39.0%]
]-10,-5]	0 (0%) 95%CI [0%;79.3%]	0 (0%) 95%CI [0%;39.0%]
]-5,5[	0 (0%) 95%CI [0%;79.3%]	4 (66.7%) 95%CI [30.0%;90.3%]
[5,10[	1 (100.0%) 95%CI [20.7%;100.0%]	2 (33.3%) 95%CI [9.7%;70.0%]
[10,15[	0 (0%) 95%CI [0%;79.3%]	0 (0%) 95%CI [0%;39.0%]
≥15	0 (0%) 95%CI [0%;79.3%]	0 (0%) 95%CI [0%;39.0%]
Missing	8	8

Abbreviations: CI: confidence interval; ETDRS: Early Treatment Diabetic Retinopathy Study.
[1]No statistical tests were performed due to the small sample size.

Characterization of nAMD switchers: CST change from baseline (in µm) at the time of switch

	Naïve Patients (n=9)	Switch patients (n=14)
CST change from baseline (in µm) at the time of switch[1]		
Valid n (Missing)	7 (2)	9 (5)
Mean [95%CI]	-126.43 [-183.27;-69.59]	-43.67 [-73.48;-13.86]
Std. dev	87.00	56.91
Med [P25,P75]	-129.00 [-157.50;-101.00]	-21.00 [-71.00;2.00]
Min / Max	-262.00 / 23.00	-165.00 / 7.00
Reduced CST at the time of switch vs baseline		
Yes	6 (85.7%) 95%CI [48.7%;97.4%]	6 (66.7%) 95%CI [35.4%;87.9%]
No	1 (14.3%) 95%CI [2.6%;51.3%]	3 (33.3%) 95%CI [12.1%;64.6%]
Missing	2	5

Abbreviations: CI: confidence interval; Std. dev: standard deviation; Med: median; P25: percentile 25; P75: percentile 75.
[1]No statistical tests were performed due to the small sample size.

Characterization of nAMD switchers: IRF, SRF and sub-RPE at the time of switch

	Naïve Patients (n=9)	Switch patients (n=14)
IRF at the time of switch		
Increased	0 (0%) 95%CI [0%;29.9%]	0 (0%) 95%CI [0%;25.9%]
Decreased	0 (0%) 95%CI [0%;29.9%]	1 (9.1%) 95%CI [1.6%;37.7%]
Maintained	2 (22.2%) 95%CI [6.3%;54.7%]	0 (0%) 95%CI [0%;25.9%]
Absent	7 (77.8%) 95%CI [45.3%;93.7%]	10 (90.9%) 95%CI [62.3%;98.4%]
Missing	0	3
In patients with presence of IRF baseline: IRF at the time of switch		
Increased	0 (0%) 95%CI [0.0%;43.4%]	0 (0%) 95%CI [0%;49.0%]
Decreased	0 (0%) 95%CI [0.0%;43.4%]	1 (25.0%) 95%CI [4.6%;69.9%]
Maintained	1 (20.0%) 95%CI [3.6%;62.4%]	0 (0%) 95%CI [0%;49.0%]
Absent	4 (80.0%) 95%CI [38.0%;96.4%]	3 (75.0%) 95%CI [30.0%;95.4%]
Missing	0	1

In patients with absence of IRF baseline: Stable of IRF at the time of switch	1 (25.0%) 95%CI [4.6%;69.9%]	0 (0%) 95%CI [0%;35.4%]
SRF at the time of switch		
Increased	1 (11.1%) 95%CI [2.0%;43.5%]	0 (0%) 95%CI [0%;24.2%]
Decreased	0 (0%) 95%CI [0%;29.9%]	0 (0%) 95%CI [0%;24.2%]
Maintained	2 (22.2%) 95%CI [6.3%;54.7%]	1 (8.3%) 95%CI [1.5%;35.4%]
Absent	6 (66.7%) 95%CI [35.4%;87.9%]	11 (91.7%) 95%CI [64.6%;98.5%]
Missing	0	2
In patients with presence of SRF baseline: SRF at the time of switch		
Increased	1 (25.0%) 95%CI [4.6%;69.9%]	0 (0%) 95%CI [0.0%;43.4%]
Decreased	0 (0%) 95%CI [0%;49.0%]	0 (0%) 95%CI [0.0%;43.4%]
Maintained	1 (25.0%) 95%CI [4.6%;69.9%]	0 (0%) 95%CI [0.0%;43.4%]
Absent	2 (50.0%) 95%CI [15.0%;85.0%]	5 (100.0%) 95%CI [57.0%;100.0%]
Missing	0	1
	1 (20.0%)	1 (14.3%)

In patients with absence of SRF baseline: Stable of SRF at the time of switch	95%CI [3.6%;62.4%]	95%CI [2.6%;51.3%]
Sub-RPE at the time of switch		
Increased	0 (0%) 95%CI [0%;29.9%]	2 (16.7%) 95%CI [4.7%;44.8%]
Decreased	0 (0%) 95%CI [0%;29.9%]	0 (0%) 95%CI [0%;24.2%]
Maintained	2 (22.2%) 95%CI [6.3%;54.7%]	3 (25.0%) 95%CI [8.9%;53.2%]
Absent	7 (77.8%) 95%CI [45.3%;93.7%]	7 (58.3%) 95%CI [32.0%;80.7%]
Missing	0	2
In patients with presence of sub-RPE baseline: Sub-RPE at the time of switch		
Increased	0 (0%) 95%CI [0%;39.0%]	1 (16.7%) 95%CI [3.0%;56.4%]
Decreased	0 (0%) 95%CI [0%;39.0%]	0 (0%) 95%CI [0%;39.0%]
Maintained	2 (33.3%) 95%CI [9.7%;70.0%]	2 (33.3%) 95%CI [9.7%;70.0%]
Absent	4 (66.7%) 95%CI [30.0%;90.3%]	3 (50.0%) 95%CI [18.8%;81.2%]
Missing	0	1
	0 (0%)	1 (16.7%)

In patients with absence of sub-RPE baseline: Stable of sub-RPE at the time of switch	95%CI [0%;56.1%]	95%CI [3.0%;56.4%]

Abbreviations: CI: confidence interval.

Characterization of nAMD switchers: CNV activity at time of switch

	Naïve Patients (n=9)	**Switch patients (n=13)**
Time to 1st reactivation (in days) of CNV since the 1st grading of inactivity during the study period		
Valid n (Missing)	4 (5)	5 (8)
Mean [95%CI]	133.50 [76.95;190.05]	109.80 [71.25;148.35]
Std. dev	86.55	70.91
Med [P25,P75]	127.00 [61.25;199.25]	133.00 [44.00;148.00]
Min / Max	56.00 / 224.00	29.00 / 195.00

Abbreviations: CI: confidence interval; Std. dev: standard deviation; Med: median; P25: percentile 25; P75: percentile 75.

Characterization of nAMD switchers: Full loading phase and injection rate at pre-switch period

	Naïve Patients (n=9)	Switch patients (n=14)
Number of injections in pre-switch period		
Valid n (Missing)	9 (0)	14 (0)
Mean [95%CI]	5.11 [3.53;6.69]	5.71 [3.54;7.89]
Std. dev	2.42	4.16
Med [P25,P75]	5.00 [3.00;7.00]	4.50 [3.00;9.00]
Min / Max	1.00 / 8.00	0.00 / 13.00
Full loading phase		
Yes	0 (0%) 95%CI [0%;29.9%]	0 (0%) 95%CI [0%;25.9%]
No	9 (100.0%) 95%CI [70.1%;100.0%]	11 (100.0%) 95%CI [74.1%;100.0%]
Missing	0	3

Abbreviations: CI: confidence interval; Std. dev: standard deviation; Med: median; P25: percentile 25; P75: percentile 75.

Switch patients from other anti-VEGF that prolonged injection intervals with brolucizumab

	Switch patients (n=25)
Nr. of injections in the last 12 months before switch	
Valid n (Missing)	25 (0)
Mean [95%CI]	5.16 [4.10;6.22]
Std. dev	2.70
Med [P25,P75]	5.00 [3.00;7.00]
Min / Max	0 / 11.00
Nr. of injections in the 12 months after switch	
Valid n (Missing)	25 (0)
Mean [95%CI]	5.08 [4.37;5.79]
Std. dev	1.80
Med [P25,P75]	5.00 [4.00;6.00]
Min / Max	2.00 / 8.00
Change in the nr of injections	
Equal or higher number of injections after switch	14 (56.0%) 95%CI [37.1%;73.3%]
Lower number of injections after switch	11 (44.0%) 95%CI [26.7%;62.9%]

Abbreviations: CI: confidence interval; Std. dev: standard deviation; Med: median; P25: percentile 25; P75: percentile 75.

6. Diagnostic OCT utilization and functional outcomes

Number of visits with/without OCT over Months 1-6, 1-12 and 13-24

	Naïve Patients (n=46)	Switch patients (n=35)
Nr. visits with OCT 1-6 M		
Valid n (Missing)	42 (0)	30 (0)
Mean [95%CI]	2.12 [1.59;2.65]	2.50 [2.12;2.88]
Std. dev	1.76	1.07
Med [P25,P75]	2.00 [1.00;3.00]	2.00 [2.00;3.00]
Min / Max	0 / 10.00	1.00 / 6.00
Nr. visits without OCT 1-6 M		
Valid n (Missing)	42 (0)	30 (0)
Mean [95%CI]	1.43 [0.99;1.87]	0.73 [0.36;1.11]
Std. dev	1.45	1.05
Med [P25,P75]	1.00 [0;2.00]	0 [0;1.00]
Min / Max	0 / 6.00	0 / 4.00
Nr. visits with OCT 1-12 M		
Valid n (Missing)	34 (0)	27 (0)
Mean [95%CI]	4.50 [3.50;5.50]	5.59 [4.81;6.38]
Std. dev	2.97	2.08
Med [P25,P75]	4.00 [3.00;6.00]	5.00 [4.00;7.00]
Min / Max	1.00 / 16.00	2.00 / 10.00
Nr. visits without OCT 1-12 M		

Valid n (Missing)	34 (0)	27 (0)
Mean [95%CI]	2.71 [1.86;3.55]	1.48 [0.73;2.23]
Std. dev	2.50	1.99
Med [P25,P75]	2.50 [0.25;4.75]	1.00 [0;2.00]
Min / Max	0 / 10.00	0 / 7.00
Nr. visits with OCT 13-14 M		
Valid n (Missing)	23 (0)	10 (0)
Mean [95%CI]	2.57 [1.84;3.29]	4.20 [2.61;5.79]
Std. dev	1.78	2.57
Med [P25,P75]	2.00 [1.50;3.50]	4.00 [2.25;4.75]
Min / Max	0 / 7.00	1.00 / 9.00
Nr. visits without OCT 13-14 M		
Valid n (Missing)	23 (0)	10 (0)
Mean [95%CI]	1.17 [0.54;1.81]	1.50 [0.12;2.88]
Std. dev	1.56	2.22
Med [P25,P75]	0 [0;2.50]	0 [0;3.25]
Min / Max	0 / 5.00	0 / 5.00

Abbreviations: CI: confidence interval; Std. dev: standard deviation; Med: median; P25: percentile 25; P75: percentile 75.

Association between number of OCT and CNV activity at month 6

	Naïve Patients (n=25)			Switch patients (n=23)		
	Nr. OCT (0-1) (n=13)	**Nr. OCT (2-3) (n=3)**	**Nr. OCT (≥4) (n=9)**	**Nr. OCT (0-1) (n=17)**	**Nr. OCT (2-3) (n=4)**	**Nr. OCT (≥4) (n=2)**
CNV active	0 (0%) 95%CI [0%;22.8%]	0 (0%) 95%CI [0%;65.8%]	3 (60.0%) 95%CI [23.0%;88.2%]	3 (17.6%) 95%CI [6.2%;41.0%]	2 (100.0%) 95%CI [34.0%;100.0%]	2 (100.0%) 95%CI [34.0%;100.0%]
CNV active (only SRF)	3 (23.1%) 95%CI [8.2%;50.3%]	0 (0%) 95%CI [0%;65.8%]	1 (20.0%) 95%CI [3.6%;62.4%]	4 (23.5%) 95%CI [9.6%;47.3%]	0 (0%) 95%CI [0%;65.8%]	0 (0%) 95%CI [0%;65.8%]
CNV active (only IRF)	4 (30.8%) 95%CI [13.0%;57.6%]	0 (0%) 95%CI [0%;65.8%]	0 (0%) 95%CI [0.0%;43.4%]	2 (11.8%) 95%CI [3.3%;34.3%]	0 (0%) 95%CI [0%;65.8%]	0 (0%) 95%CI [0%;65.8%]
CNV inactive	6 (46.2%) 95%CI [23.0%;70.9%]	2 (100.0%) 95%CI [34.0%;100.0%]	1 (20.0%) 95%CI [3.6%;62.4%]	8 (47.1%) 95%CI [26.0%;69.0%]	0 (0%) 95%CI [0%;65.8%]	0 (0%) 95%CI [0%;65.8%]
Missing	0	1	4	0	2	0

Abbreviations: CI: confidence interval.

Association between number of OCT and CNV activity at month 9

	Naïve Patients (n=21)			Switch patients (n=20)		
	Nr. OCT (0-1) (n=3)	**Nr. OCT (2-3) (n=8)**	**Nr. OCT (≥4) (n=10)**	**Nr. OCT (0-1) (n=1)**	**Nr. OCT (2-3) (n=9)**	**Nr. OCT (≥4) (n=10)**
CNV active	3 (100.0%) 95%CI [43.9%;100.0%]	2 (33.3%) 95%CI [9.7%;70.0%]	0 (0%) 95%CI [0%;29.9%]	1 (100.0%) 95%CI [20.7%;100.0%]	0 (0%) 95%CI [0%;32.4%]	1 (11.1%) 95%CI [2.0%;43.5%]

CNV active (only SRF)	0 (0%) 95%CI [0%;56.1%]	2 (33.3%) 95%CI [9.7%;70.0%]	2 (22.2%) 95%CI [6.3%;54.7%]	0 (0%) 95%CI [0%;79.3%]	1 (12.5%) 95%CI [2.2%;47.1%]	4 (44.4%) 95%CI [18.9%;73.3%]
CNV active (only IRF)	0 (0%) 95%CI [0%;56.1%]	0 (0%) 95%CI [0%;39.0%]	0 (0%) 95%CI [0%;29.9%]	0 (0%) 95%CI [0%;79.3%]	2 (25.0%) 95%CI [7.1%;59.1%]	0 (0%) 95%CI [0%;29.9%]
CNV inactive	0 (0%) 95%CI [0%;56.1%]	2 (33.3%) 95%CI [9.7%;70.0%]	7 (77.8%) 95%CI [45.3%;93.7%]	0 (0%) 95%CI [0%;79.3%]	5 (62.5%) 95%CI [30.6%;86.3%]	4 (44.4%) 95%CI [18.9%;73.3%]
Missing	0	2	1	0	1	1

Abbreviations: CI: confidence interval.

Association between number of OCT and CNV activity at month 12

	Naïve Patients (n=29)			**Switch patients (n=22)**		
	Nr. OCT (0-1) (n=4)	**Nr. OCT (2-3) (n=8)**	**Nr. OCT (≥4) (n=17)**	**Nr. OCT (0-1) (n=0)**	**Nr. OCT (2-3) (n=3)**	**Nr. OCT (≥4) (n=19)**
CNV active	4 (100.0%) 95%CI [51.0%;100.0%]	3 (50.0%) 95%CI [18.8%;81.2%]	3 (21.4%) 95%CI [7.6%;47.6%]	0 (NA%) 95%CI [NA%;NA%]	1 (50.0%) 95%CI [9.5%;90.5%]	7 (38.9%) 95%CI [20.3%;61.4%]
CNV active (only SRF)	0 (0%) 95%CI [0%;49.0%]	0 (0%) 95%CI [0%;39.0%]	2 (14.3%) 95%CI [4.0%;39.9%]	0 (NA%) 95%CI [NA%;NA%]	0 (0%) 95%CI [0%;65.8%]	4 (22.2%) 95%CI [9.0%;45.2%]
CNV active (only IRF)	0 (0%) 95%CI [0%;49.0%]	1 (16.7%) 95%CI [3.0%;56.4%]	2 (14.3%) 95%CI [4.0%;39.9%]	0 (NA%) 95%CI [NA%;NA%]	1 (50.0%) 95%CI [9.5%;90.5%]	2 (11.1%) 95%CI [3.1%;32.8%]
CNV inactive	0 (0%)	2 (33.3%)	7 (50.0%)	0 (NA%)	0 (0%)	5 (27.8%)

	95%CI [0%;49.0%]	95%CI [9.7%;70.0%]	95%CI [26.8%;73.2%]	95%CI [NA%;NA%]	95%CI [0%;65.8%]	95%CI [12.5%;50.9%]
Missing	0	2	3	0	1	1

Abbreviations: CI: confidence interval.

Association between number of OCT and CNV activity at month 18

	Naïve Patients (n=16)		**Switch patients (n=19)**	
	Nr. OCT (2-3) (n=5)	**Nr. OCT (≥4) (n=11)**	**Nr. OCT (2-3) (n=1)**	**Nr. OCT (≥4) (n=18)**
CNV active	2 (66.7%) 95%CI [20.8%;93.9%]	3 (33.3%) 95%CI [12.1%;64.6%]	1 (100.0%) 95%CI [20.7%;100.0%]	5 (31.2%) 95%CI [14.2%;55.6%]
CNV active (only SRF)	1 (33.3%) 95%CI [6.1%;79.2%]	2 (22.2%) 95%CI [6.3%;54.7%]	0 (0%) 95%CI [0%;79.3%]	3 (18.8%) 95%CI [6.6%;43.0%]
CNV active (only IRF)	0 (0%) 95%CI [0%;56.1%]	1 (11.1%) 95%CI [2.0%;43.5%]	0 (0%) 95%CI [0%;79.3%]	2 (12.5%) 95%CI [3.5%;36.0%]
CNV inactive	0 (0%) 95%CI [0%;56.1%]	3 (33.3%) 95%CI [12.1%;64.6%]	0 (0%) 95%CI [0%;79.3%]	6 (37.5%) 95%CI [18.5%;61.4%]
Missing	2	2	0	2

Abbreviations: CI: confidence interval.

Association between number of OCT and CNV activity at month 24

	Naïve Patients (n=6)	**Switch patients (n=3)**
	Nr. OCT (≥4) (n=6)	**Nr. OCT (≥4) (n=3)**
CNV active	3 (60.0%)	2 (66.7%)

	95%CI [23.0%;88.2%]	95%CI [21.0%;93.9%]
CNV active (only SRF)	1 (20.0%)	0 (0%)
	95%CI [3.6%;62.4%]	95%CI [0%;56.1%]
CNV active (only IRF)	0 (0%)	1 (33.3%)
	95%CI [0.0%;43.4%]	95%CI [6.1%;79.2%]
CNV inactive	1 (20.0%)	0 (0%)
	95%CI [3.6%;62.4%]	95%CI [0%;56.1%]
Missing	1	0

Abbreviations: CI: confidence interval.

Association between number of OCT and VA change from baseline to months 6, 9 and 12 (in ETDRS letters)

	Naïve Patients (n=25)			**Switch patients (n=23)**		
	Nr. OCT (≥4) (n=6)	**Nr. OCT (0-1) (n=6)**	**Nr. OCT (2-3) (n=13)**	**Nr. OCT (≥4) (n=2)**	**Nr. OCT (0-1) (n=3)**	**Nr. OCT (2-3) (n=18)**
VA change (in EDTRS letters) in 6M from baseline*						
≤-15	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (NA%)	0 (0%)
	95%CI [0%;65.8%]	95%CI [0%;79.3%]	95%CI [0%;32.4%]	95%CI [0%;65.8%]	95%CI [NA%;NA%]	95%CI [0%;32.4%]
]-15,-10]	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (NA%)	0 (0%)
	95%CI [0%;65.8%]	95%CI [0%;79.3%]	95%CI [0%;32.4%]	95%CI [0%;65.8%]	95%CI [NA%;NA%]	95%CI [0%;32.4%]
]-10,-5]	0 (0%)	0 (0%)	1 (12.5%)	0 (0%)	0 (NA%)	0 (0%)
	95%CI [0%;65.8%]	95%CI [0%;79.3%]	95%CI [2.2%;47.1%]	95%CI [0%;65.8%]	95%CI [NA%;NA%]	95%CI [0%;32.4%]
]-5,5[	1 (50.0%)	0 (0%)	4 (50.0%)	1 (50.0%)	0 (NA%)	5 (62.5%)
	95%CI [9.5%;90.5%]	95%CI [0%;79.3%]	95%CI [21.5%;78.5%]	95%CI [9.5%;90.5%]	95%CI [NA%;NA%]	95%CI [30.6%;86.3%]
[5,10[	0 (0%)	0 (0%)	1 (12.5%)	1 (50.0%)	0 (NA%)	1 (12.5%)

	95%CI [0%;65.8%]	95%CI [0%;79.3%]	95%CI [2.2%;47.1%]	95%CI [9.5%;90.5%]	95%CI [NA%;NA%]	95%CI [2.2%;47.1%]
[10,15[	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (NA%)	1 (12.5%)
	95%CI [0%;65.8%]	95%CI [0%;79.3%]	95%CI [0%;32.4%]	95%CI [0%;65.8%]	95%CI [NA%;NA%]	95%CI [2.2%;47.1%]
≥15	1 (50.0%)	1 (100.0%)	2 (25.0%)	0 (0%)	0 (NA%)	1 (12.5%)
	95%CI [9.5%;90.5%]	95%CI [20.7%;100.0%]	95%CI [7.1%;59.1%]	95%CI [0%;65.8%]	95%CI [NA%;NA%]	95%CI [2.2%;47.1%]
Missing	4	5	5	0	3	10
		Naïve Patients (n=21)			**Switch patients (n=20)**	
VA change (in ETDRS letters) in 9M from baseline	**Nr. OCT (≥4) (n=10)**	**Nr. OCT (0-1) (n=3)**	**Nr. OCT (2-3) (n=8)**	**Nr. OCT (≥4) (n=10)**	**Nr. OCT (0-1) (n=1)**	**Nr. OCT (2-3) (n=9)**
≤-15	0 (0%)	0 (NA%)	0 (0%)	0 (0%)	0 (NA%)	0 (0%)
	95%CI [0%;65.8%]	95%CI [NA%;NA%]	95%CI [0%;65.8%]	95%CI [0%;39.0%]	95%CI [NA%;NA%]	95%CI [0%;39.0%]
]-15,-10]	0 (0%)	0 (NA%)	0 (0%)	0 (0%)	0 (NA%)	1 (16.7%)
	95%CI [0%;65.8%]	95%CI [NA%;NA%]	95%CI [0%;65.8%]	95%CI [0%;39.0%]	95%CI [NA%;NA%]	95%CI [3.0%;56.4%]
]-10,-5]	0 (0%)	0 (NA%)	0 (0%)	0 (0%)	0 (NA%)	1 (16.7%)
	95%CI [0%;65.8%]	95%CI [NA%;NA%]	95%CI [0%;65.8%]	95%CI [0%;39.0%]	95%CI [NA%;NA%]	95%CI [3.0%;56.4%]
]-5,5[	0 (0%)	0 (NA%)	1 (50.0%)	5 (83.3%)	0 (NA%)	2 (33.3%)
	95%CI [0%;65.8%]	95%CI [NA%;NA%]	95%CI [9.5%;90.5%]	95%CI [43.6%;97.0%]	95%CI [NA%;NA%]	95%CI [9.7%;70.0%]
[5,10[	0 (0%)	0 (NA%)	0 (0%)	1 (16.7%)	0 (NA%)	2 (33.3%)
	95%CI [0%;65.8%]	95%CI [NA%;NA%]	95%CI [0%;65.8%]	95%CI [3.0%;56.4%]	95%CI [NA%;NA%]	95%CI [9.7%;70.0%]
[10,15[	2 (100.0%)	0 (NA%)	0 (0%)	0 (0%)	0 (NA%)	0 (0%)
	95%CI [34.2%;100.0%]	95%CI [NA%;NA%]	95%CI [0%;65.8%]	95%CI [0%;39.0%]	95%CI [NA%;NA%]	95%CI [0%;39.0%]
≥15	0 (0%)	0 (NA%)	1 (50.0%)	0 (0%)	0 (NA%)	0 (0%)
	95%CI [0%;65.8%]	95%CI [NA%;NA%]	95%CI [9.5%;90.5%]	95%CI [0%;39.0%]	95%CI [NA%;NA%]	95%CI [0%;39.0%]
Missing	8	3	6	4	1	3
		Naïve Patients (n=29)			**Switch patients (n=22)**	

VA change (in ETDRS letters) in 12M from baseline	Nr. OCT (≥4) (n=17)	Nr. OCT (0-1) (n=4)	Nr. OCT (2-3) (n=8)	Nr. OCT (≥4) (n=19)	Nr. OCT (0-1) (n=0)	Nr. OCT (2-3) (n=3)
≤-15	1 (16.7%) 95%CI [3.0%;56.4%]	0 (NA%) 95%CI [NA%;NA%]	0 (0%) 95%CI [0%;56.1%]	0 (0%) 95%CI [0%;32.4%]	0 (NA%) 95%CI [NA%;NA%]	1 (100.0%) 95%CI [20.7%;100.0%]
]-15,-10]	0 (0%) 95%CI [0%;39.0%]	0 (NA%) 95%CI [NA%;NA%]	0 (0%) 95%CI [0%;56.1%]	0 (0%) 95%CI [0%;32.4%]	0 (NA%) 95%CI [NA%;NA%]	0 (0%) 95%CI [0%;79.3%]
]-10,-5]	1 (16.7%) 95%CI [3.0%;56.4%]	0 (NA%) 95%CI [NA%;NA%]	0 (0%) 95%CI [0%;56.1%]	1 (12.5%) 95%CI [2.2%;47.1%]	0 (NA%) 95%CI [NA%;NA%]	0 (0%) 95%CI [0%;79.3%]
]-5,5[	1 (16.7%) 95%CI [3.0%;56.4%]	0 (NA%) 95%CI [NA%;NA%]	2 (66.7%) 95%CI [20.8%;93.9%]	5 (62.5%) 95%CI [30.6%;86.3%]	0 (NA%) 95%CI [NA%;NA%]	0 (0%) 95%CI [0%;79.3%]
[5,10[	1 (16.7%) 95%CI [3.0%;56.4%]	0 (NA%) 95%CI [NA%;NA%]	0 (0%) 95%CI [0%;56.1%]	1 (12.5%) 95%CI [2.2%;47.1%]	0 (NA%) 95%CI [NA%;NA%]	0 (0%) 95%CI [0%;79.3%]
[10,15[	2 (33.3%) 95%CI [9.7%;70.0%]	0 (NA%) 95%CI [NA%;NA%]	0 (0%) 95%CI [0%;56.1%]	0 (0%) 95%CI [0%;32.4%]	0 (NA%) 95%CI [NA%;NA%]	0 (0%) 95%CI [0%;79.3%]
≥15	0 (0%) 95%CI [0%;39.0%]	0 (NA%) 95%CI [NA%;NA%]	1 (33.3%) 95%CI [6.1%;79.2%]	1 (12.5%) 95%CI [2.2%;47.1%]	0 (NA%) 95%CI [NA%;NA%]	0 (0%) 95%CI [0%;79.3%]
Missing	11	4	5	11	0	2

Abbreviations: ETDRS: Early Treatment Diabetic Retinopathy Study; CI: confidence interval.
*No statistical tests were applied due to the elevated number of missing values.

Association between number of OCT and VA change from baseline to month 18 (in ETDRS letters)

	Naïve Patients (n=16)*		Switch patients (n=19)*	
	Nr. OCT (≥4) (n=11)	Nr. OCT (2-3) (n=5)	Nr. OCT (≥4) (n=18)	Nr. OCT (2-3) (n=1)
VA change (in ETDRS letters) in 18M from baseline				
≤-15	1 (20.0%) 95%CI [3.6%;62.4%]	0 (NA%) 95%CI [NA%;NA%]	2 (28.6%) 95%CI [8.2%;64.1%]	0 (NA%) 95%CI [NA%;NA%]
]-15,-10]	0 (0%) 95%CI [0.0%;43.4%]	0 (NA%) 95%CI [NA%;NA%]	0 (0%) 95%CI [0%;35.4%]	0 (NA%) 95%CI [NA%;NA%]
]-10,-5]	0 (0%) 95%CI [0.0%;43.4%]	0 (NA%) 95%CI [NA%;NA%]	0 (0%) 95%CI [0%;35.4%]	0 (NA%) 95%CI [NA%;NA%]
]-5,5[	3 (60.0%) 95%CI [23.0%;88.2%]	0 (NA%) 95%CI [NA%;NA%]	3 (42.9%) 95%CI [1.6e+01%;75.0%]	0 (NA%) 95%CI [NA%;NA%]
[5,10[	0 (0%) 95%CI [0.0%;43.4%]	0 (NA%) 95%CI [NA%;NA%]	1 (14.3%) 95%CI [2.6%;51.3%]	0 (NA%) 95%CI [NA%;NA%]
[10,15[	0 (0%) 95%CI [0.0%;43.4%]	0 (NA%) 95%CI [NA%;NA%]	0 (0%) 95%CI [0%;35.4%]	0 (NA%) 95%CI [NA%;NA%]
≥15	1 (20.0%) 95%CI [3.6%;62.4%]	0 (NA%) 95%CI [NA%;NA%]	1 (14.3%) 95%CI [2.6%;51.3%]	0 (NA%) 95%CI [NA%;NA%]
Missing	6	5	11	1

Abbreviations: ETDRS: Early Treatment Diabetic Retinopathy Study; CI: confidence interval.
*No statistical tests were applied due to the elevated number of missing values.

Association between number of OCT and VA change from baseline to month 24 (in ETDRS letters)*

	Naïve Patients	Switch patients
	Nr. OCT (≥4) (n=6)	Nr. OCT (≥4) (n=3)
VA change (in ETDRS letters) in 24M from baseline		
≤-15	0 (0%) 95%CI [0%;49.0%]	1 (100.0%) 95%CI [20.7%;100.0%]
]-15,-10]	0 (0%) 95%CI [0%;49.0%]	0 (0%) 95%CI [0%;79.3%]
]-10,-5]	0 (0%) 95%CI [0%;49.0%]	0 (0%) 95%CI [0%;79.3%]
]-5,5[	1 (25.0%) 95%CI [4.6%;69.9%]	0 (0%) 95%CI [0%;79.3%]
[5,10[	1 (25.0%) 95%CI [4.6%;69.9%]	0 (0%) 95%CI [0%;79.3%]
[10,15[	0 (0%) 95%CI [0%;49.0%]	0 (0%) 95%CI [0%;79.3%]
≥15	2 (50.0%) 95%CI [15.0%;85.0%]	0 (0%) 95%CI [0%;79.3%]
Missing	2	2

Abbreviations: ETDRS: Early Treatment Diabetic Retinopathy Study; CI: confidence interval.
*No statistical tests were applied due to the elevated number of missing values.

Association between number of OCT and number of injections during the months 1-6, 1-9, 1-12 and 13-24 of treatment with brolucizumab

	Naïve Patients (n=40)			Switch patients (n=30)		
	Nr. OCT (0-1) (n=16)	**Nr. OCT (2-3) (n=17)**	**Nr. OCT ≥4 (n=7)**	**Nr. OCT (0-1) (n=4)**	**Nr. OCT (2-3) (n=22)**	**Nr. OCT ≥4 (n=4)**
During months 1-6: Nr. brolucizumab injections						
Valid n (Missing)	16 (0)	17 (0)	7 (0)	4 (0)	22 (0)	4 (0)
Mean [95%CI]	2.06 [1.48;2.64]	2.71 [2.21;3.20]	3.00 [1.95;4.05]	2.25 [1.31;3.19]	2.36 [1.99;2.74]	2.75 [2.26;3.24]
Std. dev	1.18	1.05	1.41	0.96	0.90	0.50
Med [P25,P75]	2.00 [1.00;3.00]	3.00 [2.00;3.00]	4.00 [2.00;4.00]	2.50 [1.75;3.00]	2.00 [2.00;3.00]	3.00 [2.75;3.00]
Min / Max	0 / 4.00	1.00 / 5.00	1.00 / 4.00	1.00 / 3.00	1.00 / 5.00	2.00 / 3.00
	Naïve Patients (n=36)			**Switch Patients (n=30)**		
	Nr. OCT (0-1) (n=7)	**Nr. OCT (2-3) (n=15)**	**Nr. OCT ≥4 (n=14)**	**Nr. OCT (0-1) (n=1)**	**Nr. OCT (2-3) (n=13)**	**Nr. OCT ≥4 (n=16)**
During months 1-9: Nr. brolucizumab injections						
Valid n (Missing)	7 (0)	15 (0)	14 (0)	1 (0)	13 (0)	16 (0)
Mean [95%CI]	2.71 [1.79;3.64]	4.07 [3.48;4.66]	3.43 [2.56;4.29]	3.00 [NA;NA]	3.23 [2.68;3.78]	3.69 [2.91;4.46]
Std. dev	1.25	1.16	1.65	NA	1.01	1.58
Med [P25,P75]	2.00 [2.00;4.00]	4.00 [3.00;5.00]	4.00 [2.25;4.75]	3.00 [3.00;3.00]	3.00 [3.00;4.00]	4.00 [3.00;5.00]
Min / Max	1.00 / 4.00	2.00 / 6.00	1.00 / 6.00	3.00 / 3.00	2.00 / 5.00	1.00 / 7.00
	Naïve Patients (n=34)			**Switch Patients (n=27)**		
	Nr. OCT (0-1) (n=5)	**Nr. OCT (2-3) (n=9)**	**Nr. OCT ≥4 (n=20)**	**Nr. OCT (0-1) (n=0)**	**Nr. OCT (2-3) (n=4)**	**Nr. OCT ≥4 (n=23)**
During months 1-12: Nr. brolucizumab injections						
Valid n (Missing)	5 (0)	9 (0)	20 (0)	0 (0)	4 (0)	23 (0)

Mean [95%CI]	3.80 [1.90;5.70]	5.11 [4.01;6.22]	4.80 [3.82;5.78]	NA [NA;NA]	4.75 [2.05;7.45]	4.87 [4.12;5.62]
Std. dev	2.17	1.69	2.24	NA	2.75	1.84
Med [P25,P75]	5.00 [2.00;5.00]	5.00 [4.00;6.00]	5.00 [3.75;6.25]	NA [NA;NA]	4.50 [2.75;6.50]	5.00 [4.00;6.00]
Min / Max	1.00 / 6.00	3.00 / 8.00	0 / 9.00	NA / NA	2.00 / 8.00	1.00 / 8.00
	Naïve Patients (n=23)			**Switch Patients (n=10)**		
	Nr. OCT (0-1) (n=6)	**Nr. OCT (2-3) (n=11)**	**Nr. OCT ≥4 (n=6)**	**Nr. OCT (0-1) (n=1)**	**Nr. OCT (2-3) (n=3)**	**Nr. OCT ≥4 (n=6)**
During months 13-24: Nr. brolucizumab injections						
Valid n (Missing)	6 (0)	11 (0)	6 (0)	1 (0)	3 (0)	6 (0)
Mean [95%CI]	1.50 [0.19;2.81]	2.64 [1.57;3.70]	3.33 [1.93;4.73]	6.00 [NA;NA]	4.00 [2.04;5.96]	3.83 [2.90;4.77]
Std. dev	1.64	1.80	1.75	NA	1.73	1.17
Med [P25,P75]	1.00 [0.25;2.50]	2.00 [1.50;3.00]	3.50 [2.25;4.00]	6.00 [6.00;6.00]	5.00 [3.50;5.00]	4.00 [3.25;4.75]
Min / Max	0 / 4.00	1.00 / 6.00	1.00 / 6.00	6.00 / 6.00	2.00 / 5.00	2.00 / 5.00

Abbreviations: CI: confidence interval; Std. dev: standard deviation; Med: median; P25: percentile 25; P75: percentile 75.

7. Assess safety of brolucizumab during treatment

Number, nature, causes, severity, duration, treatment, resolution and outcome of AEs related to brolucizumab

	Naïve patients n=18	Switch patients n = 11
AE type		
AE	6 (33.3%) 95%CI [16.3%;56.3%]	3 (27.3%) 95%CI [9.7%;56.6%]
Ocular AE	2 (11.1%) 95%CI [3.1%;32.8%]	4 (36.4%) 95%CI [15.2%;64.6%]
Other AE not listed	10 (55.6%) 95%CI [33.7%;75.4%]	4 (36.4%) 95%CI [15.2%;64.6%]
Ocular AE		
Ocular AEs		
Blepharitis	1 (5.6%) 95%CI [1.0%;25.8%]	1 (9.1%) 95%CI [1.6%;37.7%]
Conjuctivitis	1 (5.6%) 95%CI [1.0%;25.8%]	0 (0.0%) 95%CI [0.0%;25.9%]
Vitreous floaters	0 (0.0%) 95%CI [0.0%;17.8%]	2 (18.2%) 95%CI [5.1%;47.7%]
Uveitis	0 (0.0%) 95%CI [0.0%;17.8%]	1 (9.1%) 95%CI [1.6%;37.7%]
Severity		
Mild	2 (100.0%) 95%CI [34.2%;100.0%]	3 (75.0%) 95%CI [30.1%;95.4%]
Moderate	0 (0%) 95%CI [0%;65.8%]	1 (25.0%) 95%CI [4.6%;69.9%]

Severe	0 (0%) 95%CI [0%;65.8%]	0 (0%) 95%CI [0%;49.0%]
Duration (days)		
Valid n (Missing)	2 (0)	4 (0)
Mean [95%CI]	47.50 [-8.36;103.36]	45.00 [13.27;76.73]
Std. dev	40.31	32.38
Med [P25,P75]	47.50 [33.25;61.75]	45.50 [32.75;57.75]
Min / Max	19.00 / 76.00	5.00 / 84.00
Serious AE		
Yes	0 (0%) 95%CI [0%;65.8%]	0 (0%) 95%CI [0%;49.0%]
No	2 (100.0%) 95%CI [34.2%;100.0%]	4 (100.0%) 95%CI [51.0%;100.0%]
Related to the drug of interest		
Yes	0 (0%) 95%CI [0%;65.8%]	3 (75.0%) 95%CI [30.1%;95.4%]
No	2 (100.0%) 95%CI [34.2%;100.0%]	1 (25.0%) 95%CI [4.6%;69.9%]
Loss of vision associated		
Yes	0 (0%) 95%CI [0%;65.8%]	1 (25.0%) 95%CI [4.6%;69.9%]
No	2 (100.0%) 95%CI [34.2%;100.0%]	3 (75.0%) 95%CI [30.1%;95.4%]
Action taken with Novartis product		
No action taken	2 (100.0%) 95%CI [34.2%;100.0%]	1 (25.0%) 95%CI [4.6%;69.9%]

Drug withdrawn	0 (0%) 95%CI [0%;65.8%]	3 (75.0%) 95%CI [30.1%;95.4%]
Drug interruption	0 (0%) 95%CI [0%;65.8%]	0 (0%) 95%CI [0%;49.0%]
Dose adjustment	0 (0%) 95%CI [0%;65.8%]	0 (0%) 95%CI [0%;49.0%]
Outcome		
Recovered without sequelae	2 (100.0%) 95%CI [34.2%;100.0%]	4 (100.0%) 95%CI [51.0%;100.0%]
Ongoing/Continuing	0 (0%) 95%CI [0%;65.8%]	0 (0%) 95%CI [0%;49.0%]
Recovered with sequelae	0 (0%) 95%CI [0%;65.8%]	0 (0%) 95%CI [0%;49.0%]
Lost to follow-up	0 (0%) 95%CI [0%;65.8%]	0 (0%) 95%CI [0%;49.0%]
Fatal	0 (0%) 95%CI [0%;65.8%]	0 (0%) 95%CI [0%;49.0%]
Not resolved	0 (0%) 95%CI [0%;65.8%]	0 (0%) 95%CI [0%;49.0%]
Non-Ocular AEs		
AE		
Lack of effectiveness	3 (16.7%) 95%CI [5.8%;41.4%]	2 (18.2%) 95%CI [5.1%;47.7%]
Headache	2 (11.1%) 95%CI [3.1%;32.8%]	0 (0.0%) 95%CI [0.0%;25.9%]
Pain Extremity	1 (5.6%)	0 (0.0%)

Cystitis	0 (0.0%) 0 (0.0%) 95%CI [0.0%;17.8%]	95%CI [0.0%;25.9%] 1 (9.1%) 95%CI [1.6%;37.7%]
Severity		
Mild	4 (66.7%) 95%CI [30.0%;90.3%]	3 (100.0%) 95%CI [43.9%;100.0%]
Moderate	2 (33.3%) 95%CI [9.7%;70.0%]	0 (0%) 95%CI [0%;56.1%]
Severe	0 (0%) 95%CI [0%;39.0%]	0 (0%) 95%CI [0%;56.1%]
Duration (days)		
Valid n (Missing)	2 (4)	2 (1)
Mean [95%CI]	15.50 [2.49;28.51]	70.00 [58.80;81.20]
Std. dev	16.26	9.90
Med [P25,P75]	15.50 [9.75;21.25]	70.00 [66.50;73.50]
Min / Max	4.00 / 27.00	63.00 / 77.00
Serious AE		
Yes	0 (0%) 95%CI [0%;39.0%]	0 (0%) 95%CI [0%;56.1%]
No	6 (100.0%) 95%CI [61.0%;100.0%]	3 (100.0%) 95%CI [43.9%;100.0%]
Related to the drug of interest		
Yes	4 (66.7%) 95%CI [30.0%;90.3%]	2 (66.7%) 95%CI [20.8%;93.9%]
No	2 (33.3%) 95%CI [9.7%;70.0%]	1 (33.3%) 95%CI [6.1%;79.2%]

Loss of vision associated		
Yes	1 (16.7%) 95%CI [3.0%;56.4%]	0 (0%) 95%CI [0%;65.8%]
No	5 (83.3%) 95%CI [43.6%;97.0%]	2 (100.0%) 95%CI [34.2%;100.0%]
Missing	0	1
Action taken with Novartis product		
No action taken	3 (50.0%) 95%CI [18.8%;81.2%]	1 (33.3%) 95%CI [6.1%;79.2%]
Drug interruption	0 (0%) 95%CI [0%;39.0%]	0 (0%) 95%CI [0%;56.1%]
Dose adjustment	0 (0%) 95%CI [0%;39.0%]	0 (0%) 95%CI [0%;56.1%]
Drug withdrawn	3 (50.0%) 95%CI [18.8%;81.2%]	2 (66.7%) 95%CI [20.8%;93.9%]
Outcome		
Recovered without sequelae	3 (50.0%) 95%CI [18.8%;81.2%]	2 (66.7%) 95%CI [20.8%;93.9%]
Lost to follow-up	3 (50.0%) 95%CI [18.8%;81.2%]	0 (0%) 95%CI [0%;56.1%]
Ongoing/Continuing	0 (0%) 95%CI [0%;39.0%]	1 (33.3%) 95%CI [6.1%;79.2%]
Recovered with sequelae	0 (0%) 95%CI [0%;39.0%]	0 (0%) 95%CI [0%;56.1%]
Fatal	0 (0%) 95%CI [0%;39.0%]	0 (0%) 95%CI [0%;56.1%]

Not resolved	0 (0%) 95%CI [0%;39.0%]	0 (0%) 95%CI [0%;56.1%]
Other AE not listed		
AE		
Adverse reaction to Betadine® used in the injection procedure	1 (5.6%) 95%CI [1.0%;25.8%]	0 (0.0%) 95%CI [0.0%;25.9%]
TIA	1 (5.6%) 95%CI [1.0%;25.8%]	0 (0.0%) 95%CI [0.0%;25.9%]
Cardiorespiractory arrest	1 (5.6%) 95%CI [1.0%;25.8%]	0 (0.0%) 95%CI [0.0%;25.9%]
Circle of light	1 (5.6%) 95%CI [1.0%;25.8%]	0 (0.0%) 95%CI [0.0%;25.9%]
Femur Fracture	1 (5.6%) 95%CI [1.0%;25.8%]	0 (0.0%) 95%CI [0.0%;25.9%]
Hyphema	1 (5.6%) 95%CI [1.0%;25.8%]	0 (0.0%) 95%CI [0.0%;25.9%]
Orbital fracture	1 (5.6%) 95%CI [1.0%;25.8%]	0 (0.0%) 95%CI [0.0%;25.9%]
Posterior Vitreous Detachment	1 (5.6%) 95%CI [1.0%;25.8%]	0 (0.0%) 95%CI [0.0%;25.9%]
Shoulder fracture	1 (5.6%) 95%CI [1.0%;25.8%]	0 (0.0%) 95%CI [0.0%;25.9%]
Stroke symptoms	1 (5.6%) 95%CI [1.0%;25.8%]	0 (0.0%) 95%CI [0.0%;25.9%]
Deposits on the intraocular lens	0 (0.0%) 95%CI [0.0%;17.8%]	1 (9.1%) 95%CI [1.6%;37.7%]

Endothelial precipitates	0 (0.0%) 95%CI [0.0%;17.8%]	1 (9.1%) 95%CI [1.6%;37.7%]
Hemorragic stroke	0 (0.0%) 95%CI [0.0%;17.8%]	1 (9.1%) 95%CI [1.6%;37.7%]
Worsening symptoms of dementia	0 (0.0%) 95%CI [0.0%;17.8%]	1 (9.1%) 95%CI [1.6%;37.7%]
Severity		
Mild	4 (40.0%) 95%CI [16.8%;68.7%]	0 (0%) 95%CI [0%;49.0%]
Moderate	3 (30.0%) 95%CI [10.8%;60.3%]	3 (75.0%) 95%CI [30.1%;95.4%]
Severe	3 (30.0%) 95%CI [10.8%;60.3%]	1 (25.0%) 95%CI [4.6%;69.9%]
Duration (days)		
Valid n (Missing)	6 (4)	3 (1)
Mean [95%CI]	25.67 [2.20;49.13]	13.00 [-0.58;26.58]
Std. dev	37.86	13.86
Med [P25,P75]	13.00 [9.50;16.50]	5.00 [5.00;17.00]
Min / Max	0 / 102.00	5.00 / 29.00
Serious AE		
Yes	3 (30.0%) 95%CI [10.8%;60.3%]	1 (25.0%) 95%CI [4.6%;69.9%]
No	7 (70.0%) 95%CI [39.7%;89.2%]	3 (75.0%) 95%CI [30.1%;95.4%]
Related to the drug of interest		
Yes	1 (10.0%)	3 (75.0%)

	95%CI [1.8%;40.4%]	95%CI [30.1%;95.4%]
No	9 (90.0%) 95%CI [59.6%;98.2%]	1 (25.0%) 95%CI [4.6%;69.9%]
Loss of vision associated		
Yes	1 (10.0%) 95%CI [1.8%;40.4%]	0 (0%) 95%CI [0%;49.0%]
No	9 (90.0%) 95%CI [59.6%;98.2%]	4 (100.0%) 95%CI [51.0%;100.0%]
Action taken with Novartis product		
No action taken	7 (70.0%) 95%CI [4.0e+01%;89.2%]	0 (0%) 95%CI [0%;49.0%]
Drug interruption	2 (20.0%) 95%CI [5.7e+00%;51.0%]	1 (25.0%) 95%CI [4.6e+00%;69.9%]
Drug withdrawn	1 (10.0%) 95%CI [1.8e+00%;40.4%]	3 (75.0%) 95%CI [3.0e+01%;95.4%]
Dose adjustment	0 (0%) 95%CI [2.0e-15%;27.8%]	0 (0%) 95%CI [0%;49.0%]
Outcome		
Recovered without sequelae	7 (70.0%) 95%CI [4.0e+01%;89.2%]	3 (75.0%) 95%CI [3.0e+01%;95.4%]
Ongoing/Continuing	1 (10.0%) 95%CI [1.8e+00%;40.4%]	1 (25.0%) 95%CI [4.6e+00%;69.9%]
Lost to follow-up	1 (10.0%) 95%CI [1.8e+00%;40.4%]	0 (0%) 95%CI [0%;49.0%]
Fatal	1 (10.0%) 95%CI [1.8e+00%;40.4%]	0 (0%) 95%CI [0%;49.0%]

Recovered with sequelae	0 (0%) 95%CI [2.0e-15%;27.8%]	0 (0%) 95%CI [0%;49.0%]
Not resolved	0 (0%) 95%CI [2.0e-15%;27.8%]	0 (0%) 95%CI [0%;49.0%]

Abbreviations: CI: confidence interval; Std. dev: standard deviation; Med: median; P25: percentile 25; P75: percentile 75; TIA: transient ischemic attack.

Safety Results

Refer to Secondary Outcome Results.

Adverse Events by System Organ Class

Not applicable

Most Frequently Reported AEs Overall by Preferred Term n (%)

Not applicable

Serious Adverse Events and Deaths

Not applicable

Other Relevant Findings

Not applicable

Conclusion

Despite its limitations, the *BlueSky* study offers valuable insights into the real-world use of brolucizumab for neovascular age-related macular degeneration (nAMD) patients in Portugal, highlighting differences between treatment-naïve and switch patients. Key findings, such as fluid resolution, central subfield thickness (CST) reduction, and visual acuity (VA) gains, align with existing literature. However, high dropout rates, small sample size, and missing data suggests these conclusions should be interpreted cautiously. Larger, multicenter studies are needed to validate these trends and enhance understanding of brolucizumab's real-world efficacy. Nonetheless, the study provides important evidence for clinicians, especially regarding extended injection intervals and managing switch patients.

Date of Clinical Study Report

03 February 2025