Clinical trial results:
LUMINA: A Phase III, Multicenter, Sham-Controlled, Randomized, Double-Masked Study Assessing the Efficacy and Safety of Intravitreal Injections of 440 µg DE-109 for the Treatment of Active, Non-Infectious Uveitis of the Posterior Segment of the Eye.

Summary

EudraCT number	2019-003638-18
Trial protocol	IT
Global end of trial date	14 June 2022

Results information

Result version number	v1 (current)
This version publication date	09 September 2023
First version publication date	09 September 2023

Trial information

Trial identification

Sponsor protocol code	010906IN

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03711929
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Santen Pharmaceuticals
Sponsor organisation address	6401 Hollis Street, Suite 125, Emeryville, United States,
Public contact	VP, Vitreous & Retina TA Strategy, Santen Incorporated, +1 447485321710, salman.anzer@santen.com
Scientific contact	VP, Vitreous & Retina TA Strategy, Santen Incorporated, 7485321710 447485321710, salman.anzer@santen.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	14 June 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 June 2022
Global end of trial reached?	Yes
Global end of trial date	14 June 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of intravitreal injection of 440 µg DE-109 every 2 months as compared with sham.

Protection of trial subjects:

Informed consent was being obtained in compliance with "21 CFR Part 50.25 – PROTECTION OF HUMAN SUBJECTS, Elements of Informed Consent". Subjects were assigned a unique identifier by Santen. Any subject records or datasets that are transferred to Santen contained the identifier only; subject names or any information which would make the subject identifiable were not be transferred.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 November 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	Italy: 5
Country: Number of subjects enrolled	United States: 71
Country: Number of subjects enrolled	Argentina: 24
Country: Number of subjects enrolled	India: 45
Worldwide total number of subjects	145
EEA total number of subjects	5

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)	126

From 65 to 84 years	19
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 340 subjects were enrolled, of whom 146 were randomized into the double-masked portion of the study; 16 subjects discontinued from the study before completion of the Month 5 (Exit) visit. A total of 194 subjects were considered screen failure. A total of 103subjects enrolled into the open-label period, 19 of whom discontinued.

Pre-assignment period milestones

Number of subjects started	145
Number of subjects completed	145

Period 1

Period 1 title	Double-Masked Treatment Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Test Arm: DE-109 Injectable Solution

Arm description:

DE-109 Injectable Solution
Intravitreal injection of DE-109 440 µg in the study eye(s) every 2 months
(Day 1, Month 2, and Month 4)

Arm type	Experimental
Investigational medicinal product name	DE-109
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

DE-109 440 µg IVT injection

Arm title	Sham Procedure

Arm description:

Sham procedure administered to the study eye(s) every 2 months (Day 1,
Month 2, and Month 4). The sham procedure
mimics an intravitreal injection without penetrating the eye.

Arm type	Control Arm
Investigational medicinal product name	Sham Procedure
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

The sham procedure mimics an intravitreal injection without penetrating the eye.

Arm title	Dummy Arm: DE-109 Injectable Solution

Arm description:

Intravitreal injection of DE-109 at an undisclosed, fixed dose (within the range of 44 µg to 880 µg) in the study eye(s) every 2 months (Day 1, Month 2, and Month 4). This study arm (which has the same route of administration and frequency as the test arm).

Arm type	Dummy Arm
Investigational medicinal product name	DE-109
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

Undisclosed Fixed Dose of DE-109 Injectable Solution (range of 44 ug to 880 ug)

Number of subjects in period 1	Test Arm: DE-109 Injectable Solution	Sham Procedure	Dummy Arm: DE-109 Injectable Solution
Started	57	59	29
Completed	51	48	24
Not completed	6	11	5
Study terminated	3	8	3
Consent withdrawn by subject	-	1	-
Adverse Event	-	-	1
Adverse event, non-fatal	1	1	-
Other	1	-	-
Non- compliance with Study Drug	1	-	-
Lost to follow-up	-	1	1

Period 2

Period 2 title	Open-Label Treatment Period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Test Arm: DE-109 Injectable Solution

Arm description:

DE-109 Injectable Solution
Intravitreal injection of DE-109 440 µg in the study eye(s) every 2 months (Day 1, Month 2, and Month 4)

Arm type	Experimental

Investigational medicinal product name	DE-109
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

440 ug of DE-109 Injectable Solution

Arm title	Sham Procedure

Arm description:

Sham procedure administered to the study eye(s) every 2 months (Day 1, Month 2, and Month 4). The sham procedure mimics an intravitreal injection without penetrating the eye.

Arm type	Control Arm
Investigational medicinal product name	Sham Procedure
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

The sham procedure mimics an intravitreal injection without penetrating the eye.

Arm title	Dummy Arm: DE-109 Injectable Solution

Arm description:

Intravitreal injection of DE-109 at an undisclosed, fixed dose (within the range of 44 µg to 880 µg) in the study eye(s) every 2 months (Day 1, Month 2, and Month 4).

Arm type	Dummy Arm
Investigational medicinal product name	DE-109
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

Undisclosed Fixed Dose of DE-109 Injectable Solution (range of 44 ug to 880 ug)

Number of subjects in period 2[1]	Test Arm: DE-109 Injectable Solution	Sham Procedure	Dummy Arm: DE-109 Injectable Solution
Started	42	40	21
Completed	34	35	15
Not completed	8	5	6
Study terminated	5	4	4
Consent withdrawn by subject	1	1	1
Other	-	-	1
LTF	2	-	-

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Some participants exited the study after Double-Masked Treatment period at month 6, hence, less participants entered the Open-Label Treatment Period.

Baseline characteristics

Reporting groups	
Reporting group title	Test Arm: DE-109 Injectable Solution
Reporting group description:	
DE-109 Injectable Solution Intravitreal injection of DE-109 440 µg in the study eye(s) every 2 months (Day 1, Month 2, and Month 4)	
Reporting group title	Sham Procedure
Reporting group description:	
Sham procedure administered to the study eye(s) every 2 months (Day 1, Month 2, and Month 4). The sham procedure mimics an intravitreal injection without penetrating the eye.	
Reporting group title	Dummy Arm: DE-109 Injectable Solution
Reporting group description:	
Intravitreal injection of DE-109 at an undisclosed, fixed dose (within the range of 44 µg to 880 µg) in the study eye(s) every 2 months (Day 1, Month 2, and Month 4). This study arm (which has the same route of administration and frequency as the test arm).	

Reporting group values	Test Arm: DE-109 Injectable Solution	Sham Procedure	Dummy Arm: DE-109 Injectable Solution
Number of subjects	57	59	29
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)	47	52	27
From 65-84 years	10	7	2
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	46.8	46.2	47
standard deviation	± 17.26	± 14.40	± 14.27
Gender categorical Units: Subjects			
Female	36	35	14
Male	21	24	15
Race/Ethnicity, Customized Units: Subjects			
Asian	19	18	11
Black or African American	8	7	6
Native Hawaiian or Other Pacific Islander	1	0	0
White	29	33	12
Other	0	1	0

Region of Enrollment Units: Subjects			
Argentina	12	9	3
United States	26	31	14
Italy	1	3	1
India	18	16	11

Reporting group values	Total		
Number of subjects	145		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	126		
From 65-84 years	19		
85 years and over	0		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	85		
Male	60		
Race/Ethnicity, Customized Units: Subjects			
Asian	48		
Black or African American	21		
Native Hawaiian or Other Pacific Islander	1		
White	74		
Other	1		
Region of Enrollment Units: Subjects			
Argentina	24		
United States	71		
Italy	5		
India	45		

End points

End points reporting groups

Reporting group title	Test Arm: DE-109 Injectable Solution
Reporting group description:	
DE-109 Injectable Solution Intravitreal injection of DE-109 440 µg in the study eye(s) every 2 months (Day 1, Month 2, and Month 4)	
Reporting group title	Sham Procedure
Reporting group description:	
Sham procedure administered to the study eye(s) every 2 months (Day 1, Month 2, and Month 4). The sham procedure mimics an intravitreal injection without penetrating the eye.	
Reporting group title	Dummy Arm: DE-109 Injectable Solution
Reporting group description:	
Intravitreal injection of DE-109 at an undisclosed, fixed dose (within the range of 44 µg to 880 µg) in the study eye(s) every 2 months (Day 1, Month 2, and Month 4). This study arm (which has the same route of administration and frequency as the test arm).	
Reporting group title	Test Arm: DE-109 Injectable Solution
Reporting group description:	
DE-109 Injectable Solution Intravitreal injection of DE-109 440 µg in the study eye(s) every 2 months (Day 1, Month 2, and Month 4)	
Reporting group title	Sham Procedure
Reporting group description:	
Sham procedure administered to the study eye(s) every 2 months (Day 1, Month 2, and Month 4). The sham procedure mimics an intravitreal injection without penetrating the eye.	
Reporting group title	Dummy Arm: DE-109 Injectable Solution
Reporting group description:	
Intravitreal injection of DE-109 at an undisclosed, fixed dose (within the range of 44 µg to 880 µg) in the study eye(s) every 2 months (Day 1, Month 2, and Month 4).	

Primary: VH 0 Response at Month 5

End point title	VH 0 Response at Month 5[1][2]
End point description:	
Response rates are DE-109 (15.7%), sham (12.2%) and DE-109 fixed dose (28.7%). Rate differences between Sham and other groups are reported as results.	
End point type	Primary
End point timeframe:	
VH 0 Response at Month 5	

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: There are no statistical analyses for Open-Label Treatment period.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There is no data point for the Sham arm because the Test and Dummy arms are percent Rate Difference from the Sham arm.

End point values	Test Arm: DE-109 Injectable Solution	Dummy Arm: DE-109 Injectable Solution		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57[3]	29[4]		
Units: Rate Difference				
arithmetic mean (standard error)	3.8 (± 6.9)	16.1 (± 10.2)		

Notes:

[3] - 65 eyes are analyzed as FAS.

[4] - 32 eyes are analyzed as FAS.

Statistical analyses

No statistical analyses for this end point

Secondary: Composite score at Month 5

End point title	Composite score at Month 5[5]

End point description:

End point type	Secondary

End point timeframe:

Composite Score at Month 5

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There is no data point for the Sham arm because the Test and Dummy arms are percent Rate Difference from the Sham arm.

End point values	Test Arm: DE-109 Injectable Solution	Dummy Arm: DE-109 Injectable Solution		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57[6]	29[7]		
Units: Mean Difference				
arithmetic mean (standard error)	0.1 (± 0.2)	0.4 (± 0.3)		

Notes:

[6] - 65 eyes are analyzed as FAS.

[7] - 32 eyes are analyzed as FAS.

Statistical analyses

No statistical analyses for this end point

Secondary: VH 0 Response at Month 3

End point title	VH 0 Response at Month 3[8]

End point description:

Response rates are DE-109 (14.7%), sham (5.5%) and DE-109 fixed dose (15.4%). Rate differences between Sham and other groups are reported as results.

End point type	Secondary

End point timeframe:

VH 0 Response at Month 3

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There is no data point for the Sham arm because the Test and Dummy arms are percent Rate Difference from the Sham arm.

End point values	Test Arm: DE-109 Injectable Solution	Dummy Arm: DE-109 Injectable Solution		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57[9]	29[10]		
Units: Rate Difference				
arithmetic mean (standard error)	9.2 (± 5.6)	9.7 (± 8.0)		

Notes:

[9] - 65 eyes are analyzed as FAS.

[10] - 32 eyes are analyzed as FAS.

Statistical analyses

No statistical analyses for this end point

Secondary: Composite score at Month 3

End point title	Composite score at Month 3[11]

End point description:

End point type	Secondary

End point timeframe:

Composite score at Month 3

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There is no data point for the Sham arm because the Test and Dummy arms are percent Rate Difference from the Sham arm.

End point values	Test Arm: DE-109 Injectable Solution	Dummy Arm: DE-109 Injectable Solution		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57[12]	29[13]		
Units: Mean Difference				
arithmetic mean (standard error)	0.2 (± 0.2)	0.2 (± 0.2)		

Notes:

[12] - 65 eyes are analyzed as FAS.

[13] - 32 eyes are analyzed as FAS.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events in this study were collected from the time of informed consent and until subject withdrew or the scheduled exit visit.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Double Masked -DE-109 440 µg
Reporting group description: -	
Reporting group title	Double Masked- Sham
Reporting group description: -	
Reporting group title	Double Masked- DE-109 Fixed Dose
Reporting group description: -	
Reporting group title	Open Label -DE-109 440 µg
Reporting group description: -	
Reporting group title	Open Label- Sham
Reporting group description: -	
Reporting group title	Open Label- DE-109 Fixed Dose

Reporting group description:

This reporting group has 13 subject affected by non-adverse events, however 7 is entered as subjects affected by non-serious adverse events. The threshold for reporting non-serious adverse events is 5%, therefore 7 subjects are reported and 6 subjects are not needed to report. However, system validation notified the error message "The total number of subjects affected by the non-serious adverse events is less than the total number of subjects affected by non-serious adverse events for the reporting group. Account for all subjects affected or correct the total number of subjects for the reporting group". Therefore, the number of subjects was entered 7.

Serious adverse events	Double Masked -DE-109 440 µg	Double Masked- Sham	Double Masked- DE-109 Fixed Dose
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 57 (12.28%)	3 / 59 (5.08%)	5 / 29 (17.24%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Toxic anterior segment syndrome			
subjects affected / exposed	0 / 57 (0.00%)	0 / 59 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Brain injury			

subjects affected / exposed	1 / 57 (1.75%)	0 / 59 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraesthesia			
subjects affected / exposed	1 / 57 (1.75%)	0 / 59 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 57 (0.00%)	0 / 59 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Strangulated hernia			
subjects affected / exposed	0 / 57 (0.00%)	0 / 59 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Uveitis			
subjects affected / exposed	2 / 57 (3.51%)	0 / 59 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	3 / 3	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cataract			
subjects affected / exposed	0 / 57 (0.00%)	0 / 59 (0.00%)	2 / 29 (6.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angle closure glaucoma			
subjects affected / exposed	1 / 57 (1.75%)	0 / 59 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Birdshot chorioretinopathy			
subjects affected / exposed	1 / 57 (1.75%)	0 / 59 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Blindness			
subjects affected / exposed	0 / 57 (0.00%)	1 / 59 (1.69%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iridocyclitis			
subjects affected / exposed	1 / 57 (1.75%)	0 / 59 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-infectious endophthalmitis			
subjects affected / exposed	0 / 57 (0.00%)	0 / 59 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	0 / 57 (0.00%)	1 / 59 (1.69%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Endophthalmitis			
subjects affected / exposed	1 / 57 (1.75%)	0 / 59 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 57 (0.00%)	0 / 59 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chorioretinitis			
subjects affected / exposed	0 / 57 (0.00%)	1 / 59 (1.69%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Conjunctivitis			
subjects affected / exposed	0 / 57 (0.00%)	0 / 59 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Eye abscess			
subjects affected / exposed	1 / 57 (1.75%)	0 / 59 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Open Label -DE-109 440 µg	Open Label- Sham	Open Label- DE-109 Fixed Dose
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 42 (7.14%)	1 / 40 (2.50%)	0 / 21 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Toxic anterior segment syndrome			
subjects affected / exposed	0 / 42 (0.00%)	1 / 40 (2.50%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Brain injury			
subjects affected / exposed	0 / 42 (0.00%)	0 / 40 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraesthesia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 40 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 42 (0.00%)	0 / 40 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Strangulated hernia			
subjects affected / exposed	1 / 42 (2.38%)	0 / 40 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			

Uveitis			
subjects affected / exposed	1 / 42 (2.38%)	0 / 40 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cataract			
subjects affected / exposed	0 / 42 (0.00%)	0 / 40 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angle closure glaucoma			
subjects affected / exposed	0 / 42 (0.00%)	0 / 40 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Birdshot chorioretinopathy			
subjects affected / exposed	0 / 42 (0.00%)	0 / 40 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blindness			
subjects affected / exposed	0 / 42 (0.00%)	0 / 40 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iridocyclitis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 40 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-infectious endophthalmitis			
subjects affected / exposed	1 / 42 (2.38%)	0 / 40 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	0 / 42 (0.00%)	0 / 40 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			

Endophthalmitis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 40 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 40 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chorioretinitis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 40 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Conjunctivitis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 40 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye abscess			
subjects affected / exposed	0 / 42 (0.00%)	0 / 40 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Double Masked -DE-109 440 µg	Double Masked-Sham	Double Masked- DE-109 Fixed Dose
Total subjects affected by non-serious adverse events			
subjects affected / exposed	47 / 57 (82.46%)	45 / 59 (76.27%)	22 / 29 (75.86%)
Investigations			
Intraocular pressure increased			
subjects affected / exposed	15 / 57 (26.32%)	8 / 59 (13.56%)	3 / 29 (10.34%)
occurrences (all)	20	9	7
Product residue present			
subjects affected / exposed	4 / 57 (7.02%)	1 / 59 (1.69%)	4 / 29 (13.79%)
occurrences (all)	4	1	5
SARS-CoV-2 test positive			

subjects affected / exposed	0 / 57 (0.00%)	0 / 59 (0.00%)	2 / 29 (6.90%)
occurrences (all)	0	0	2
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 57 (5.26%)	1 / 59 (1.69%)	1 / 29 (3.45%)
occurrences (all)	3	2	1
Eye disorders			
Uveitis			
subjects affected / exposed	9 / 57 (15.79%)	12 / 59 (20.34%)	5 / 29 (17.24%)
occurrences (all)	12	16	5
Cystoid macular oedema			
subjects affected / exposed	6 / 57 (10.53%)	11 / 59 (18.64%)	1 / 29 (3.45%)
occurrences (all)	8	14	2
Conjunctival haemorrhage			
subjects affected / exposed	7 / 57 (12.28%)	5 / 59 (8.47%)	4 / 29 (13.79%)
occurrences (all)	7	5	5
Iridocyclitis			
subjects affected / exposed	7 / 57 (12.28%)	4 / 59 (6.78%)	3 / 29 (10.34%)
occurrences (all)	8	4	4
Cataract			
subjects affected / exposed	4 / 57 (7.02%)	1 / 59 (1.69%)	4 / 29 (13.79%)
occurrences (all)	5	1	5
Cataract subcapsular			
subjects affected / exposed	3 / 57 (5.26%)	3 / 59 (5.08%)	3 / 29 (10.34%)
occurrences (all)	4	5	3
Eye pain			
subjects affected / exposed	4 / 57 (7.02%)	1 / 59 (1.69%)	1 / 29 (3.45%)
occurrences (all)	4	1	2
Macular oedema			
subjects affected / exposed	1 / 57 (1.75%)	4 / 59 (6.78%)	1 / 29 (3.45%)
occurrences (all)	1	5	2
Ocular hyperaemia			
subjects affected / exposed	4 / 57 (7.02%)	0 / 59 (0.00%)	1 / 29 (3.45%)
occurrences (all)	7	0	2
Vitreous floaters			

subjects affected / exposed	0 / 57 (0.00%)	3 / 59 (5.08%)	0 / 29 (0.00%)
occurrences (all)	0	7	0
Iris adhesions			
subjects affected / exposed	2 / 57 (3.51%)	1 / 59 (1.69%)	2 / 29 (6.90%)
occurrences (all)	2	1	2
Visual impairment			
subjects affected / exposed	3 / 57 (5.26%)	0 / 59 (0.00%)	1 / 29 (3.45%)
occurrences (all)	4	0	1
Eye irritation			
subjects affected / exposed	1 / 57 (1.75%)	0 / 59 (0.00%)	2 / 29 (6.90%)
occurrences (all)	1	0	2
Keratic precipitates			
subjects affected / exposed	0 / 57 (0.00%)	2 / 59 (3.39%)	2 / 29 (6.90%)
occurrences (all)	0	2	2
Infections and infestations			
Chorioretinitis			
subjects affected / exposed	1 / 57 (1.75%)	5 / 59 (8.47%)	1 / 29 (3.45%)
occurrences (all)	1	8	2

Non-serious adverse events	Open Label -DE-109 440 µg	Open Label- Sham	Open Label- DE-109 Fixed Dose
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 42 (73.81%)	25 / 40 (62.50%)	8 / 21 (38.10%)
Investigations			
Intraocular pressure increased			
subjects affected / exposed	9 / 42 (21.43%)	8 / 40 (20.00%)	1 / 21 (4.76%)
occurrences (all)	12	12	1
Product residue present			
subjects affected / exposed	1 / 42 (2.38%)	2 / 40 (5.00%)	1 / 21 (4.76%)
occurrences (all)	1	5	1
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 42 (0.00%)	0 / 40 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 42 (0.00%)	2 / 40 (5.00%)	0 / 21 (0.00%)
occurrences (all)	0	4	0
Eye disorders			

Uveitis			
subjects affected / exposed	5 / 42 (11.90%)	4 / 40 (10.00%)	2 / 21 (9.52%)
occurrences (all)	6	5	3
Cystoid macular oedema			
subjects affected / exposed	3 / 42 (7.14%)	4 / 40 (10.00%)	0 / 21 (0.00%)
occurrences (all)	4	5	0
Conjunctival haemorrhage			
subjects affected / exposed	6 / 42 (14.29%)	4 / 40 (10.00%)	1 / 21 (4.76%)
occurrences (all)	9	4	2
Iridocyclitis			
subjects affected / exposed	2 / 42 (4.76%)	2 / 40 (5.00%)	1 / 21 (4.76%)
occurrences (all)	2	3	1
Cataract			
subjects affected / exposed	4 / 42 (9.52%)	3 / 40 (7.50%)	0 / 21 (0.00%)
occurrences (all)	4	3	0
Cataract subcapsular			
subjects affected / exposed	2 / 42 (4.76%)	1 / 40 (2.50%)	0 / 21 (0.00%)
occurrences (all)	4	2	0
Eye pain			
subjects affected / exposed	0 / 42 (0.00%)	2 / 40 (5.00%)	1 / 21 (4.76%)
occurrences (all)	0	5	1
Macular oedema			
subjects affected / exposed	0 / 42 (0.00%)	1 / 40 (2.50%)	0 / 21 (0.00%)
occurrences (all)	0	1	0
Ocular hyperaemia			
subjects affected / exposed	0 / 42 (0.00%)	1 / 40 (2.50%)	0 / 21 (0.00%)
occurrences (all)	0	2	0
Vitreous floaters			
subjects affected / exposed	0 / 42 (0.00%)	4 / 40 (10.00%)	1 / 21 (4.76%)
occurrences (all)	0	5	1
Iris adhesions			
subjects affected / exposed	1 / 42 (2.38%)	2 / 40 (5.00%)	0 / 21 (0.00%)
occurrences (all)	1	2	0
Visual impairment			
subjects affected / exposed	3 / 42 (7.14%)	0 / 40 (0.00%)	0 / 21 (0.00%)
occurrences (all)	4	0	0

Eye irritation			
subjects affected / exposed	0 / 42 (0.00%)	1 / 40 (2.50%)	0 / 21 (0.00%)
occurrences (all)	0	2	0
Keratic precipitates			
subjects affected / exposed	1 / 42 (2.38%)	1 / 40 (2.50%)	0 / 21 (0.00%)
occurrences (all)	1	2	0
Infections and infestations			
Chorioretinitis			
subjects affected / exposed	1 / 42 (2.38%)	2 / 40 (5.00%)	0 / 21 (0.00%)
occurrences (all)	2	3	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 July 2021	Protocol Amendment

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
14 June 2022	Study was terminated for business reasons.	-

Notes:

Limitations and caveats

None reported