Clinical trial results:
A Phase 3 Multicenter Randomized, Sham-Controlled Study to Determine the Safety and Efficacy of NT-501 in Macular Telangiectasia type 2

Summary

EudraCT number	2017-003260-12
Trial protocol	DE
Global end of trial date	07 September 2022

Results information

Result version number	v1 (current)
This version publication date	04 August 2024
First version publication date	04 August 2024

Trial information

Trial identification

Sponsor protocol code	NTMT-03-B

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03319849
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Neurotech Pharmaceuticals Inc
Sponsor organisation address	900 Highland Corporate Drive, Suite 101, Cumberland, United States,
Public contact	Kevin Hibbert, Neurotech Pharmaceuticals Inc, k.hibbert@neurotechusa.com
Scientific contact	Kevin Hibbert, Neurotech Pharmaceuticals Inc, k.hibbert@neurotechusa.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	30 November 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 September 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The overall objective of this study is to evaluate the efficacy and safety of NT-501 for the treatment of MacTel.

Primary objective:
• To determine the rate of change in the ellipsoid zone (EZ; inner segment/outer segment [IS/OS]) area loss over 24 months, as measured by study eye spectral-domain optical coherence tomography (SD-OCT) in participants with MacTel

Protection of trial subjects:

Ethics committee approval

Background therapy:

None

Evidence for comparator:

A sham surgical procedure was performed to mimic the implant procedure; there was no comparator product,

Actual start date of recruitment	22 January 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 25
Country: Number of subjects enrolled	United States: 73
Country: Number of subjects enrolled	Germany: 21
Worldwide total number of subjects	119
EEA total number of subjects	21

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)	79
From 65 to 84 years	40
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Screening period for up to 30 days

Pre-assignment

Screening details:

NTMT-03-B: 119 subjects enrolled (6 participants withdrew after randomization) but prior to the implantation/sham surgery procedure; 59 subjects in NT-501 arm and 54 subjects in sham arm.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind[1]
Roles blinded	Data analyst, Carer, Assessor, Subject

Blinding implementation details:

The subjects and all personnel at the image reading center remained masked to the treatment assignment throughout the study. In addition, the refractionist, VA examiner, and photographers/imagers were masked to treatment assignment (NT-501 implantation or sham procedure) at all follow-up visits. The ophthalmologist, surgeon, and clinic coordinator were instructed not to discuss the assigned treatment with the subject.

Arms

Are arms mutually exclusive?	Yes
Arm title	NT-501

Arm description:

Test product

Arm type	Experimental
Investigational medicinal product name	NT-501 Implant
Investigational medicinal product code	NT-501
Other name	
Pharmaceutical forms	Implant
Routes of administration	Intravitreal use

Dosage and administration details:

Each implant consisting of hCNTF-secreting NTC-201-6A.02 cells encapsulated within supportive matrices and surrounded by a semipermeable polymer membrane.
The NTC-201-6A cells continuously secrete CNTF from the NT-501 implant into the vitreous cavity.
Implanted by a qualified Health Care Professional.

Arm title	Sham Procedure

Arm description:

A sham surgical procedure was performed to mimic the implant procedure; there was no comparator product.

Arm type	Sham surgical procedure
Investigational medicinal product name	Sham procedure
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Implant
Routes of administration	Intravitreal use

Dosage and administration details:

The sham surgery involved a superficial conjunctival incision performed under local anesthetic and closure with a single suture.

Notes:

[1] - The number of roles blinded appears inconsistent with a single blinded trial. It is expected that there will be one role blinded in a single blind trial.

Justification: The subjects and all personnel at the image reading center remained masked to the treatment assignment throughout the study. In addition, the refractionist, VA examiner, and photographers/imagers were masked to treatment assignment (NT-501 implantation or sham procedure) at all follow-up visits. The ophthalmologist, surgeon, and clinic coordinator were instructed not to discuss the assigned treatment with the subject.

Number of subjects in period 1	NT-501	Sham Procedure
Started	60	59
Completed	57	49
Not completed	3	10
Adverse event, serious fatal	1	-
Physician decision	-	1
Consent withdrawn by subject	-	1
COVID-19	-	1
Other	1	2
Eligible and did not enrol in amendment	1	3
Lost to follow-up	-	2

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	119	119	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	79	79	
From 65-84 years	40	40	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	84	84	
Male	35	35	

Subject analysis sets	
Subject analysis set title	Safety population
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety population included all randomized subjects who underwent either NT-501 implantation surgery or sham surgery and had at least 1 safety measurement.

Subject analysis set title	Modified Intention-to-Treat population
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The mITT population comprised all randomized subjects who underwent either NT-501 implantation surgery or sham surgery

Subject analysis set title	Per Protocol Population
Subject analysis set type	Per protocol

Subject analysis set description:

The PP population included all subjects in the mITT population who had no important protocol deviations (ie, deviations that may have had a substantial impact on the primary efficacy endpoint).

Reporting group values	Safety population	Modified Intention-to-Treat population	Per Protocol Population
Number of subjects	113	113	105
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)	78	78	74
From 65-84 years	35	35	31
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	82	82	76
Male	31	31	29

End points

End points reporting groups

Reporting group title	NT-501
Reporting group description:	
Test product	
Reporting group title	Sham Procedure
Reporting group description:	
A sham surgical procedure was performed to mimic the implant procedure; there was no comparator product.	
Subject analysis set title	Safety population
Subject analysis set type	Safety analysis
Subject analysis set description:	
The safety population included all randomized subjects who underwent either NT-501 implantation surgery or sham surgery and had at least 1 safety measurement.	
Subject analysis set title	Modified Intention-to-Treat population
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
The mITT population comprised all randomized subjects who underwent either NT-501 implantation surgery or sham surgery	
Subject analysis set title	Per Protocol Population
Subject analysis set type	Per protocol
Subject analysis set description:	
The PP population included all subjects in the mITT population who had no important protocol deviations (ie, deviations that may have had a substantial impact on the primary efficacy endpoint).	

Primary: Primary Efficacy Endpoint

End point title	Primary Efficacy Endpoint
End point description:	
The rate of change in the area of EZ loss (IS/OS; macular photoreceptor loss) from baseline through month 24, as assessed using SD-OCT in the study eye of subjects with MacTel.	
End point type	Primary
End point timeframe:	
End point timeframe is 2 years Baseline, Month 6, 12, 16, 20 and 24. Month 6 was collected but not included in the primary analyses.	

End point values	NT-501	Sham Procedure		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	54		
Units: mm2				
number (not applicable)	0.111	0.160		

Statistical analyses

Statistical analysis title	Statistical Analysis - NT-501 vs Sham Procedure

Statistical analysis description:

The efficacy and safety of the NT-501 implant that delivers a daily dose of CNTF in comparison to sham surgery with no implant, in participants with confirmed MacTel.

Comparison groups	Sham Procedure v NT-501
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0186
Method	longitudinal mixed model
Parameter estimate	Mean difference (net)
Point estimate	-0.049
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.089
upper limit	-0.0082
Variability estimate	Standard error of the mean
Dispersion value	0.0206

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
During the Clinical Trial	
Adverse event reporting additional description:	
Please note that only non-ocular and ocular events in the study eye have been reported. The Adverse events reported are those that occurred through month 24.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups	
Reporting group title	NT-501
Reporting group description:	
Test product	
Reporting group title	Sham Procedure
Reporting group description:	
A sham surgical procedure was performed to mimic the implant procedure; there was no comparator product.	

Serious adverse events	NT-501	Sham Procedure	
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 59 (18.64%)	10 / 54 (18.52%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Injury, poisoning and procedural complications			
Suture related complication			
subjects affected / exposed	3 / 59 (5.08%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Palpitations			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Transient ischaemic attack			
subjects affected / exposed	2 / 59 (3.39%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Small intestinal obstruction			

subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Endometriosis			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 59 (1.69%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Goitre			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			

subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device extrusion			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (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			
Cellulitis			
subjects affected / exposed	1 / 59 (1.69%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	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	NT-501	Sham Procedure	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	56 / 59 (94.92%)	48 / 54 (88.89%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Blepharal papilloma			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Basal cell carcinoma			
subjects affected / exposed	1 / 59 (1.69%)	1 / 54 (1.85%)	
occurrences (all)	1	1	
Melanocytic naevus			

subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 59 (6.78%)	1 / 54 (1.85%)	
occurrences (all)	4	1	
Hot flush			
subjects affected / exposed	0 / 59 (0.00%)	2 / 54 (3.70%)	
occurrences (all)	0	2	
Prehypertension			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	2 / 59 (3.39%)	0 / 54 (0.00%)	
occurrences (all)	2	0	
Oedema peripheral			
subjects affected / exposed	0 / 59 (0.00%)	2 / 54 (3.70%)	
occurrences (all)	0	2	
Adverse drug reaction			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Fatigue			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Pain			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	2 / 59 (3.39%)	0 / 54 (0.00%)	
occurrences (all)	2	0	
Drug hypersensitivity			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Social circumstances			

Menopause			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Prostatomegaly			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Vaginal haemorrhage			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	2 / 59 (3.39%)	1 / 54 (1.85%)	
occurrences (all)	2	1	
Cough			
subjects affected / exposed	1 / 59 (1.69%)	2 / 54 (3.70%)	
occurrences (all)	1	2	
Respiratory tract congestion			
subjects affected / exposed	3 / 59 (5.08%)	0 / 54 (0.00%)	
occurrences (all)	3	0	
Sleep apnoea syndrome			
subjects affected / exposed	1 / 59 (1.69%)	1 / 54 (1.85%)	
occurrences (all)	1	1	
Hypopnoea			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Rhinitis allergic			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Sinus congestion			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	

Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 59 (0.00%)	2 / 54 (3.70%)	
occurrences (all)	0	2	
Agitation			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Product issues			
Product deposit			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Investigations			
Intraocular pressure increased			
subjects affected / exposed	2 / 59 (3.39%)	1 / 54 (1.85%)	
occurrences (all)	2	1	
Blood cholesterol increased			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Mammogram abnormal			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Suture related complication			
subjects affected / exposed	14 / 59 (23.73%)	2 / 54 (3.70%)	
occurrences (all)	14	2	
Conjunctival scar			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Corneal abrasion			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Arthropod bite			
subjects affected / exposed	1 / 59 (1.69%)	1 / 54 (1.85%)	
occurrences (all)	1	1	
Muscle strain			

subjects affected / exposed	1 / 59 (1.69%)	1 / 54 (1.85%)	
occurrences (all)	1	1	
Ankle fracture			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Contusion			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Joint dislocation			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Limb injury			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Muscle rupture			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Scar			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Tooth fracture			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Congenital, familial and genetic disorders			
Macular dystrophy congenital			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 59 (1.69%)	2 / 54 (3.70%)	
occurrences (all)	1	2	
Ventricular extrasystoles			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Nervous system disorders			

Aura			
subjects affected / exposed	2 / 59 (3.39%)	0 / 54 (0.00%)	
occurrences (all)	2	0	
Headache			
subjects affected / exposed	7 / 59 (11.86%)	6 / 54 (11.11%)	
occurrences (all)	7	6	
Dizziness			
subjects affected / exposed	2 / 59 (3.39%)	2 / 54 (3.70%)	
occurrences (all)	2	2	
Paraesthesia			
subjects affected / exposed	0 / 59 (0.00%)	2 / 54 (3.70%)	
occurrences (all)	0	2	
Transient ischaemic attack			
subjects affected / exposed	2 / 59 (3.39%)	0 / 54 (0.00%)	
occurrences (all)	2	0	
Ageusia			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Carotid artery stenosis			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Essential tremor			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Hypoaesthesia			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Migraine			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Migraine with aura			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Neuropathy peripheral			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	

Sciatica			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Tremor			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Deafness unilateral			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Vertigo			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	19 / 59 (32.20%)	10 / 54 (18.52%)	
occurrences (all)	19	10	
Foreign body sensation in eyes			
subjects affected / exposed	14 / 59 (23.73%)	8 / 54 (14.81%)	
occurrences (all)	14	8	
Conjunctival hyperaemia			
subjects affected / exposed	12 / 59 (20.34%)	7 / 54 (12.96%)	
occurrences (all)	12	7	
Eye pain			
subjects affected / exposed	12 / 59 (20.34%)	6 / 54 (11.11%)	
occurrences (all)	12	6	
Delayed dark adaptation			
subjects affected / exposed	15 / 59 (25.42%)	2 / 54 (3.70%)	
occurrences (all)	15	2	
Conjunctival oedema			
subjects affected / exposed	4 / 59 (6.78%)	6 / 54 (11.11%)	
occurrences (all)	4	6	
Vision blurred			
subjects affected / exposed	6 / 59 (10.17%)	3 / 54 (5.56%)	
occurrences (all)	6	3	
Dry eye			

subjects affected / exposed	6 / 59 (10.17%)	2 / 54 (3.70%)	
occurrences (all)	6	2	
Miosis			
subjects affected / exposed	8 / 59 (13.56%)	0 / 54 (0.00%)	
occurrences (all)	8	0	
Conjunctival irritation			
subjects affected / exposed	3 / 59 (5.08%)	3 / 54 (5.56%)	
occurrences (all)	3	3	
Swelling of eyelid			
subjects affected / exposed	3 / 59 (5.08%)	3 / 54 (5.56%)	
occurrences (all)	3	3	
Visual impairment			
subjects affected / exposed	3 / 59 (5.08%)	3 / 54 (5.56%)	
occurrences (all)	3	3	
Vitreous floaters			
subjects affected / exposed	6 / 59 (10.17%)	0 / 54 (0.00%)	
occurrences (all)	6	0	
Vitreous haemorrhage			
subjects affected / exposed	6 / 59 (10.17%)	0 / 54 (0.00%)	
occurrences (all)	6	0	
Choroidal neovascularisation			
subjects affected / exposed	2 / 59 (3.39%)	1 / 54 (1.85%)	
occurrences (all)	2	1	
Eye irritation			
subjects affected / exposed	2 / 59 (3.39%)	3 / 54 (5.56%)	
occurrences (all)	2	3	
Metamorphopsia			
subjects affected / exposed	1 / 59 (1.69%)	4 / 54 (7.41%)	
occurrences (all)	1	4	
Ocular discomfort			
subjects affected / exposed	4 / 59 (6.78%)	1 / 54 (1.85%)	
occurrences (all)	4	1	
Eye discharge			
subjects affected / exposed	2 / 59 (3.39%)	1 / 54 (1.85%)	
occurrences (all)	2	1	
Eye pruritus			

subjects affected / exposed	2 / 59 (3.39%)	1 / 54 (1.85%)	
occurrences (all)	2	1	
Lacrimation increased			
subjects affected / exposed	0 / 59 (0.00%)	3 / 54 (5.56%)	
occurrences (all)	0	3	
Retinal haemorrhage			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Vitreous detachment			
subjects affected / exposed	2 / 59 (3.39%)	0 / 54 (0.00%)	
occurrences (all)	2	0	
Anterior chamber cell			
subjects affected / exposed	2 / 59 (3.39%)	0 / 54 (0.00%)	
occurrences (all)	2	0	
Anterior chamber flare			
subjects affected / exposed	2 / 59 (3.39%)	0 / 54 (0.00%)	
occurrences (all)	2	0	
Asthenopia			
subjects affected / exposed	0 / 59 (0.00%)	2 / 54 (3.70%)	
occurrences (all)	0	2	
Blepharitis			
subjects affected / exposed	1 / 59 (1.69%)	1 / 54 (1.85%)	
occurrences (all)	1	1	
Cataract			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Cataract subcapsular			
subjects affected / exposed	2 / 59 (3.39%)	0 / 54 (0.00%)	
occurrences (all)	2	0	
Diplopia			
subjects affected / exposed	2 / 59 (3.39%)	0 / 54 (0.00%)	
occurrences (all)	2	0	
Meibomian gland dysfunction			
subjects affected / exposed	2 / 59 (3.39%)	0 / 54 (0.00%)	
occurrences (all)	2	0	
Photophobia			

subjects affected / exposed	0 / 59 (0.00%)	2 / 54 (3.70%)	
occurrences (all)	0	2	
Photopsia			
subjects affected / exposed	1 / 59 (1.69%)	1 / 54 (1.85%)	
occurrences (all)	1	1	
Punctate keratitis			
subjects affected / exposed	1 / 59 (1.69%)	1 / 54 (1.85%)	
occurrences (all)	1	1	
Visual field defect			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Amaurosis fugax			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Anterior chamber collapse			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Blepharospasm			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Cataract cortical			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Chorioretinal folds			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Conjunctival cyst			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Corneal deposits			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Corneal epithelium defect			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Corneal erosion			

subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Corneal opacity			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Delayed light adaptation			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Epiretinal membrane			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Eye swelling			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Eyelid margin crusting			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Eyelid pain			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Eyelids pruritus			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Hypotony of eye			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Lenticular opacities			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Mydriasis			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Night blindness			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Periorbital pain			

subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Pinguecula			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Presbyopia			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Retinal artery embolism			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Retinal vasculitis			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Scleral thinning			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Visual acuity reduced			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Vitreoretinal traction syndrome			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Vitreous haze			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 59 (3.39%)	0 / 54 (0.00%)	
occurrences (all)	2	0	
Haemorrhoids			
subjects affected / exposed	0 / 59 (0.00%)	2 / 54 (3.70%)	
occurrences (all)	0	2	
Abdominal discomfort			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	

Abdominal pain upper			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Colitis			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Intestinal obstruction			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Large intestine polyp			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Periodontal inflammation			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Tooth erosion			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Actinic keratosis			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Dermatitis contact			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Hyperhidrosis			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Pruritus			

subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Sebaceous gland disorder			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Stasis dermatitis			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Eczema			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 59 (1.69%)	1 / 54 (1.85%)	
occurrences (all)	1	1	
Endocrine disorders			
Autoimmune thyroiditis			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Hypothyroidism			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 59 (5.08%)	3 / 54 (5.56%)	
occurrences (all)	3	3	
Osteoarthritis			
subjects affected / exposed	1 / 59 (1.69%)	5 / 54 (9.26%)	
occurrences (all)	1	5	
Back pain			
subjects affected / exposed	1 / 59 (1.69%)	3 / 54 (5.56%)	
occurrences (all)	1	3	
Intervertebral disc protrusion			

subjects affected / exposed	1 / 59 (1.69%)	2 / 54 (3.70%)	
occurrences (all)	1	2	
Rotator cuff syndrome			
subjects affected / exposed	2 / 59 (3.39%)	1 / 54 (1.85%)	
occurrences (all)	2	1	
Arthritis			
subjects affected / exposed	0 / 59 (0.00%)	2 / 54 (3.70%)	
occurrences (all)	0	2	
Bursitis			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Lumbar spinal stenosis			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal stiffness			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Neck pain			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Pain in extremity			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Spinal osteoarthritis			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Spondylitis			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Tendon disorder			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Trigger finger			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Infections and infestations			

Adenoviral conjunctivitis			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Conjunctivitis bacterial			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Conjunctivitis viral			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Periorbital cellulitis			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			
subjects affected / exposed	5 / 59 (8.47%)	3 / 54 (5.56%)	
occurrences (all)	5	3	
COVID-19			
subjects affected / exposed	1 / 59 (1.69%)	3 / 54 (5.56%)	
occurrences (all)	1	3	
Influenza			
subjects affected / exposed	0 / 59 (0.00%)	4 / 54 (7.41%)	
occurrences (all)	0	4	
Urinary tract infection			
subjects affected / exposed	1 / 59 (1.69%)	3 / 54 (5.56%)	
occurrences (all)	1	3	
Cellulitis			
subjects affected / exposed	1 / 59 (1.69%)	2 / 54 (3.70%)	
occurrences (all)	1	2	
Ear infection			
subjects affected / exposed	0 / 59 (0.00%)	3 / 54 (5.56%)	
occurrences (all)	0	3	
Sinusitis			
subjects affected / exposed	1 / 59 (1.69%)	2 / 54 (3.70%)	
occurrences (all)	1	2	
Staphylococcal infection			
subjects affected / exposed	1 / 59 (1.69%)	1 / 54 (1.85%)	
occurrences (all)	1	1	

Tooth abscess			
subjects affected / exposed	2 / 59 (3.39%)	0 / 54 (0.00%)	
occurrences (all)	2	0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 59 (1.69%)	1 / 54 (1.85%)	
occurrences (all)	1	1	
Candida infection			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Croup infectious			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Cystitis			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Diverticulitis			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Erysipelas			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Gastroenteritis viral			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Gingivitis			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Localised infection			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Pilonidal disease			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Pulpitis dental			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	

Bronchitis			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	2 / 59 (3.39%)	1 / 54 (1.85%)	
occurrences (all)	2	1	
Hyperglycaemia			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Hypercalcaemia			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Hypoglycaemia			
subjects affected / exposed	0 / 59 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Magnesium deficiency			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Vitamin D deficiency			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Hypocalcaemia			
subjects affected / exposed	1 / 59 (1.69%)	0 / 54 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 June 2019	Version 4.0
12 April 2021	Version 6.1
31 August 2021	Version 7.0

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported