NOVARTIS

Sponsor

Novartis Pharmaceuticals

Generic Drug Name

Brolucizumab / RTH258

Trial Indication(s)

Suboptimal anatomically controlled neovascular age-related macular degeneration

Protocol Number

CRTH258ADE01

Protocol Title

A 52-week, two arm, randomized, open-label, multicenter study assessing the efficacy and safety of two different brolucizumab 6 mg dosing regimens for patients with suboptimal anatomically controlled neovascular age-related macular degeneration

Clinical Trial Phase

Phase 4

Phase of Drug Development

Phase IV

Study Start/End Dates

Study Start Date: July 13, 2021 (Actual)

Primary Completion Date: January 31, 2024 (Actual)
Study Completion Date: January 31, 2024 (Actual)

Reason for Termination (If applicable)

Enrollment was early terminated by Amendment 2 (dated 30-Nov-2022) due to a slow recruitment when only 47 of the initially planned 490 patients were actually enrolled since Jul 2021. All patients randomized by then were allowed to stay in the study and continue study treatment until week 52.

Study Design/Methodology

This study was a 52-week randomized, open-label, multi-center, two-arm study for pretreated patients with suboptimal anatomically controlled neovascular, age-related macular degeneration (nAMD). Patients who consented were screened to evaluate eligibility. Eligible patients were randomized in a 1:1 ratio to one of the two treatment arms:

- Brolucizumab 6 mg “loading arm”: 3 x 4-weekly initial injections followed by an injection every 12 weeks
- Brolucizumab 6 mg “non-loading arm”: one initial injection followed by an injection every 12 weeks

There were three periods in this study:

- Screening period: from day -14 to baseline
- Open-label treatment period: from baseline (day 1) to week 48
- Post-treatment follow-up period: from week 48 to week 52

In both study arms, treatment intervals after the initiation phase were either 8 weeks or 12 weeks depending on disease activity status. More frequent injections, i.e., treatment intervals of < 8 weeks were not allowed after the initiation phase.

The initial plan was to screen approximately 598 adult patients and randomize approximately 490 patients. At the time of early termination, 88 patients were enrolled and 52 randomized (25 to the loading arm and 27 to the non-loading arm). As a consequence of the low patient number, the primary endpoint and all analyses were performed in a purely descriptive manner.

NOVARTIS

Centers

19 centers in 2 countries: Germany(16), Switzerland(3)

Objectives:

The objective of this clinical study report is to provide results of the final analysis of the terminated study, when all patients randomized by 30-Nov-2022 had had the opportunity to complete the 52-week study period.

Primary objective was:

- To evaluate the difference in best corrected visual activity (BCVA) change from baseline for brolucizumab 6 mg with one (initial) injection followed by treatment every 12 weeks as compared to brolucizumab 6 mg with three monthly loading injections followed by treatment every 12 weeks.
  - Endpoint: Mean change in BCVA from baseline to mean of visits at weeks 40 to 52.

Secondary objectives were:

- To evaluate treatment interval prolongation compared to previous treatment
  - Endpoint: Mean treatment interval (overall as well as per study group comparing treatment intervals from baseline to week 52 in the study vs. 24 weeks to baseline prior to enrollment)
  - Endpoint: Rate of patients (overall and per group) with prolonged interval compared to mean treatment interval in last 24 weeks prior to enrollment
- To estimate the proportions of patients maintained at every 12 weeks treatment frequency in the two brolucizumab groups
  - Endpoint: Comparison of proportions of patients maintained at a q12w interval at week 52 between the two arms
  - Endpoint: Distributions of patients at q8w/q12w intervals from baseline to week 52
- To evaluate the functional outcomes comparing the two brolucizumab groups
  - Endpoint: Average change in BCVA from baseline to week 52
  - Endpoint: Proportions of patients with BCVA improvements of ≥5, ≥ 10, and ≥ 15 letters from baseline to week 52

- Endpoint: Proportions of patients with BCVA ≥ 69 letters at week 52
- Endpoint: Mean change in BCVA from baseline to mean of visits at week 16 to week 28

- To evaluate the anatomical outcomes comparing the two brolucizumab groups
  - Endpoint: Change from baseline in Central subfield thickness (CST) as assessed by spectral domain optical coherence tomography (SD-OCT) per visit up to week 52
  - Endpoint: Absence of Intraretinal fluid (IRF), Subretinal fluid (SRF), and sub- retinal pigment epithelium (RPE) fluid as assessed by SD-OCT per visit up to week 52

Endpoint: Presence of active choroidal neovascularization (CNV) leakage as assessed by fluorescein angiography at week 52

- To evaluate the safety and tolerability of brolucizumab
  - Endpoint: Incidence of ocular and non-ocular adverse events (AEs) up to week 52

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

Brolucizumab 6 mg/0.05 mL was administered as intravitreal injections to all randomized patients (non-loading arm as test regimen and loading arm as reference):

Brolucizumab 6 mg loading - 3 x 4-weekly initial injections followed by an injection every 12 weeks

Brolucizumab 6 mg non-loading - One initial injection followed by treatment every 12 weeks

Statistical Methods

The following analysis sets were defined:

- Randomized set (RAS): All randomized patients.
- Full analysis set (FAS): All subjects who received at least one intravitreal IVT injection of study treatment, where “treatment received” was defined as the actual treatment regime.
- Safety set (SAF): All subjects who received at least one dose of study treatment. Subjects were analyzed according to the study treatment received.

Due to the low patient number, all analyses were descriptive.

For the analysis of the primary endpoint in terms of mean change in BCVA from baseline to mean of visits at week 40 through week 52, a two-sided 95% confidence interval for the treatment difference was derived from a mixed model with repeated measures (MMRM) with factors treatment arm, baseline BCVA and age. An unstructured covariance structure shared across treatment arms was used to model the within-patient errors.

Secondary endpoints were analyzed using adequate descriptive statistics. Missing values were not replaced in these analyses.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:

•Male or female patients ≥ 50 years of age at screening

•Active choroidal neovascularization (CNV) secondary to AMD that affects the central subfield, including retinal angiomatous proliferation (RAP) with a CNV component, confirmed by presence of active leakage from CNV seen by fluorescein angiography and sequellae of CNV, e.g. pigment epithelial detachment (PED), subretinal or sub-retinal pigment epithelium (sub-RPE) hemorrhage, blocked fluorescence, macular edema (intraretinal fluid (IRF) and/or subretinal fluid (SRF) and/or sub-retinal pigment epithelium (sub-RPE) fluid that affects the central subfield, as seen by spectral domain optical coherence tomography (SD-OCT)) at screening, as confirmed by central reading center (study eye). If active CNV according to the above explained activity criteria is not detectable in screening image data (no IRF and no SRF), presence of residual and/or recurrent fluid (IRF and / or SRF) within the last 6 months before baseline visit is also considered eligible. In this case, historical images must be submitted for analysis by the central reading center.

•Pretreatment with any anti-VEGF drug for a maximum of five years (60 months). Patients should have shown functional and/or anatomical treatment response to the pretreatment(s), prior to participating in this study.

•The treatment initiation phase with the current anti-VEGF must have been completed for at least 6 months with continuous treatment

in a ≥ q4w to ≤ q12w injection interval (±2-day window, i.e., 26 to 86 days inclusive) before the baseline visit. At least 4 weeks (minimum 26 days) must have passed between the last anti-VEGF pretreatment and baseline.
•Best-corrected visual acuity (BCVA) score between 83 and 38 letters, inclusive, using Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity testing charts at both screening and baseline visit (study eye)

Exclusion Criteria:

•Any active intraocular or periocular infection or active intraocular inflammation, at screening or baseline (study eye)
•Uncontrolled glaucoma defined as intraocular pressure (IOP) > 25 mmHg on medication, or according to investigator's judgement, at screening or baseline (study eye)
•Presence of amblyopia, amaurosis or ocular disorders in the fellow eye with BCVA <20/200 at screening (except when due to conditions whose surgery may improve VA, e.g. cataract)
•Ocular treatments: treatment with anti-VEGF drugs for > 5 years in the study eye, pretreatment with brolucizumab at any time in the study eye, previous treatment with investigational drugs in the last 6 months, intraocular or periocular steroids at any time, macular laser photocoagulation or photodynamic therapy at any time, peripheral laser photocoagulation within 3 months prior to baseline, intraocular surgery within 3 months prior to baseline, vitreoretinal surgery at any time, aphakia with the absence of posterior capsule (study eye)
•Stroke or myocardial infarction during the 6 month period prior to baseline
•Systemic anti-VEGF therapy during the 3-month period prior to baseline

Participant Flow Table

Overall Study

	Brolucizumab 6 mg loading	Brolucizumab 6 mg non-loading	Total
Arm/Group Description	3 x 4-weekly initial injections followed by an injection every 12 weeks	One initial injection followed by treatment every 12 weeks	
Started	25	27	52
Completed	25	26	51
Not Completed	0	1	1
Death	0	1	1

Baseline Characteristics

	Brolucizumab 6 mg loading	Brolucizumab 6 mg non-loading	Total
Arm/Group Description	3 x 4-weekly initial injections followed by an injection every 12 weeks	One initial injection followed by treatment every 12 weeks	
Number of Participants [units: participants]	25	27	52
Baseline Analysis Population Description			
Age Continuous (units: years) Analysis Population Type: Participants Mean ± Standard Deviation			
	77.6±6.3	77.4±8.3	77.5±7.3
Sex: Female, Male (units:) Analysis Population Type: Participants Count of Participants (Not Applicable)			
Female	14	18	32
Male	11	9	20

Race (NIH/OMB)
(units:)
Analysis Population Type: Participants
Count of Participants (Not Applicable)

American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	25	27	52
More than one race	0	0	0
Unknown or Not Reported	0	0	0

Primary Outcome Result(s)

Week 40 to Week 52: LS mean change from baseline in best corrected visual acuity (BCVA) in the study eye

Description	BCVA was assessed using Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity testing charts. Visual function of the study eye was assessed using the ETDRS protocol. Participants with a BCVA ETDRS letter score between 78 and 23 ETDRS letters (inclusive) at Screening and Baseline in the study eye were included. Min and max possible scores are 0-100 respectively. A higher score represents better functioning.
Time Frame	Baseline, Week 40 to Week 52
Analysis Population Description	full analysis set - included all patients with a valid assessment without a protocol deviation with impact

	Brolucizumab 6 mg loading	Brolucizumab 6 mg non-loading
Arm/Group Description	3 x 4-weekly initial injections followed by an injection every 12 weeks	One initial injection followed by treatment every 12 weeks

Number of Participants Analyzed [units: participants]	25	26
Week 40 to Week 52: LS mean change from baseline in best corrected visual acuity (BCVA) in the study eye (units: Letters read)	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**
Week 40	3.24 ± 1.32	-0.50 ± 1.28
Week 44	3.88 ± 1.66	-0.27 ± 1.60
Week 48	3.12 ± 1.71	-2.23 ± 1.65
Week 52	2.76 ± 1.64	-1.43 ± 1.58

Statistical Analysis

Groups	Brolucizumab 6 mg loading, Brolucizumab 6 mg non-loading	Week 40
Type of Statistical Test	Other	
Non-Inferiority/Equivalence Test	Analysis was purely descriptive.	
Method	Other MMRM model	
Other Difference	-3.74	
Standard Error of the mean	1.84	
95 % Confidence Interval 2-Sided	-7.47 to -0.01	

Statistical Analysis

Groups	Brolucizumab 6 mg loading, Brolucizumab 6 mg non-loading	Week 44
Type of Statistical Test	Other	

Non-Inferiority/Equivalence Test	Analysis was purely descriptive.
Method	Other MMRM model
Other Difference	-4.15
Standard Error of the mean	2.30
95 % Confidence Interval 2-Sided	-8.78 to -0.48

Statistical Analysis

Groups	Brolucizumab 6 mg loading, Brolucizumab 6 mg non-loading	Week 48
Type of Statistical Test	Other	
Non-Inferiority/Equivalence Test	Analysis was purely descriptive.	
Method	Other MMRM model	
Other Difference	-5.35	
Standard Error of the mean	2.38	
95 % Confidence Interval 2-Sided	-10.13 to -0.58	

Statistical Analysis

Groups	Brolucizumab 6 mg loading, Brolucizumab 6 mg non-loading	Week 52
Type of Statistical Test	Other	

Non-Inferiority/Equivalence Test	Analysis was purely descriptive.
Method	Other MMRM model
Other Difference	-4.19
Standard Error of the mean	2.28
95 % Confidence Interval 2-Sided	-8.77 to 0.39

Statistical Analysis

Groups	Brolucizumab 6 mg loading, Brolucizumab 6 mg non-loading	Mean of Week 40 to Week 52
Type of Statistical Test	Other	
Non-Inferiority/Equivalence Test	Analysis was purely descriptive.	
Method	Other MMRM model	
Other Difference	-4.36	
Standard Error of the mean	2.09	
95 % Confidence Interval 2-Sided	-8.56 to -0.16	

NOVARTIS

Secondary Outcome Result(s)

Treatment intervals before and during the study

Description	Treatment interval distribution. Treatment interval during the study, within 24 weeks prior to baseline and interval between the last 2 injections in the study. In the loading arm, data from the loading period was excluded.
Time Frame	-24 Weeks, Baseline, Week 52
Analysis Population Description	full analysis set

	Brolucizumab 6 mg loading	**Brolucizumab 6 mg non-loading**
Arm/Group Description	3 x 4-weekly initial injections followed by an injection every 12 weeks	One initial injection followed by treatment every 12 weeks
Number of Participants Analyzed [units: participants]	25	27
Treatment intervals before and during the study (units: days)	**Median (Full Range)**	**Median (Full Range)**
within 24 weeks prior to baseline	54.7 (40.0 to 152.0)	68.5 (37.2 to 165.0)
from baseline to week 52 (n=23,25)	64.8 (47.5 to 85.3)	77.8 (55.8 to 85.8)
Last treatment interval during the study (n=25,25)	56.0 (28.0 to 88.0)	65.0 (56.0 to 91.0)

Number of patients with prolonged interval

Description	Treatment interval distribution. Prolongation was calculated by comparing the mean treatment interval in last 24 weeks prior to first brolucizumab injection (a) with the mean of the average treatment interval during the study (loading phase excluded in the loading arm) and (b) with the last treatment interval during the study. Patients with only 1 injection during the treatment period were calculated as non-responders (no prolon-gation).

Time Frame	Baseline, Week 52
Analysis Population Description	full analysis set - included all patients with a valid assessment without a protocol deviation with impact

	Brolucizumab 6 mg loading	Brolucizumab 6 mg non-loading
Arm/Group Description	3 x 4-weekly initial injections followed by an injection every 12 weeks	One initial injection followed by treatment every 12 weeks
Number of Participants Analyzed [units: participants]	25	27
Number of patients with prolonged interval (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
from baseline to week 52	18 (72%)	12 (44.44%)
Last treatment interval during the study	13 (52%)	10 (37.04%)

Proportion of patients who maintained on q12w regimen.

Description	Treatment interval distribution up to Week 52. Proportion of patients maintained on q12w treatment frequency in the two brolucizumab groups up to week 52. Patients who discontinued treatment before week 52 were rated as non-responders, i.e., as patients who did not maintain the q12w regimen. In the loading arm, the loading period up to week 12 was not considered in the analysis.
Time Frame	Up to week 52
Analysis Population Description	full analysis set

	Brolucizumab 6 mg loading	Brolucizumab 6 mg non-loading
Arm/Group Description	3 x 4-weekly initial injections followed by an injection every 12 weeks	One initial injection followed by treatment every 12 weeks

Number of Participants Analyzed [units: participants]	25	27
Proportion of patients who maintained on q12w regimen. (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
Patients who maintained on q12w regimen up to week 52	8 (32%)	6 (22.22%)

Distribution of patients at every 8 weeks / every 12 weeks intervals - Frequency of switches in treatment intervals between baseline and week 52

Description	Treatment interval distribution
Time Frame	Up to Week 52
Analysis Population Description	full analysis set

	Brolucizumab 6 mg loading	**Brolucizumab 6 mg non-loading**
Arm/Group Description	3 x 4-weekly initial injections followed by an injection every 12 weeks	One initial injection followed by treatment every 12 weeks
Number of Participants Analyzed [units: participants]	25	27
Distribution of patients at every 8 weeks / every 12 weeks intervals - Frequency of switches in treatment intervals between baseline and week 52 (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
Switch q12w to q8w (overall)	15 (60%)	19 (70.37%)
Switch q8w to q12w (overall)	3 (12%)	6 (22.22%)

Mean change in best-corrected visual acuity

Description	BCVA was assessed using Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity testing charts. Visual function of the study eye was assessed using the ETDRS protocol. Participants with a BCVA ETDRS letter score between 78 and 23 ETDRS letters (inclusive) at Screening and Baseline in the study eye were included. Min and max possible scores are 0-100 respectively. A higher score represents better functioning.
Time Frame	Baseline, Weeks 16 to 28, Week 52
Analysis Population Description	full analysis set

	Brolucizumab 6 mg loading	**Brolucizumab 6 mg non-loading**
Arm/Group Description	3 x 4-weekly initial injections followed by an injection every 12 weeks	One initial injection followed by treatment every 12 weeks
Number of Participants Analyzed [units: participants]	25	27
Mean change in best-corrected visual acuity (units: Letters read)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
Baseline	72.0 ± 8.7	71.6 ± 11.5
Mean of weeks 16 to 28	74.9 ± 9.2	71.2 ± 12.9
Week 52	74.8 ± 9.1	69.8 ± 16.1

Number of patients with best-corrected visual acuity improvements of >= 5, >= 10 and >= 15 letters

Description	BCVA was assessed using Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity testing charts. Visual function of the study eye was assessed using the ETDRS protocol. Participants with a BCVA ETDRS letter score between 78 and 23 ETDRS letters (inclusive) at Screening and Baseline in the study eye were included. Min and max possible scores are 0-100 respectively. A higher score represents better functioning.
Time Frame	Baseline, up to Week 52
Analysis Population Description	full analysis set

	Brolucizumab 6 mg loading	Brolucizumab 6 mg non-loading
Arm/Group Description	3 x 4-weekly initial injections followed by an injection every 12 weeks	One initial injection followed by treatment every 12 weeks
Number of Participants Analyzed [units: participants]	25	27
Number of patients with best-corrected visual acuity improvements of >= 5, >= 10 and >= 15 letters (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
BCVA ≥ 5 ETDRS letters improvement during the study	9 (36%)	5 (18.52%)
BCVA ≥ 10 ETDRS letters improvement during the study	2 (8%)	2 (7.41%)
BCVA ≥ 15 ETDRS letters improvement during the study	1 (4%)	0 (%)

Number of patients with best-corrected visual acuity >= 69 letters

Description	BCVA was assessed using Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity testing charts. Visual function of the study eye was assessed using the ETDRS protocol. Participants with a BCVA ETDRS letter score between 78 and 23 ETDRS letters (inclusive) at Screening and Baseline in the study eye were included. Min and max possible scores are 0-100 respectively. A higher score represents better functioning.
Time Frame	Baseline, up to Week 52
Analysis Population Description	full analysis set

	Brolucizumab 6 mg loading	Brolucizumab 6 mg non-loading
Arm/Group Description	3 x 4-weekly initial injections followed by an injection every 12 weeks	One initial injection followed by treatment every 12 weeks
Number of Participants Analyzed [units: participants]	25	27

Number of patients with best-corrected visual acuity >= 69 letters (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
BCVA ≥ 69 ETDRS letters during the study	20 (80%)	19 (70.37%)

LS mean change in best-corrected visual acuity from Baseline at Week 52

Description	BCVA was assessed using Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity testing charts. Visual function of the study eye was assessed using the ETDRS protocol. Participants with a BCVA ETDRS letter score between 78 and 23 ETDRS letters (inclusive) at Screening and Baseline in the study eye were included. Min and max possible scores are 0-100 respectively. A higher score represents better functioning.
Time Frame	Baseline, Week 52
Analysis Population Description	full analysis set - included all patients with a valid assessment without a protocol deviation with impact

	Brolucizumab 6 mg loading	**Brolucizumab 6 mg non-loading**
Arm/Group Description	3 x 4-weekly initial injections followed by an injection every 12 weeks	One initial injection followed by treatment every 12 weeks
Number of Participants Analyzed [units: participants]	25	26
LS mean change in best-corrected visual acuity from Baseline at Week 52 (units: Letters read)	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**
Week 52	2.76 ± 1.64	-1.43 ± 1.58

Statistical Analysis

Groups	Brolucizumab 6 mg loading, Brolucizumab 6 mg non-loading	Week 52
Type of Statistical Test	Other	

Non-Inferiority/Equivalence Test	Analysis was purely descriptive.
Method	Other MMRM model
Other Difference	-4.19
Standard Error of the mean	2.28
95 % Confidence Interval 2-Sided	-8.77 to -0.39

Change in central subfield thickness from Baseline at Weeks 12, 16, 28 and 52

Description	Change in central subfield thickness was measured by Spectral domain optical coherence tomography.
Time Frame	Baseline, Weeks 12, 16, 28 and 52
Analysis Population Description	full analysis set

	Brolucizumab 6 mg loading	**Brolucizumab 6 mg non-loading**
Arm/Group Description	3 x 4-weekly initial injections followed by an injection every 12 weeks	One initial injection followed by treatment every 12 weeks
Number of Participants Analyzed [units: participants]	25	27
Change in central subfield thickness from Baseline at Weeks 12, 16, 28 and 52 (units: µm)	**Median** **(Full Range)**	**Median** **(Full Range)**
Week 12	-74.0 (-275 to 27)	-8.5 (-232 to 650)
Week 16	-20.0 (-240 to 208)	-51.0 (-317 to 80)
Week 28	-21.0 (-273 to 393)	-53.0 (-357 to 60)

Week 52	-15.0 (-268 to 269)	-49.5 (-359 to 30)

Absence of intraretinal fluid in the central subfield

Description	Change in fluids was measured by Spectral domain optical coherence tomography.
Time Frame	Every 4 weeks from baseline up to Week 52
Analysis Population Description	full analysis set

	Brolucizumab 6 mg loading	**Brolucizumab 6 mg non-loading**
Arm/Group Description	3 x 4-weekly initial injections followed by an injection every 12 weeks	One initial injection followed by treatment every 12 weeks
Number of Participants Analyzed [units: participants]	25	27
Absence of intraretinal fluid in the central subfield (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
Baseline	13 (52%)	16 (59.26%)
Week 4	19 (76%)	22 (81.48%)
Week 8	17 (68%)	16 (59.26%)
Week 12	21 (84%)	16 (59.26%)
Week 16	12 (48%)	21 (77.78%)
Week 20	16 (64%)	20 (74.07%)
Week 24	17 (68%)	18 (66.67%)

Week 28	16 (64%)	20 (74.07%)
Week 32	18 (72%)	17 (62.96%)
Week 36	17 (68%)	17 (62.96%)
Week 40	16 (64%)	21 (77.78%)
Week 44	16 (64%)	19 (70.37%)
Week 48	19 (76%)	19 (70.37%)
Week 52	16 (64%)	21 (77.78%)

Absence of subretinal fluid in the central subfield

Description	Change in fluids was measured by Spectral domain optical coherence tomography.
Time Frame	Every 4 weeks from baseline up to Week 52
Analysis Population Description	full analysis set

	Brolucizumab 6 mg loading	**Brolucizumab 6 mg non-loading**
Arm/Group Description	3 x 4-weekly initial injections followed by an injection every 12 weeks	One initial injection followed by treatment every 12 weeks
Number of Participants Analyzed [units: participants]	25	27
Absence of subretinal fluid in the central subfield (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
Baseline	5 (20%)	6 (22.22%)

Week 4	13 (52%)	18 (66.67%)
Week 8	18 (72%)	12 (44.44%)
Week 12	20 (80%)	6 (22.22%)
Week 16	8 (32%)	15 (55.56%)
Week 20	3 (12%)	12 (44.44%)
Week 24	13 (52%)	12 (44.44%)
Week 28	9 (36%)	13 (48.15%)
Week 32	11 (44%)	14 (51.85%)
Week 36	11 (44%)	14 (51.85%)
Week 40	10 (40%)	15 (55.56%)
Week 44	8 (32%)	10 (37.04%)
Week 48	10 (40%)	15 (55.56%)
Week 52	9 (36%)	16 (59.26%)

Absence of sub-retinal pigment epithelium fluid in the central subfield

Description	Change in fluids was measured by Spectral domain optical coherence tomography.
Time Frame	Every 4 weeks from baseline up to Week 52

Analysis Population Description: full analysis set

	Brolucizumab 6 mg loading	Brolucizumab 6 mg non-loading
Arm/Group Description	3 x 4-weekly initial injections followed by an injection every 12 weeks	One initial injection followed by treatment every 12 weeks
Number of Participants Analyzed [units: participants]	25	27
Absence of sub-retinal pigment epithelium fluid in the central subfield (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
Baseline	15 (60%)	13 (48.15%)
Week 4	20 (80%)	21 (77.78%)
Week 8	18 (72%)	16 (59.26%)
Week 12	20 (80%)	17 (62.96%)
Week 16	20 (80%)	14 (51.85%)
Week 20	17 (68%)	16 (59.26%)
Week 24	18 (72%)	16 (59.26%)
Week 28	19 (76%)	21 (77.78%)
Week 32	19 (76%)	20 (74.07%)
Week 36	18 (72%)	19 (70.37%)

Week 40	22 (88%)	18 (66.67%)
Week 44	18 (72%)	18 (66.67%)
Week 48	21 (84%)	18 (66.67%)
Week 52	17 (68%)	16 (59.26%)

Presence of active choroidal neovascularization leakage

Description	Presence of active choroidal neovascularization leakage was measured by Fluorescein angiography. CNV = choroidal neovascularization; MNV = macular neovascularization
Time Frame	At Week 52
Analysis Population Description	full analysis set

	Brolucizumab 6 mg loading	**Brolucizumab 6 mg non-loading**
Arm/Group Description	3 x 4-weekly initial injections followed by an injection every 12 weeks	One initial injection followed by treatment every 12 weeks
Number of Participants Analyzed [units: participants]	25	27
Presence of active choroidal neovascularization leakage (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
Active CNV leakage at week 52 - Yes	17 (68%)	15 (55.56%)
Active CNV leakage at week 52 - No	7 (28%)	10 (37.04%)
Active CNV leakage at week 52 - missing	1 (4%)	2 (7.41%)

CNV location at week 52 - Subfoveal	11 (44%)	10 (37.04%)
CNV location at week 52 - Extrafoveal	6 (24%)	5 (18.52%)
CNV location at week 52 - Not applicable	7 (28%)	10 (37.04%)
CNV location at week 52 - Missing	1 (4%)	2 (7.41%)
CNV subtype at week 52 - Type 1 MNV	12 (48%)	9 (33.33%)
CNV subtype at week 52 - Mixed type 1 and type 2 MNV	2 (8%)	1 (3.7%)
CNV subtype at week 52 -Type 3 MNV	3 (12%)	5 (18.52%)
CNV subtype at week 52 - Not applicable	7 (28%)	10 (37.04%)
CNV subtype at week 52 - Missing	1 (4%)	2 (7.41%)

Overview of TEAEs

Description	An adverse event (AE) is any untoward medical occurrence (e.g. any unfavorable and unintended sign (including abnormal laboratory findings), symptom or disease) in a subject or clinical investigation subject after providing written informed consent for participation in the study. Treatment-emergent AEs are AEs that developed on or after first study treatment administration, or any event previously present that worsened following exposure to the study treatment.
Time Frame	Adverse events are reported from first dose of study treatment until end of study treatment plus 30 days post treatment, up to a maximum timeframe of approximately 52 weeks.
Analysis Population Description	safety analysis set

	Brolucizumab 6 mg loading	**Brolucizumab 6 mg non-loading**

Arm/Group Description	3 x 4-weekly initial injections followed by an injection every 12 weeks	One initial injection followed by treatment every 12 weeks
Number of Participants Analyzed [units: participants]	25	27
Overview of TEAEs (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
Any AE	23 (92%)	26 (96.3%)
Ocular AE(s) in the study eye	17 (68%)	19 (70.37%)
Ocular AE(s) in the fellow eye	4 (16%)	9 (33.33%)
Non-ocular AE(s)	20 (80%)	19 (70.37%)
AE(s) related to injection procedure	11 (44%)	12 (44.44%)
AE(s) related to study drug	9 (36%)	12 (44.44%)
SAE(s)	5 (20%)	6 (22.22%)
Ocular SAE(s) in the study eye	1 (4%)	4 (14.81%)
Non-ocular SAE(s)	4 (16%)	2 (7.41%)
Death	0 (%)	1 (3.7%)
Non-fatal SAE(s)	5 (20%)	6 (22.22%)
Discontinuation of study treatment due to any AE(s)	2 (8%)	5 (18.52%)
Discontinuation of study treatment due to non-serious AE(s)	0 (%)	4 (14.81%)
Discontinuation of study treatment due to any SAE(s)	2 (8%)	2 (7.41%)

NOVARTIS

Ocular TEAEs in the study eye by primary system organ class

Description	An adverse event (AE) is any untoward medical occurrence (e.g. any unfavorable and unintended sign (including abnormal laboratory findings), symptom or disease) in a subject or clinical investigation subject after providing written informed consent for participation in the study. Treatment-emergent AEs are AEs that developed on or after first study treatment administration, or any event previously present that worsened following exposure to the study treatment.
Time Frame	Adverse events are reported from first dose of study treatment until end of study treatment plus 30 days post treatment, up to a maximum timeframe of approximately 52 weeks.
Analysis Population Description	safety analysis set

	Brolucizumab 6 mg loading	**Brolucizumab 6 mg non-loading**
Arm/Group Description	3 x 4-weekly initial injections followed by an injection every 12 weeks	One initial injection followed by treatment every 12 weeks
Number of Participants Analyzed [units: participants]	25	27
Ocular TEAEs in the study eye by primary system organ class (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
Total	17 (68%)	19 (70.37%)
Eye disorders	16 (64%)	17 (62.96%)
General disorders and administration site conditions	0 (%)	1 (3.7%)
Infections and infestations	2 (8%)	2 (7.41%)
Injury, poisoning and procedural complications	2 (8%)	1 (3.7%)
Investigations	2 (8%)	4 (14.81%)

NOVARTIS

Ocular TEAEs in the study eye by preferred term (at least 5% in any group)

Description	An adverse event (AE) is any untoward medical occurrence (e.g. any unfavorable and unintended sign (including abnormal laboratory findings), symptom or disease) in a subject or clinical investigation subject after providing written informed consent for participation in the study. Treatment-emergent AEs are AEs that developed on or after first study treatment administration, or any event previously present that worsened following exposure to the study treatment.
Time Frame	Adverse events are reported from first dose of study treatment until end of study treatment plus 30 days post treatment, up to a maximum timeframe of approximately 52 weeks.
Analysis Population Description	safety analysis set

	Brolucizumab 6 mg loading	**Brolucizumab 6 mg non-loading**
Arm/Group Description	3 x 4-weekly initial injections followed by an injection every 12 weeks	One initial injection followed by treatment every 12 weeks
Number of Participants Analyzed [units: participants]	25	27
Ocular TEAEs in the study eye by preferred term (at least 5% in any group) (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
Conjunctival haemorrhage	7 (28%)	5 (18.52%)
Visual acuity reduced	2 (8%)	3 (11.11%)
Eye inflammation	1 (4%)	3 (11.11%)
Intraocular pressure increased	1 (4%)	3 (11.11%)
Retinal oedema	1 (4%)	3 (11.11%)
Dry Eye	1 (4%)	2 (7.41%)

Neovascular age-related macular degeneration	1 (4%)	2 (7.41%)
Vitreous detachment	2 (8%)	1 (3.7%)
Cataract	0 (%)	2 (7.41%)
Conjunctivitis	0 (%)	2 (7.41%)
Retinal exudates	0 (%)	2 (7.41%)
Vitreous floaters	0 (%)	2 (7.41%)

Non-ocular TEAEs - total

Description	An adverse event (AE) is any untoward medical occurrence (e.g. any unfavorable and unintended sign (including abnormal laboratory findings), symptom or disease) in a subject or clinical investigation subject after providing written informed consent for participation in the study. Treatment-emergent AEs are AEs that developed on or after first study treatment administration, or any event previously present that worsened following exposure to the study treatment.
Time Frame	Adverse events are reported from first dose of study treatment until end of study treatment plus 30 days post treatment, up to a maximum timeframe of approximately 52 weeks.
Analysis Population Description	safety analysis set

	Brolucizumab 6 mg loading	**Brolucizumab 6 mg non-loading**
Arm/Group Description	3 x 4-weekly initial injections followed by an injection every 12 weeks	One initial injection followed by treatment every 12 weeks
Number of Participants Analyzed [units: participants]	25	27
Non-ocular TEAEs - total (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**

	20 (80%)	19 (70.37%)

Ocular TEAEs in the study eye of moderate or severe intensity

Description	An adverse event (AE) is any untoward medical occurrence (e.g. any unfavorable and unintended sign (including abnormal laboratory findings), symptom or disease) in a subject or clinical investigation subject after providing written informed consent for participation in the study. Treatment-emergent AEs are AEs that developed on or after first study treatment administration, or any event previously present that worsened following exposure to the study treatment.
Time Frame	Adverse events are reported from first dose of study treatment until end of study treatment plus 30 days post treatment, up to a maximum timeframe of approximately 52 weeks.
Analysis Population Description	safety analysis set

	Brolucizumab 6 mg loading	**Brolucizumab 6 mg non-loading**
Arm/Group Description	3 x 4-weekly initial injections followed by an injection every 12 weeks	One initial injection followed by treatment every 12 weeks
Number of Participants Analyzed [units: participants]	25	27
Ocular TEAEs in the study eye of moderate or severe intensity (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
Any AE of moderate intensity	3 (12%)	8 (29.63%)
Cataract - moderate intensity	0 (%)	2 (7.41%)
Conjunctival haemorrhage - moderate intensity	0 (%)	1 (3.7%)
Conjunctival irritation - moderate intensity	1 (4%)	0 (%)
Conjunctivitis allergic - moderate intensity	0 (%)	1 (3.7%)

Dry eye - moderate intensity	1 (4%)	1 (3.7%)
Eye inflammation - moderate intensity	0 (%)	1 (3.7%)
Eye pain - moderate intensity	0 (%)	1 (3.7%)
Neovascular age-related macular degeneration - moderate intensity	0 (%)	1 (3.7%)
Retinal vasculitis - moderate intensity	0 (%)	2 (7.41%)
Subretinal fluid - moderate intensity	0 (%)	1 (3.7%)
Visual acuity reduced - moderate intensity	1 (4%)	0 (%)
Vital dye staining cornea present - moderate intensity	0 (%)	1 (3.7%)
Vitreous opacities - moderate intensity	0 (%)	1 (3.7%)
Any AE of severe intensity	1 (4%)	2 (7.41%)
Endophthalmitis - severe intensity	1 (4%)	0 (%)
Eye inflammation - severe intensity	1 (4%)	1 (3.7%)
Intraocular pressure increased - severe intensity	0 (%)	1 (3.7%)
Retinal haemorrhage - severe intensity	0 (%)	1 (3.7%)
Retinal neovascularization - severe intensity	0 (%)	1 (3.7%)
Visual acuity reduced - severe intensity	0 (%)	1 (3.7%)

Other Pre-Specified Outcome Result(s)

No data identified.

Post-Hoc Outcome Result(s)

All collected deaths

Description	On-treatment deaths are reported from first dose of study treatment until end of study treatment plus 30 days after last treatment, up to a maximum timeframe of approximately 52 weeks. Post-treatment death data are reported from day 31 after last treatment to end of study (Week 52).
Time Frame	Fatality data are reported from first dose of study treatment until approximately Week 52.
Analysis Population Description	safety analysis set

	Brolucizumab 6 mg loading	**Brolucizumab 6 mg non-loading**
Arm/Group Description	3 x 4-weekly initial injections followed by an injection every 12 weeks	One initial injection followed by treatment every 12 weeks
Number of Participants Analyzed [units: participants]	25	27
All collected deaths (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
On-treatment Deaths	0 (%)	0 (%)
Post-treatment Deaths	0 (%)	1 (3.7%)
Total Deaths	0 (%)	1 (3.7%)

Safety Results

Time Frame	Adverse events are reported from first dose of study treatment until end of study treatment plus 30 days post treatment, up to a maximum timeframe of approximately 52 weeks.
Source Vocabulary for Table Default	MedDRA (27.0)
Collection Approach for Table Default	Systematic Assessment

All-Cause Mortality

	Brolucizumab 6 mg loading N = 25	**Brolucizumab 6 mg non-loading N = 27**
Arm/Group Description	3 x 4-weekly initial injections followed by an injection every 12 weeks	One initial injection followed by treatment every 12 weeks
Total Number Affected	0	1
Total Number At Risk	25	27

Serious Adverse Events

Time Frame	Adverse events are reported from first dose of study treatment until end of study treatment plus 30 days post treatment, up to a maximum timeframe of approximately 52 weeks.
Source Vocabulary for Table Default	MedDRA (27.0)

NOVARTIS

Collection Approach for Table Default Systematic Assessment

	Brolucizumab 6 mg loading N = 25	Brolucizumab 6 mg non-loading N = 27
Arm/Group Description	3 x 4-weekly initial injections followed by an injection every 12 weeks	One initial injection followed by treatment every 12 weeks
Total # Affected by any Serious Adverse Event	5	6
Total # at Risk by any Serious Adverse Event	25	27
Eye disorders		
Eye inflammation- Study Eye	1 (4.00%)	1 (3.70%)
Iridocyclitis- Study Eye	0 (0.00%)	1 (3.70%)
Retinal haemorrhage- Study Eye	0 (0.00%)	1 (3.70%)
Retinal neovascularisation- Study Eye	0 (0.00%)	1 (3.70%)
Retinal vasculitis- Study Eye	0 (0.00%)	1 (3.70%)
Visual acuity reduced- Study Eye	0 (0.00%)	1 (3.70%)
Gastrointestinal disorders		
Colitis ischaemic	0 (0.00%)	1 (3.70%)
Diverticulum intestinal	0 (0.00%)	1 (3.70%)
Lower gastrointestinal haemorrhage	0 (0.00%)	1 (3.70%)
General disorders and administration site conditions		
Pyrexia	0 (0.00%)	1 (3.70%)

Infections and infestations		
Endophthalmitis- Study Eye	1 (4.00%)	0 (0.00%)
Kidney infection	0 (0.00%)	1 (3.70%)
Urosepsis	0 (0.00%)	1 (3.70%)
Investigations		
Intraocular pressure increased- Study Eye	0 (0.00%)	1 (3.70%)
Musculoskeletal and connective tissue disorders		
Osteoarthritis	0 (0.00%)	1 (3.70%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Chromophobe renal cell carcinoma	1 (4.00%)	0 (0.00%)
Hepatic neoplasm	1 (4.00%)	0 (0.00%)
Nervous system disorders		
Ballismus	1 (4.00%)	0 (0.00%)
Cerebrovascular accident	1 (4.00%)	0 (0.00%)
Renal and urinary disorders		
Hydronephrosis	0 (0.00%)	1 (3.70%)

Other (Not Including Serious) Adverse Events

Time Frame	Adverse events are reported from first dose of study treatment until end of study treatment plus 30 days post treatment, up to a maximum timeframe of approximately 52 weeks.

Source Vocabulary for Table Default	MedDRA (27.0)
Collection Approach for Table Default	Systematic Assessment
Frequent Event Reporting Threshold	0%

	Brolucizumab 6 mg loading N = 25	**Brolucizumab 6 mg non-loading N = 27**
Arm/Group Description	3 x 4-weekly initial injections followed by an injection every 12 weeks	One initial injection followed by treatment every 12 weeks
Total # Affected by any Other Adverse Event	23	26
Total # at Risk by any Other Adverse Event	25	27
Eye disorders		
Anterior chamber cell- Study Eye	1 (4.00%)	0 (0.00%)
Blepharitis- Bilateral	0 (0.00%)	1 (3.70%)
Cataract- Bilateral	0 (0.00%)	1 (3.70%)
Cataract- Study Eye	0 (0.00%)	1 (3.70%)
Chalazion- Study Eye	1 (4.00%)	0 (0.00%)
Conjunctival haemorrhage- Study Eye	7 (28.00%)	5 (18.52%)
Conjunctival hyperaemia- Fellow Eye	0 (0.00%)	1 (3.70%)
Conjunctival irritation- Study Eye	1 (4.00%)	0 (0.00%)
Conjunctivitis allergic- Bilateral	0 (0.00%)	2 (7.41%)

Corneal epithelial microcysts- Study Eye	0 (0.00%)	1 (3.70%)
Corneal erosion- Study Eye	1 (4.00%)	0 (0.00%)
Detachment of retinal pigment epithelium- Study Eye	0 (0.00%)	1 (3.70%)
Dry eye- Bilateral	1 (4.00%)	2 (7.41%)
Eczema eyelids- Fellow Eye	0 (0.00%)	1 (3.70%)
Eczema eyelids- Study Eye	0 (0.00%)	1 (3.70%)
Episcleritis- Study Eye	0 (0.00%)	1 (3.70%)
Eye inflammation- Bilateral	0 (0.00%)	1 (3.70%)
Eye inflammation- Study Eye	0 (0.00%)	2 (7.41%)
Eye irritation- Study Eye	1 (4.00%)	0 (0.00%)
Eye pain	0 (0.00%)	1 (3.70%)
Eye pain- Study Eye	0 (0.00%)	1 (3.70%)
Eye ulcer- Fellow Eye	0 (0.00%)	1 (3.70%)
Foreign body sensation in eyes- Study Eye	0 (0.00%)	1 (3.70%)
Macular oedema- Fellow Eye	0 (0.00%)	1 (3.70%)
Macular oedema- Study Eye	1 (4.00%)	1 (3.70%)
Neovascular age-related macular degeneration- Fellow Eye	3 (12.00%)	1 (3.70%)
Neovascular age-related macular degeneration- Study Eye	1 (4.00%)	2 (7.41%)
Ocular hyperaemia- Fellow Eye	1 (4.00%)	0 (0.00%)
Posterior capsule opacification- Fellow Eye	0 (0.00%)	1 (3.70%)
Retinal aneurysm- Fellow Eye	0 (0.00%)	1 (3.70%)
Retinal aneurysm- Study Eye	0 (0.00%)	1 (3.70%)
Retinal cyst- Fellow Eye	0 (0.00%)	2 (7.41%)
Retinal exudates- Bilateral	0 (0.00%)	1 (3.70%)
Retinal exudates- Study Eye	0 (0.00%)	1 (3.70%)
Retinal haemorrhage- Study Eye	1 (4.00%)	1 (3.70%)

Retinal oedema- Fellow Eye	0 (0.00%)	1 (3.70%)
Retinal oedema- Study Eye	1 (4.00%)	3 (11.11%)
Retinal vasculitis- Study Eye	0 (0.00%)	2 (7.41%)
Retinopathy hypertensive	1 (4.00%)	0 (0.00%)
Scleritis- Study Eye	0 (0.00%)	1 (3.70%)
Subretinal fibrosis- Study Eye	0 (0.00%)	1 (3.70%)
Subretinal fluid- Fellow Eye	1 (4.00%)	1 (3.70%)
Subretinal fluid- Study Eye	1 (4.00%)	1 (3.70%)
Vision blurred- Study Eye	0 (0.00%)	1 (3.70%)
Visual acuity reduced- Bilateral	1 (4.00%)	0 (0.00%)
Visual acuity reduced- Fellow Eye	0 (0.00%)	1 (3.70%)
Visual acuity reduced- Study Eye	1 (4.00%)	3 (11.11%)
Vitreal cells- Study Eye	0 (0.00%)	1 (3.70%)
Vitreous detachment- Study Eye	2 (8.00%)	1 (3.70%)
Vitreous floaters- Bilateral	0 (0.00%)	1 (3.70%)
Vitreous floaters- Study Eye	0 (0.00%)	2 (7.41%)
Vitreous haemorrhage- Fellow Eye	1 (4.00%)	0 (0.00%)
Vitreous opacities- Study Eye	0 (0.00%)	1 (3.70%)
Gastrointestinal disorders		
Tooth impacted	0 (0.00%)	1 (3.70%)
General disorders and administration site conditions		
Application site wound	0 (0.00%)	1 (3.70%)
Injection site pain- Study Eye	0 (0.00%)	1 (3.70%)
Oedema peripheral	1 (4.00%)	1 (3.70%)
Retention cyst- Fellow Eye	0 (0.00%)	1 (3.70%)

Hepatobiliary disorders		
Hyperbilirubinaemia	1 (4.00%)	0 (0.00%)
Infections and infestations		
Arthritis bacterial	1 (4.00%)	0 (0.00%)
Bronchitis	1 (4.00%)	1 (3.70%)
Conjunctivitis- Study Eye	0 (0.00%)	2 (7.41%)
COVID-19	6 (24.00%)	5 (18.52%)
Cystitis	1 (4.00%)	2 (7.41%)
Gastrointestinal viral infection	1 (4.00%)	0 (0.00%)
Herpes virus infection	0 (0.00%)	1 (3.70%)
Herpes zoster	0 (0.00%)	1 (3.70%)
Hordeolum- Study Eye	1 (4.00%)	0 (0.00%)
Influenza	0 (0.00%)	1 (3.70%)
Lyme disease	1 (4.00%)	0 (0.00%)
Nasopharyngitis	6 (24.00%)	5 (18.52%)
Oral herpes	0 (0.00%)	1 (3.70%)
Otitis media	0 (0.00%)	1 (3.70%)
Respiratory tract infection	0 (0.00%)	1 (3.70%)
Sialoadenitis	1 (4.00%)	0 (0.00%)
Upper respiratory tract infection	0 (0.00%)	1 (3.70%)
Injury, poisoning and procedural complications		
Arthropod sting	1 (4.00%)	0 (0.00%)
Bone contusion	0 (0.00%)	1 (3.70%)
Contusion	1 (4.00%)	0 (0.00%)

Epicondylitis	1 (4.00%)	0 (0.00%)
Expired product administered- Study Eye	1 (4.00%)	1 (3.70%)
Fall	1 (4.00%)	2 (7.41%)
Intra-ocular injection complication- Fellow Eye	0 (0.00%)	1 (3.70%)
Intra-ocular injection complication- Study Eye	1 (4.00%)	0 (0.00%)
Ligament sprain	0 (0.00%)	1 (3.70%)
Meniscus injury	0 (0.00%)	1 (3.70%)
Rib fracture	1 (4.00%)	0 (0.00%)
Skin laceration	1 (4.00%)	0 (0.00%)
Stress fracture	1 (4.00%)	0 (0.00%)
Investigations		
Blood pressure increased	2 (8.00%)	0 (0.00%)
Intraocular pressure increased- Fellow Eye	0 (0.00%)	1 (3.70%)
Intraocular pressure increased- Study Eye	1 (4.00%)	2 (7.41%)
Vital dye staining cornea present- Study Eye	1 (4.00%)	1 (3.70%)
Metabolism and nutrition disorders		
Glucose tolerance impaired	1 (4.00%)	0 (0.00%)
Gout	0 (0.00%)	1 (3.70%)
Musculoskeletal and connective tissue disorders		
Arthralgia	2 (8.00%)	1 (3.70%)
Arthritis	0 (0.00%)	1 (3.70%)
Back pain	1 (4.00%)	2 (7.41%)
Intervertebral disc protrusion	1 (4.00%)	0 (0.00%)
Jaw cyst	0 (0.00%)	1 (3.70%)

Joint swelling	0 (0.00%)	1 (3.70%)
Muscle tightness	0 (0.00%)	1 (3.70%)
Osteoarthritis	2 (8.00%)	1 (3.70%)
Pain in extremity	1 (4.00%)	0 (0.00%)
Synovial cyst	0 (0.00%)	1 (3.70%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Basal cell carcinoma	0 (0.00%)	1 (3.70%)
Blepharal papilloma- Fellow Eye	0 (0.00%)	1 (3.70%)
Nervous system disorders		
Dizziness	1 (4.00%)	0 (0.00%)
Headache	0 (0.00%)	1 (3.70%)
Hypoaesthesia	1 (4.00%)	0 (0.00%)
Neuralgia	1 (4.00%)	0 (0.00%)
Restless legs syndrome	1 (4.00%)	0 (0.00%)
Psychiatric disorders		
Depression	0 (0.00%)	1 (3.70%)
Insomnia	0 (0.00%)	1 (3.70%)
Renal and urinary disorders		
Incontinence	0 (0.00%)	1 (3.70%)
Reproductive system and breast disorders		
Benign prostatic hyperplasia	1 (4.00%)	0 (0.00%)
Respiratory, thoracic and mediastinal disorders		
Cough	1 (4.00%)	2 (7.41%)

Rhinitis allergic	0 (0.00%)	1 (3.70%)
Skin and subcutaneous tissue disorders		
Dermatitis contact	1 (4.00%)	0 (0.00%)
Eczema	0 (0.00%)	1 (3.70%)
Palmar erythema	1 (4.00%)	0 (0.00%)
Vascular disorders		
Haematoma	1 (4.00%)	0 (0.00%)
Hypertension	3 (12.00%)	3 (11.11%)
Hypertensive crisis	1 (4.00%)	0 (0.00%)
Thrombophlebitis	0 (0.00%)	1 (3.70%)

Other Relevant Findings

Conclusion:

- Due to the early recruitment stop, when only 11% of the initially planned patient number were enrolled, the results of the analyses of data are to be interpreted descriptively only.
- Functional outcomes assessed by the changes in best corrected visual activity (BCVA) up to week 52 were qualitatively in favor of the loading regimen (q12w preceded by 3 monthly injections) even in patients pre-treated with another anti-vascular endothelial growth factor (VEGF) drug.
- Omission of the monthly loading may also be effective in a subset of patients and is not necessarily associated with the requirement to shorten treatment intervals.
- A switch to treatment with brolucizumab allows a prolongation of the treatment interval in more than 50% patients when compared to the 24 weeks prior to the switch.

- Anatomical outcomes assessed by spectral domain optical coherence tomography (SD-OCT) and fluorescein angiography (FA) showed trends towards improvements on brolucizumab treatment.
- Safety data were consistent with the known safety profile of brolucizumab and there were no new or unexpected findings.

Date of Clinical Trial Report

16 Jan 2025