Clinical trial results:
A one-year, single-arm, open-label, multicenter study assessing the effect of brolucizumab 6 mg on disease control in adult patients with suboptimal anatomically controlled neovascular age-related macular degeneration (SWIFT)

Summary

EudraCT number	2019-004145-33
Trial protocol	FR
Global end of trial date	

Results information

Result version number	v1
This version publication date	12 October 2023
First version publication date	12 October 2023

Trial information

Trial identification

Sponsor protocol code	CRTH258AFR03

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04264819
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	Interim
Date of interim/final analysis	05 October 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 October 2022
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

The Primary objective is to evaluate the effect of brolucizumab 6 mg on disease control.

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	14 December 2020
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Ethical reason, Safety, Regulatory reason, Scientific research
Long term follow-up duration	7 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 295
Worldwide total number of subjects	295
EEA total number of subjects	295

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)	22
From 65 to 84 years	217
85 years and over	56

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Before inclusion, patients underwent a 4-to-8-Week Washout Period (from 26 to 62 days) from the last administration of a licensed anti-VEGF drug (i.e., Lucentis®, Eylea®).

Period 1

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

Arms

Arm title	RTH258/Brolucizumab

Arm description:

This is a single arm study in which all patients are treated with brolucizumab 6mg; 3 loading injections (at Screening/Baseline, week 4 and week 8) followed by treat-to-control phase with adjustable treatment frequency based on disease activity from every 8 to up to 16 weeks; last treatment at week 44/46 based on the treatment regimen.

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 (RTH258 6 mg /0.05 mL)

Number of subjects in period 1	RTH258/Brolucizumab
Started	295
Full Analysis Set (FAS)	289
Completed	281
Not completed	14
Physician decision	4
Consent withdrawn by subject	4
Adverse event, non-fatal	5
Lost to follow-up	1

Baseline characteristics

Reporting groups	
Reporting group title	RTH258/Brolucizumab
Reporting group description:	
This is a single arm study in which all patients are treated with brolucizumab 6mg; 3 loading injections (at Screening/Baseline, week 4 and week 8) followed by treat-to-control phase with adjustable treatment frequency based on disease activity from every 8 to up to 16 weeks; last treatment at week 44/46 based on the treatment regimen.	

Reporting group values	RTH258/Brolucizumab	Total	
Number of subjects	295	295	
Age Categorical Units: Participants			
<=18 years	0	0	
Between 18 and 65 years	22	22	
>=65 years	273	273	
Age Continuous Units: Years			
arithmetic mean	76.2		
standard deviation	± 8.13	-	
Sex: Female, Male Units: Participants			
Female	183	183	
Male	112	112	
Race and Ethnicity Not Collected Units: Participants			
arithmetic mean	99999		
standard deviation	± 99999	-	

End points

End points reporting groups

Reporting group title	RTH258/Brolucizumab

Reporting group description:

This is a single arm study in which all patients are treated with brolucizumab 6mg; 3 loading injections (at Screening/Baseline, week 4 and week 8) followed by treat-to-control phase with adjustable treatment frequency based on disease activity from every 8 to up to 16 weeks; last treatment at week 44/46 based on the treatment regimen.

Primary: Number of patients with no disease activity at Week 16

End point title	Number of patients with no disease activity at Week 16[1]

End point description:

Disease activity criteria were assessed by the Investigator based on whether nAMD was still active or had been re-activated. The disease was defined as active if at least one of the following criteria was observed:
- BCVA decrease ≥ 5 letters from the best value since Baseline due to disease activity
- Any significant increase in CRT
- Retinal hemorrhage
- Intraretinal fluid or SRF due to disease activity (degenerative cysts allowed)
- Increase of sub-RPE fluid

These criteria were for guidance only, Investigators could define disease activity based on their own assessment.

End point type	Primary

End point timeframe:

Week 16

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Not applicable for a single arm study.

End point values	RTH258/Brolucizumab			
Subject group type	Reporting group			
Number of subjects analysed	289			
Units: Participants	88			

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 – up to 20 weeks; Post-treatment - greater than 30 days after last treatment, up to a maximum timeframe of 81 days after treatment

End point type	Post-hoc

End point timeframe:

On-treatment – up to 20 weeks; Post-treatment - greater than 30 days after last treatment, up to 81 days post-treatment

End point values	RTH258/Brolucizumab			
Subject group type	Reporting group			
Number of subjects analysed	295			
Units: Participants				
On-Treatment Deaths	0			
Post-Treatment Deaths	2			
All Deaths	2			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

For in the interim results reporting, AEs are reported from first dose of study treatment to 16 weeks, for the last-enrolled pt, and 50 weeks for the earlier-enrolled pts, for a maximum timeframe of approx. 50 weeks. The study is still ongoing.

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	25.1

Reporting groups

Reporting group title	Overall Study

Reporting group description:

RTH258/Brolucizumab

Serious adverse events	Overall Study		
Total subjects affected by serious adverse events			
subjects affected / exposed	28 / 295 (9.49%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung adenocarcinoma			
subjects affected / exposed	1 / 295 (0.34%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastric cancer			
subjects affected / exposed	1 / 295 (0.34%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Glioblastoma			
subjects affected / exposed	1 / 295 (0.34%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatic cancer			

subjects affected / exposed	1 / 295 (0.34%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Thyroid cancer			
subjects affected / exposed	1 / 295 (0.34%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Traumatic intracranial haematoma			
subjects affected / exposed	1 / 295 (0.34%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	2 / 295 (0.68%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Cardiomyopathy			
subjects affected / exposed	1 / 295 (0.34%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 295 (0.34%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Presyncope			
subjects affected / exposed	1 / 295 (0.34%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Headache			
subjects affected / exposed	1 / 295 (0.34%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Cerebrovascular accident				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
General disorders and administration site conditions				
Chest pain				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Cyclitis - Study eye				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Eye haematoma - Study eye				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Uveitis - Study eye				
subjects affected / exposed	7 / 295 (2.37%)			
occurrences causally related to treatment / all	7 / 7			
deaths causally related to treatment / all	0 / 0			
Retinal occlusive vasculitis - Study eye				
subjects affected / exposed	2 / 295 (0.68%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Retinal artery occlusion - Study eye				
subjects affected / exposed	2 / 295 (0.68%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Iridocyclitis - Study eye				

subjects affected / exposed	1 / 295 (0.34%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Eye inflammation - Study eye			
subjects affected / exposed	1 / 295 (0.34%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Vitritis - Study eye			
subjects affected / exposed	3 / 295 (1.02%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	1 / 295 (0.34%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Muscle spasms			
subjects affected / exposed	1 / 295 (0.34%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 295 (0.34%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Overall Study		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	148 / 295 (50.17%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Uterine leiomyoma subjects affected / exposed occurrences (all)	1 / 295 (0.34%) 1		
Vascular disorders Hypotension subjects affected / exposed occurrences (all) Hypertension subjects affected / exposed occurrences (all) Arterial stenosis subjects affected / exposed occurrences (all) White coat hypertension subjects affected / exposed occurrences (all)	 1 / 295 (0.34%) 1 11 / 295 (3.73%) 12 1 / 295 (0.34%) 1 1 / 295 (0.34%) 1		
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all)	 1 / 295 (0.34%) 1		
Immune system disorders Allergy to arthropod sting subjects affected / exposed occurrences (all) Allergy to synthetic fabric subjects affected / exposed occurrences (all) Drug hypersensitivity subjects affected / exposed occurrences (all) Seasonal allergy subjects affected / exposed occurrences (all)	 1 / 295 (0.34%) 1 1 / 295 (0.34%) 1 1 / 295 (0.34%) 1 1 / 295 (0.34%) 1		
Reproductive system and breast disorders Benign prostatic hyperplasia			

subjects affected / exposed	1 / 295 (0.34%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 295 (0.34%)		
occurrences (all)	1		
Bronchospasm			
subjects affected / exposed	1 / 295 (0.34%)		
occurrences (all)	1		
Psychiatric disorders			
Hallucination			
subjects affected / exposed	1 / 295 (0.34%)		
occurrences (all)	1		
Investigations			
Intraocular pressure increased - Both eye			
subjects affected / exposed	1 / 295 (0.34%)		
occurrences (all)	1		
Intraocular pressure increased - Study eye			
subjects affected / exposed	6 / 295 (2.03%)		
occurrences (all)	8		
Prostatic specific antigen increased			
subjects affected / exposed	1 / 295 (0.34%)		
occurrences (all)	1		
SARS-CoV-2 test positive			
subjects affected / exposed	1 / 295 (0.34%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Foreign body in eye - Both eye			
subjects affected / exposed	1 / 295 (0.34%)		
occurrences (all)	1		
Procedural pain - Study eye			
subjects affected / exposed	2 / 295 (0.68%)		
occurrences (all)	2		
Spinal fracture			

subjects affected / exposed occurrences (all) Thermal burn - Both eye subjects affected / exposed occurrences (all) Upper limb fracture subjects affected / exposed occurrences (all)	1 / 295 (0.34%) 1 1 / 295 (0.34%) 1 1 / 295 (0.34%) 1		
Cardiac disorders Atrial fibrillation subjects affected / exposed occurrences (all) Arrhythmia subjects affected / exposed occurrences (all)	 1 / 295 (0.34%) 1 2 / 295 (0.68%) 2		
Nervous system disorders Amnesia subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Psychomotor skills impaired subjects affected / exposed occurrences (all) Sciatica subjects affected / exposed occurrences (all) Tremor subjects affected / exposed occurrences (all)	 1 / 295 (0.34%) 1 3 / 295 (1.02%) 3 1 / 295 (0.34%) 1 3 / 295 (1.02%) 3 1 / 295 (0.34%) 1		
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	 1 / 295 (0.34%) 2		
Eye disorders			

Age-related macular degeneration - Fellow eye				
subjects affected / exposed	3 / 295 (1.02%)			
occurrences (all)	3			
Anterior chamber cell - Study eye				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Blepharitis				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Cataract - Both eye				
subjects affected / exposed	4 / 295 (1.36%)			
occurrences (all)	4			
Dry eye - Both eye				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Diplopia - Both eye				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Conjunctival haemorrhage - Study eye				
subjects affected / exposed	2 / 295 (0.68%)			
occurrences (all)	2			
Chalazion				
subjects affected / exposed	2 / 295 (0.68%)			
occurrences (all)	2			
Dry eye - Study eye				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Cataract - Study eye				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Cataract - Fellow eye				
subjects affected / exposed	2 / 295 (0.68%)			
occurrences (all)	2			
Keratitis - Study eye				

subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Iridocyclitis - Study eye				
subjects affected / exposed	4 / 295 (1.36%)			
occurrences (all)	4			
Glaucoma - Both eye				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Eyelid irritation				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Eye pruritus - Study eye				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Eye pain - Study eye				
subjects affected / exposed	3 / 295 (1.02%)			
occurrences (all)	3			
Eye irritation - Study eye				
subjects affected / exposed	3 / 295 (1.02%)			
occurrences (all)	3			
Eye irritation - Both eye				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Eye inflammation - Study eye				
subjects affected / exposed	3 / 295 (1.02%)			
occurrences (all)	3			
Dyschromatopsia - Both eye				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Lacrimation increased - Both eye				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Neovascular age-related macular degeneration - Fellow eye				
subjects affected / exposed	11 / 295 (3.73%)			
occurrences (all)	11			

Macular hole - Study eye				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Neovascular age-related macular degeneration - Study eye				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Vision blurred - Both eye				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Ocular hypertension - Both eye				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Ocular hypertension - Fellow eye				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Ocular hypertension - Study eye				
subjects affected / exposed	10 / 295 (3.39%)			
occurrences (all)	14			
Ocular vasculitis - Study eye				
subjects affected / exposed	2 / 295 (0.68%)			
occurrences (all)	2			
Posterior capsule opacification - Both eye				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Posterior capsule opacification - Fellow eye				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Posterior capsule opacification - Study eye				
subjects affected / exposed	3 / 295 (1.02%)			
occurrences (all)	3			
Retinal degeneration - Study eye				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Retinal detachment - Study eye				

subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Retinal drusen - Study eye				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Retinal haemorrhage - Fellow eye				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Retinal haemorrhage - Study eye				
subjects affected / exposed	4 / 295 (1.36%)			
occurrences (all)	5			
Retinal occlusive vasculitis - Study eye				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Retinal perivascular sheathing - Fellow eye				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Retinal perivascular sheathing - Study eye				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Retinal pigment epithelial tear - Study eye				
subjects affected / exposed	2 / 295 (0.68%)			
occurrences (all)	2			
Retinal tear - Study eye				
subjects affected / exposed	2 / 295 (0.68%)			
occurrences (all)	2			
Retinal vasculitis - Study eye				
subjects affected / exposed	2 / 295 (0.68%)			
occurrences (all)	2			
Serous retinal detachment - Fellow eye				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Uveitis - Study eye				

subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Swelling of eyelid				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Ocular hyperaemia - Study eye				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Vision blurred - Fellow eye				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Vision blurred - Study eye				
subjects affected / exposed	3 / 295 (1.02%)			
occurrences (all)	3			
Visual acuity reduced - Study eye				
subjects affected / exposed	2 / 295 (0.68%)			
occurrences (all)	2			
Visual field defect - Study eye				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Vitreous detachment - Study eye				
subjects affected / exposed	9 / 295 (3.05%)			
occurrences (all)	9			
Vitreous floaters - Both eye				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Vitreous floaters - Study eye				
subjects affected / exposed	12 / 295 (4.07%)			
occurrences (all)	13			
Vitreous haemorrhage - Study eye				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Vitreous opacities - Study eye				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Vitritis - Study eye				

subjects affected / exposed occurrences (all)	5 / 295 (1.69%) 6		
Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all)	 1 / 295 (0.34%) 1		
Constipation subjects affected / exposed occurrences (all)	 2 / 295 (0.68%) 2		
Diarrhoea subjects affected / exposed occurrences (all)	 3 / 295 (1.02%) 3		
Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	 3 / 295 (1.02%) 3		
Gingival erosion subjects affected / exposed occurrences (all)	 1 / 295 (0.34%) 1		
Inguinal hernia subjects affected / exposed occurrences (all)	 1 / 295 (0.34%) 1		
Irritable bowel syndrome subjects affected / exposed occurrences (all)	 1 / 295 (0.34%) 1		
Nausea subjects affected / exposed occurrences (all)	 2 / 295 (0.68%) 2		
Rectal polyp subjects affected / exposed occurrences (all)	 1 / 295 (0.34%) 1		
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all)	 1 / 295 (0.34%) 1		
Rash			

subjects affected / exposed	1 / 295 (0.34%)		
occurrences (all)	1		
Purpura			
subjects affected / exposed	1 / 295 (0.34%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	1 / 295 (0.34%)		
occurrences (all)	1		
Erythema			
subjects affected / exposed	1 / 295 (0.34%)		
occurrences (all)	1		
Eczema			
subjects affected / exposed	1 / 295 (0.34%)		
occurrences (all)	1		
Dermatitis allergic			
subjects affected / exposed	1 / 295 (0.34%)		
occurrences (all)	1		
Psoriasis			
subjects affected / exposed	1 / 295 (0.34%)		
occurrences (all)	1		
Renal and urinary disorders			
Urinary tract polyp			
subjects affected / exposed	1 / 295 (0.34%)		
occurrences (all)	1		
Urinary incontinence			
subjects affected / exposed	1 / 295 (0.34%)		
occurrences (all)	1		
Renal cyst			
subjects affected / exposed	1 / 295 (0.34%)		
occurrences (all)	1		
Nephrolithiasis			
subjects affected / exposed	1 / 295 (0.34%)		
occurrences (all)	1		
Hydronephrosis			
subjects affected / exposed	1 / 295 (0.34%)		
occurrences (all)	1		

Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 295 (0.34%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Limb discomfort			
subjects affected / exposed	1 / 295 (0.34%)		
occurrences (all)	1		
Intervertebral disc protrusion			
subjects affected / exposed	1 / 295 (0.34%)		
occurrences (all)	1		
Back pain			
subjects affected / exposed	4 / 295 (1.36%)		
occurrences (all)	4		
Arthralgia			
subjects affected / exposed	2 / 295 (0.68%)		
occurrences (all)	2		
Myalgia			
subjects affected / exposed	1 / 295 (0.34%)		
occurrences (all)	1		
Osteoarthritis			
subjects affected / exposed	2 / 295 (0.68%)		
occurrences (all)	2		
Osteoporosis			
subjects affected / exposed	1 / 295 (0.34%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	1 / 295 (0.34%)		
occurrences (all)	1		
Tendonitis			
subjects affected / exposed	1 / 295 (0.34%)		
occurrences (all)	1		
Infections and infestations			
Asymptomatic COVID-19			
subjects affected / exposed	1 / 295 (0.34%)		
occurrences (all)	1		

Bronchitis				
subjects affected / exposed	4 / 295 (1.36%)			
occurrences (all)	4			
Dermatophytosis				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Conjunctivitis - Study eye				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Conjunctivitis - Both eye				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
COVID-19				
subjects affected / exposed	7 / 295 (2.37%)			
occurrences (all)	7			
Gastroenteritis				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Herpes ophthalmic - Study eye				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Herpes zoster				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Influenza				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Nasopharyngitis				
subjects affected / exposed	3 / 295 (1.02%)			
occurrences (all)	3			
Onychomycosis				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			
Otitis externa				
subjects affected / exposed	1 / 295 (0.34%)			
occurrences (all)	1			

Periodontitis subjects affected / exposed occurrences (all) Sinusitis subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all) Cystitis subjects affected / exposed occurrences (all)	1 / 295 (0.34%) 1 1 / 295 (0.34%) 1 3 / 295 (1.02%) 3 1 / 295 (0.34%) 1		
Metabolism and nutrition disorders Hyperuricaemia subjects affected / exposed occurrences (all) Diabetes mellitus subjects affected / exposed occurrences (all) Hypokalaemia subjects affected / exposed occurrences (all)	1 / 295 (0.34%) 1 3 / 295 (1.02%) 3 1 / 295 (0.34%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 January 2020	The purpose of this amendment was to incorporate changes requested by Regulatory Authorities. Clarification of the washout period between the last dose of the anti-VEGF treatment received by the patient prior to be included in the study and the first dose of brolucizumab 6 mg administrated in the study. Clarification on the number of mandatory visits and on the data to collect for the fellow eye.
21 October 2020	The purpose was to provide clarification and guidance on safety assessments in accordance to the urgent safety measures regarding the post-marketing reports with brolucizumab 6 mg (Beovu®) in the treatment of nAMD. Restrictions in the use of corticosteroids were removed to provide flexibility using systemic steroids for the treatment of AEs at the Investigator's discretion. Additional guidance was added to emphasize that if any sign of IOI was present, an IVT injection were not to be performed and patients were to be treated for IOI according to clinical practice. Additional examinations and assessments were included to fully characterize cases of IOI. The number of study sites was increased from 50 to 75 to ensure the feasibility of patient recruitment in a 9-month period. Instructions on ophthalmic examinations in case of symptoms of IOI were added.
01 September 2021	As per the urgent safety measures, clarification and guidance were provided on the early discontinuation of study treatment required for those patients who were on q4w dosing beyond the first 3-monthly loading phase or would need q4w dosing beyond the "loading phase" based on the Investigator's assessment. Discontinuation of study treatment for patients who develop RV and/or RVO was added in line with the urgent safety measures. The safety sections were updated throughout the protocol including updating the Risks and Benefits section and creating a new section under Safety Monitoring to consolidate all the information regarding the risk mitigation into one section in the protocol and require close monitoring of patients with IOI. Clarification was provided on record of prior Intraocular or periocular use of corticosteroids in the study eye and remove of the study timelines and number of sites.
25 November 2021	The optional Patient reported outcome (PRO) self-assessment of BCNVA by the patient at home was removed because of the scarce use by the elderly population of the study, which would not allow valid conclusions from data collected. The Warnings and Precautions for Use section of the Beovu® brolucizumab 6 mg EU SmPC was updated to indicate that patients treated with Beovu with a medical history of IOI and/or RVO should be closely monitored, and for patients who develop IOI, even if not associated with RV and/or RVO, treatment with Beovu should be discontinued and the events promptly managed. Information on gender imbalance on IOI following brolucizumab 6 mg treatment was added.
05 April 2022	Due to COVID-19 and the urgent safety measures, the originally planned number of patients could not be achieved. Thus, the sample size was reassessed.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported