Clinical trial results:
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 (FALCON)

Summary

EudraCT number	2019-004767-53
Trial protocol	DE
Global end of trial date	31 January 2024

Results information

Result version number	v1 (current)
This version publication date	01 January 2025
First version publication date	01 January 2025

Trial information

Trial identification

Sponsor protocol code	CRTH258ADE01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04679935
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	Novartis Campus, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	31 January 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 January 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary objective was to evaluate the difference in 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.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 July 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 47
Country: Number of subjects enrolled	Switzerland: 5
Worldwide total number of subjects	52
EEA total number of subjects	47

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	3
From 65 to 84 years	40

85 years and over	9

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

If both eyes were eligible as per the inclusion and exclusion criteria, the eye with the worse visual acuity should have been selected for study eye, unless the investigator deemed it more appropriate to select the eye with better visual acuity, based on medical reasons or local
ethical requirements.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Brolucizumab 6 mg loading

Arm description:

3 x 4-weekly initial injections followed by an injection every 12 weeks

Arm type	Experimental
Investigational medicinal product name	Brolucizumab
Investigational medicinal product code	RTH258
Other name	Beovu
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

Brolucizumab 6 mg loading

Arm title	Brolucizumab 6 mg non-loading

Arm description:

One initial injection followed by treatment every 12 weeks

Arm type	Experimental
Investigational medicinal product name	Brolucizumab
Investigational medicinal product code	RTH258
Other name	Beovu
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

Brolucizumab 6 mg non-loading

Number of subjects in period 1	Brolucizumab 6 mg loading	Brolucizumab 6 mg non-loading
Started	25	27
Completed	25	26
Not completed	0	1
Adverse event, serious fatal	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Brolucizumab 6 mg loading
Reporting group description:	
3 x 4-weekly initial injections followed by an injection every 12 weeks	
Reporting group title	Brolucizumab 6 mg non-loading
Reporting group description:	
One initial injection followed by treatment every 12 weeks	

Reporting group values	Brolucizumab 6 mg loading	Brolucizumab 6 mg non-loading	Total
Number of subjects	25	27	52
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	3	3
From 65-84 years	21	19	40
85 years and over	4	5	9
Age Continuous Units: years			
arithmetic mean	77.6	77.4	
standard deviation	± 6.3	± 8.3	-
Sex: Female, Male Units:			
Female	14	18	32
Male	11	9	20
Race (NIH/OMB) Units: Subjects			
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

End points

End points reporting groups

Reporting group title	Brolucizumab 6 mg loading
Reporting group description:	
3 x 4-weekly initial injections followed by an injection every 12 weeks	
Reporting group title	Brolucizumab 6 mg non-loading
Reporting group description:	
One initial injection followed by treatment every 12 weeks	

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

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

End point 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.

End point type	Primary
End point timeframe:	
Baseline, Week 40 to Week 52	

End point values	Brolucizumab 6 mg loading	Brolucizumab 6 mg non-loading		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	26		
Units: Letters read				
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 analyses

Statistical analysis title	Brolucizumab loading v Brolucizumab non-loading
Statistical analysis description:	
Week 44	
Comparison groups	Brolucizumab 6 mg loading v Brolucizumab 6 mg non-loading

Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	
Method	MMRM model
Parameter estimate	Difference
Point estimate	-4.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.78
upper limit	-0.48
Variability estimate	Standard error of the mean
Dispersion value	2.3

Statistical analysis title	Brolucizumab loading v Brolucizumab non-loading
Statistical analysis description:	
Week 40	
Comparison groups	Brolucizumab 6 mg loading v Brolucizumab 6 mg non-loading
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	
Method	MMRM model
Parameter estimate	Difference
Point estimate	-3.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.47
upper limit	-0.01
Variability estimate	Standard error of the mean
Dispersion value	1.84

Statistical analysis title	Brolucizumab loading v Brolucizumab non-loading
Statistical analysis description:	
Week 52	
Comparison groups	Brolucizumab 6 mg loading v Brolucizumab 6 mg non-loading
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	
Method	MMRM model
Parameter estimate	Difference
Point estimate	-4.19

Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.77
upper limit	0.39
Variability estimate	Standard error of the mean
Dispersion value	2.28

Statistical analysis title	Brolucizumab loading v Brolucizumab non-loading
Statistical analysis description: Mean of Week 40 to Week 52	
Comparison groups	Brolucizumab 6 mg loading v Brolucizumab 6 mg non-loading
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	
Method	MMRM model
Parameter estimate	Difference
Point estimate	-4.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.56
upper limit	-0.16
Variability estimate	Standard error of the mean
Dispersion value	2.09

Statistical analysis title	Brolucizumab loading v Brolucizumab non-loading
Statistical analysis description: Week 48	
Comparison groups	Brolucizumab 6 mg loading v Brolucizumab 6 mg non-loading
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	
Method	MMRM model
Parameter estimate	Difference
Point estimate	-5.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.13
upper limit	-0.58
Variability estimate	Standard error of the mean
Dispersion value	2.38

Secondary: Treatment intervals before and during the study

End point title	Treatment intervals before and during the study

End point 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.

End point type	Secondary

End point timeframe:

-24 Weeks, Baseline, Week 52

End point values	Brolucizumab 6 mg loading	Brolucizumab 6 mg non-loading		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	27		
Units: days				
median (full range (min-max))				
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)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with prolonged interval

End point title	Number of patients with prolonged interval

End point 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).

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Brolucizumab 6 mg loading	Brolucizumab 6 mg non-loading		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	27		
Units: Participants				
from baseline to week 52	18	12		
Last treatment interval during the study	13	10		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of patients who maintained on q12w regimen.

End point title	Proportion of patients who maintained on q12w regimen.

End point 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.

End point type	Secondary

End point timeframe:

Up to week 52

End point values	Brolucizumab 6 mg loading	Brolucizumab 6 mg non-loading		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	27		
Units: Participants	8	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change in best-corrected visual acuity

End point title	Mean change in best-corrected visual acuity

End point 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.

End point type	Secondary
End point timeframe: Baseline, Weeks 16 to 28, Week 52	

End point values	Brolucizumab 6 mg loading	Brolucizumab 6 mg non-loading		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	27		
Units: Letters read				
arithmetic 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)		

Statistical analyses

No statistical analyses for this end point

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

End point title	Distribution of patients at every 8 weeks / every 12 weeks intervals - Frequency of switches in treatment intervals between baseline and week 52
End point description: Treatment interval distribution	
End point type	Secondary
End point timeframe: Up to Week 52	

End point values	Brolucizumab 6 mg loading	Brolucizumab 6 mg non-loading		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	27		
Units: Participants				
Switch q12w to q8w (overall)	15	19		
Switch q8w to q12w (overall)	3	6		

Statistical analyses

No statistical analyses for this end point

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

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

End point 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.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Brolucizumab 6 mg loading	Brolucizumab 6 mg non-loading		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	26		
Units: Letters read				
least squares mean (standard error)	2.76 (± 1.64)	-1.43 (± 1.58)		

Statistical analyses

Statistical analysis title	Brolucizumab loading v Brolucizumab non-loading
Statistical analysis description:	
Week 52	
Comparison groups	Brolucizumab 6 mg loading v Brolucizumab 6 mg non-loading
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	
Method	MMRM model
Parameter estimate	Difference
Point estimate	-4.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.77
upper limit	-0.39
Variability estimate	Standard error of the mean
Dispersion value	2.28

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

End point title	Number of patients with best-corrected visual acuity >= 69

	letters

End point 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.

End point type	Secondary

End point timeframe:

Baseline, up to Week 52

End point values	Brolucizumab 6 mg loading	Brolucizumab 6 mg non-loading		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	27		
Units: Participants	20	19		

Statistical analyses

No statistical analyses for this end point

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

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

End point 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.

End point type	Secondary

End point timeframe:

Baseline, up to Week 52

End point values	Brolucizumab 6 mg loading	Brolucizumab 6 mg non-loading		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	27		
Units: Participants				

BCVA ≥ 5 ETDRS letters improvement during study	9	5		
BCVA ≥ 10 ETDRS letters improvement during study	2	2		
BCVA ≥ 15 ETDRS letters improvement during study	1	0		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Change in central subfield thickness was measured by Spectral domain optical coherence tomography.

End point type	Secondary

End point timeframe:

Baseline, Weeks 12, 16, 28 and 52

End point values	Brolucizumab 6 mg loading	Brolucizumab 6 mg non-loading		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	27		
Units: µm				
median (full range (min-max))				
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)		

Statistical analyses

No statistical analyses for this end point

Secondary: Absence of intraretinal fluid in the central subfield

End point title	Absence of intraretinal fluid in the central subfield

End point description:

Change in fluids was measured by Spectral domain optical coherence tomography.

End point type	Secondary

End point timeframe:
Every 4 weeks from baseline up to Week 52

End point values	Brolucizumab 6 mg loading	Brolucizumab 6 mg non-loading		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	27		
Units: Participants				
Baseline	13	16		
Week 4	19	22		
Week 8	17	16		
Week 12	21	16		
Week 16	12	21		
Week 20	16	20		
Week 24	17	18		
Week 28	16	20		
Week 32	18	17		
Week 36	17	17		
Week 40	16	21		
Week 44	16	19		
Week 48	19	19		
Week 52	16	21		

Statistical analyses

No statistical analyses for this end point

Secondary: Absence of subretinal fluid in the central subfield

End point title	Absence of subretinal fluid in the central subfield

End point description:
Change in fluids was measured by Spectral domain optical coherence tomography.

End point type	Secondary

End point timeframe:
Every 4 weeks from baseline up to Week 52

End point values	Brolucizumab 6 mg loading	Brolucizumab 6 mg non-loading		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	27		
Units: Participants				
Baseline	5	6		
Week 4	13	18		
Week 8	18	12		

Week 12	20	6		
Week 16	8	15		
Week 20	3	12		
Week 24	13	12		
Week 28	9	13		
Week 32	11	14		
Week 36	11	14		
Week 40	10	15		
Week 44	8	10		
Week 48	10	15		
Week 52	9	16		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Change in fluids was measured by Spectral domain optical coherence tomography.

End point type	Secondary

End point timeframe:

Every 4 weeks from baseline up to Week 52

End point values	Brolucizumab 6 mg loading	Brolucizumab 6 mg non-loading		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	27		
Units: Participants				
Baseline	15	13		
Week 4	20	21		
Week 8	18	16		
Week 12	20	17		
Week 16	20	14		
Week 20	17	16		
Week 24	18	16		
Week 28	19	21		
Week 32	19	20		
Week 36	18	19		
Week 40	22	18		
Week 44	18	18		
Week 48	21	18		
Week 52	17	16		

Statistical analyses

No statistical analyses for this end point

Secondary: Presence of active choroidal neovascularization leakage

End point title	Presence of active choroidal neovascularization leakage

End point description:

Presence of active choroidal neovascularization leakage was measured by Fluorescein angiography.

CNV = choroidal neovascularization; MNV = macular neovascularization; Wk = Week

End point type	Secondary

End point timeframe:

At Week 52

End point values	Brolucizumab 6 mg loading	Brolucizumab 6 mg non-loading		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	27		
Units: Participants				
Active CNV leakage at week 52 - Yes	17	15		
Active CNV leakage at week 52 - No	7	10		
Active CNV leakage at week 52 - missing	1	2		
CNV location at week 52 - Subfoveal	11	10		
CNV location at week 52 - Extrafoveal	6	5		
CNV location at week 52 - Not applicable	7	10		
CNV location at week 52 - Missing	1	2		
CNV subtype at week 52 - Type 1 MNV	12	9		
CNV subtype at Wk 52 - Mixed type 1 and type 2 MNV	2	1		
CNV subtype at week 52 -Type 3 MNV	3	5		
CNV subtype- Wk 52 - Not applicable	7	10		
CNV subtype at week 52 - Missing	1	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Overview of TEAEs

End point title	Overview of TEAEs

End point 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.

Disc. = discontinuation

End point type	Secondary

End point timeframe:

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.

End point values	Brolucizumab 6 mg loading	Brolucizumab 6 mg non-loading		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	27		
Units: Participants				
Any AE	23	26		
Ocular AE(s) in the study eye	17	19		
Ocular AE(s) in the fellow eye	4	9		
Non-ocular AE(s)	20	19		
AE(s) related to injection procedure	11	12		
AE(s) related to study drug	9	12		
SAE(s)	5	6		
Ocular SAE(s) in the study eye	1	4		
Non-ocular SAE(s)	4	2		
Death	0	1		
Non-fatal SAE(s)	5	6		
Disc.of study treatment due to any AE(s)	2	5		
Disc.of study treatment due to non-serious AE(s)	0	4		
Disc.of study treatment due to any SAE(s)	2	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Ocular TEAEs in the study eye by primary system organ class

End point title	Ocular TEAEs in the study eye by primary system organ class

End point 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.
Adm. = administration

End point type	Secondary

End point timeframe:

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.

End point values	Brolucizumab 6 mg loading	Brolucizumab 6 mg non-loading		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	27		
Units: Participants				
Total	17	19		
Eye disorders	16	17		
General disorders and adm. site conditions	0	1		
Infections and infestations	2	2		
Injury, poisoning and procedural complications	2	1		
Investigations	2	4		

Statistical analyses

No statistical analyses for this end point

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

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

End point 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.

End point type	Secondary

End point timeframe:

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.

End point values	Brolucizumab 6 mg loading	Brolucizumab 6 mg non-loading		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	27		
Units: Participants				
Conjunctival haemorrhage	7	5		
Visual acuity reduced	2	3		

Eye inflammation	1	3		
Intraocular pressure increased	1	3		
Retinal oedema	1	3		
Dry Eye	1	2		
Neovascular age-related macular degeneration	1	2		
Vitreous detachment	2	1		
Cataract	0	2		
Conjunctivitis	0	2		
Retinal exudates	0	2		
Vitreous floaters	0	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Non-ocular TEAEs - total

End point title	Non-ocular TEAEs - total

End point 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.

End point type	Secondary

End point timeframe:

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.

End point values	Brolucizumab 6 mg loading	Brolucizumab 6 mg non-loading		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	27		
Units: Participants	20	19		

Statistical analyses

No statistical analyses for this end point

Secondary: Ocular TEAEs in the study eye of moderate or severe intensity

End point title	Ocular TEAEs in the study eye of moderate or severe intensity

End point 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.

MD = macular degeneration
int. = intensity

End point type	Secondary

End point timeframe:

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.

End point values	Brolucizumab 6 mg loading	Brolucizumab 6 mg non-loading		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	27		
Units: Participants				
Any AE of moderate intensity	3	8		
Cataract - moderate intensity	0	2		
Conjunctival haemorrhage - moderate intensity	0	1		
Conjunctival irritation - moderate intensity	1	0		
Conjunctivitis allergic - moderate intensity	0	1		
Dry eye - moderate intensity	1	1		
Eye inflammation - moderate intensity	0	1		
Eye pain - moderate intensity	0	1		
Neovascular age-related MD - moderate intensity	0	1		
Retinal vasculitis - moderate intensity	0	2		
Subretinal fluid - moderate intensity	0	1		
Visual acuity reduced - moderate intensity	1	0		
Vital dye staining cornea present-moderate int.	0	1		
Vitreous opacities - moderate intensity	0	1		
Any AE of severe intensity	1	2		
Endophthalmitis - severe intensity	1	0		
Eye inflammation - severe intensity	1	1		
Intraocular pressure increased - severe intensity	0	1		
Retinal haemorrhage - severe intensity	0	1		
Retinal neovascularization - severe intensity	0	1		
Visual acuity reduced - severe intensity	0	1		

Statistical analyses

No statistical analyses for this end point

Post-hoc: All collected deaths

End point title	All collected deaths

End point 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).

End point type	Post-hoc

End point timeframe:

Fatality data are reported from first dose of study treatment until approximately Week 52.

End point values	Brolucizumab 6 mg loading	Brolucizumab 6 mg non-loading		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	27		
Units: Participants				
On-treatment Deaths	0	0		
Post-treatment Deaths	0	1		
Total Deaths	0	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

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.

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	Non-Loading Arm

Reporting group description:

Non-Loading Arm

Reporting group title	Loading Arm

Reporting group description:

Loading Arm

Serious adverse events	Non-Loading Arm	Loading Arm	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 27 (22.22%)	5 / 25 (20.00%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Chromophobe renal cell carcinoma			
subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic neoplasm			
subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Intraocular pressure increased-Study Eye			

subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ballismus			
subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Eye inflammation- Study Eye			
subjects affected / exposed	1 / 27 (3.70%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iridocyclitis- Study Eye			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal haemorrhage- Study Eye			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal neovascularisation- Study Eye			

subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal vasculitis- Study Eye			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Visual acuity reduced- Study Eye			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colitis ischaemic			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Lower gastrointestinal haemorrhage			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Diverticulum intestinal			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infections and infestations			
Endophthalmitis- Study Eye			
subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney infection			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Non-Loading Arm	Loading Arm	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 27 (96.30%)	23 / 25 (92.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Blepharal papilloma- Fellow Eye			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Hypertension			
subjects affected / exposed	3 / 27 (11.11%)	3 / 25 (12.00%)	
occurrences (all)	3	3	
Hypertensive crisis			

subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Thrombophlebitis			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	1 / 27 (3.70%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Application site wound			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Retention cyst- Fellow Eye			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Injection site pain- Study Eye			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 27 (7.41%)	1 / 25 (4.00%)	
occurrences (all)	2	1	
Rhinitis allergic			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Insomnia			

subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Investigations			
Blood pressure increased			
subjects affected / exposed	0 / 27 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	2	
Intraocular pressure increased-Study Eye			
subjects affected / exposed	2 / 27 (7.41%)	1 / 25 (4.00%)	
occurrences (all)	6	1	
Vital dye staining cornea present-Study Eye			
subjects affected / exposed	1 / 27 (3.70%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Intraocular pressure increased-Fellow Eye			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Injury, poisoning and procedural complications			
Stress fracture			
subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Skin laceration			
subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Rib fracture			
subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Meniscus injury			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Ligament sprain			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Fall			
subjects affected / exposed	2 / 27 (7.41%)	1 / 25 (4.00%)	
occurrences (all)	2	1	

Contusion			
subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Bone contusion			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Arthropod sting			
subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Epicondylitis			
subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Intra-ocular injection complication-Study Eye			
subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Intra-ocular injection complication-Fellow Eye			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Expired product administered- Study Eye			
subjects affected / exposed	1 / 27 (3.70%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Hypoaesthesia			
subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Neuralgia			
subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Restless legs syndrome			

subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Eye disorders			
Retinopathy hypertensive			
subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Eye pain			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Corneal erosion- Study Eye			
subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Detachment of retinal pigment epithelium- Study Eye			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Eczema eyelids- Fellow Eye			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Eczema eyelids- Study Eye			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Episcleritis- Study Eye			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Eye inflammation- Study Eye			
subjects affected / exposed	2 / 27 (7.41%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Eye irritation- Study Eye			
subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Anterior chamber cell- Study Eye			
subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Cataract- Study Eye			

subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)		
occurrences (all)	1	0		
Chalazion- Study Eye				
subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)		
occurrences (all)	0	1		
Conjunctival haemorrhage- Study Eye				
subjects affected / exposed	5 / 27 (18.52%)	7 / 25 (28.00%)		
occurrences (all)	5	7		
Conjunctival hyperaemia- Fellow Eye				
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)		
occurrences (all)	1	0		
Conjunctival irritation- Study Eye				
subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)		
occurrences (all)	0	1		
Corneal epithelial microcysts- Study Eye				
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)		
occurrences (all)	1	0		
Eye pain- Study Eye				
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)		
occurrences (all)	1	0		
Eye ulcer- Fellow Eye				
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)		
occurrences (all)	1	0		
Vitreous opacities- Study Eye				
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)		
occurrences (all)	1	0		
Vitreous haemorrhage- Fellow Eye				
subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)		
occurrences (all)	0	1		
Vitreous floaters- Study Eye				
subjects affected / exposed	2 / 27 (7.41%)	0 / 25 (0.00%)		
occurrences (all)	2	0		
Vitreous detachment- Study Eye				

subjects affected / exposed	1 / 27 (3.70%)	2 / 25 (8.00%)	
occurrences (all)	1	2	
Vitreal cells- Study Eye			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Visual acuity reduced- Study Eye			
subjects affected / exposed	3 / 27 (11.11%)	1 / 25 (4.00%)	
occurrences (all)	3	2	
Visual acuity reduced- Fellow Eye			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Vision blurred- Study Eye			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Subretinal fluid- Study Eye			
subjects affected / exposed	1 / 27 (3.70%)	1 / 25 (4.00%)	
occurrences (all)	1	2	
Subretinal fluid- Fellow Eye			
subjects affected / exposed	1 / 27 (3.70%)	1 / 25 (4.00%)	
occurrences (all)	3	2	
Subretinal fibrosis- Study Eye			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Scleritis- Study Eye			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Retinal vasculitis- Study Eye			
subjects affected / exposed	2 / 27 (7.41%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Retinal oedema- Study Eye			
subjects affected / exposed	3 / 27 (11.11%)	1 / 25 (4.00%)	
occurrences (all)	4	2	
Retinal oedema- Fellow Eye			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Retinal haemorrhage- Study Eye			

subjects affected / exposed	1 / 27 (3.70%)	1 / 25 (4.00%)	
occurrences (all)	1	2	
Retinal exudates- Study Eye			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Retinal cyst- Fellow Eye			
subjects affected / exposed	2 / 27 (7.41%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Foreign body sensation in eyes- Study Eye			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Macular oedema- Fellow Eye			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Macular oedema- Study Eye			
subjects affected / exposed	1 / 27 (3.70%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Neovascular age-related macular degeneration- Fellow Eye			
subjects affected / exposed	1 / 27 (3.70%)	3 / 25 (12.00%)	
occurrences (all)	1	3	
Neovascular age-related macular degeneration- Study Eye			
subjects affected / exposed	2 / 27 (7.41%)	1 / 25 (4.00%)	
occurrences (all)	2	1	
Ocular hyperaemia- Fellow Eye			
subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Posterior capsule opacification- Fellow Eye			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Retinal aneurysm- Fellow Eye			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Retinal aneurysm- Study Eye			

subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Vitreous floaters- Bilateral			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Visual acuity reduced- Bilateral			
subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Retinal exudates- Bilateral			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Eye inflammation- Bilateral			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Dry eye- Bilateral			
subjects affected / exposed	2 / 27 (7.41%)	1 / 25 (4.00%)	
occurrences (all)	2	1	
Conjunctivitis allergic- Bilateral			
subjects affected / exposed	2 / 27 (7.41%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Cataract- Bilateral			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Blepharitis- Bilateral			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Tooth impacted			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			

Dermatitis contact			
subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Eczema			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Palmar erythema			
subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Incontinence			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Synovial cyst			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Osteoarthritis			
subjects affected / exposed	1 / 27 (3.70%)	2 / 25 (8.00%)	
occurrences (all)	1	2	
Muscle tightness			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Joint swelling			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Jaw cyst			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Intervertebral disc protrusion			
subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Back pain			

subjects affected / exposed	2 / 27 (7.41%)	1 / 25 (4.00%)	
occurrences (all)	3	1	
Arthritis			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Arthralgia			
subjects affected / exposed	1 / 27 (3.70%)	2 / 25 (8.00%)	
occurrences (all)	1	2	
Infections and infestations			
Arthritis bacterial			
subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	2	
Bronchitis			
subjects affected / exposed	1 / 27 (3.70%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Upper respiratory tract infection			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Sialoadenitis			
subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Respiratory tract infection			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Otitis media			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Oral herpes			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			
subjects affected / exposed	5 / 27 (18.52%)	6 / 25 (24.00%)	
occurrences (all)	5	6	
Lyme disease			
subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	

Influenza			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Herpes zoster			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Herpes virus infection			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal viral infection			
subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Cystitis			
subjects affected / exposed	2 / 27 (7.41%)	1 / 25 (4.00%)	
occurrences (all)	3	1	
COVID-19			
subjects affected / exposed	5 / 27 (18.52%)	6 / 25 (24.00%)	
occurrences (all)	5	6	
Hordeolum- Study Eye			
subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Conjunctivitis- Study Eye			
subjects affected / exposed	2 / 27 (7.41%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	1 / 27 (3.70%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Glucose tolerance impaired			
subjects affected / exposed	0 / 27 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 October 2021	(1) Implementation of the Urgent Safety Measures (USM) described in the 10-Aug-2021 Dear Investigator Letter into the study protocol. The USM were implemented for ongoing studies not achieving Last Patient Last Visit (LPLV) by 11-Aug-2021 and in response to the identification of a causal immune-mediated mechanism of the previously identified risk of retinal vasculitis, and/or retinal vascular occlusion, typically in the presence of intraocular inflammation.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported