Clinical trial results:
A Comparison of Bimatoprost SR to Selective Laser Trabeculoplasty in Patients With Open-Angle Glaucoma or Ocular Hypertension

Summary

EudraCT number	2015-002131-18
Trial protocol	GB DE DK PL FR
Global end of trial date	31 May 2023

Results information

Result version number	v1 (current)
This version publication date	03 April 2024
First version publication date	03 April 2024

Trial information

Trial identification

Sponsor protocol code	192024-093

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02507687
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Allergan Limited
Sponsor organisation address	Marlow International The Parkway, Marlow Buckinghamshire, United Kingdom, SL7 1YL
Public contact	Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.com
Scientific contact	Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	31 May 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 May 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study will evaluate the intraocular pressure (IOP)-lowering effect and safety of bimatoprost SR compared with selective laser trabeculoplasty in patients with open-angle glaucoma or ocular hypertension who are not adequately managed with topical IOP-lowering medication for reasons other than medication efficacy (e.g., due to intolerance or nonadherence).

Protection of trial subjects:

Subject and/or legal guardian read and understood the information provided about the study and gave written permission.

Background therapy:

Procedure/Surgery: Selective Laser Trabeculoplasty
SLT is a laser procedure that targets the pigment in specific cells of the eye. An ophthalmologist performed 360 degrees of SLT using a standardized method.

Procedure/Surgery: Sham Selective Laser Trabeculoplasty
Sham SLT is performed on the contralateral eye using the same method as for SLT, with the exception that the laser is not switched to the active state.

Evidence for comparator: -

Actual start date of recruitment	27 August 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 20
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	Denmark: 1
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Germany: 11
Country: Number of subjects enrolled	Israel: 6
Country: Number of subjects enrolled	New Zealand: 12
Country: Number of subjects enrolled	Philippines: 8
Country: Number of subjects enrolled	Poland: 2
Country: Number of subjects enrolled	United Kingdom: 9
Country: Number of subjects enrolled	United States: 165
Worldwide total number of subjects	240
EEA total number of subjects	18

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)	128
From 65 to 84 years	109
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

Participants were randomized at 61 sites in 11 countries (Australia, Canada, Germany, Denmark, France, Great Britain, Israel, New Zealand, Philippines, Poland, and the US).

The eye with the higher IOP at Baseline was assigned as the primary (PR) eye. If Baseline IOP was the same in both eyes, the right eye was the PR eye.

Pre-assignment

Screening details:

The PR eye was randomized to receive bimatoprost SR or SLT using a 1:1 ratio. If the PR eye received bimatoprost SR, the contralateral (CL) eye received SLT. If the PR eye received SLT, the CL eye received bimatoprost SR.

Period 1

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

Blinding implementation details:

Prior to initiation of any study procedures, each subject was assigned a number that served as the subject's identification number on all study documents. For determination of stratification group assignment for the PR eye for each subject, sites were required to enter Baseline IOP (at Hour 0) data for both eyes into an automated interactive response system.

Arms

Are arms mutually exclusive?	Yes
Arm title	Stage 1: SLT (PR Eye)/Bimatoprost SR 15 µg (CL Eye)

Arm description:

Participants enrolled prior to implementation of Protocol Amendment 3 received the following treatment in each eye:
Assigned PR Eye: SLT administered on Day 1 followed by up to three sham bimatoprost SR administrations.
CL Eye: Sham SLT administered on Day 1 followed by up to three bimatoprost SR 15 µg administrations.

Bimatoprost SR/sham bimatoprost SR was administered on Day 4 (Cycle 1) and at Week 16 (Cycle 2) and Week 32 (Cycle 3; participants who reached Week 32 prior to implementation of Protocol Amendment 3 only).

Arm type	Experimental
Investigational medicinal product name	Bimatoprost SR
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Implant
Routes of administration	Intracameral use

Dosage and administration details:

Bimatoprost SR is a biodegradable, sustained-release, preservative free bimatoprost implant, preloaded in an applicator for administration. The Bimatoprost SR implant is administered into the anterior chamber via the corneal limbus using the prefilled applicator.

Investigational medicinal product name	Sham Bimatoprost
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Implant
Routes of administration	Intracameral use

Dosage and administration details:

Sham bimatoprost SR performed using the same procedure as for Bimatoprost SR using an needleless applicator that touches the eye at the area of insertion but does not deliver an implant into the anterior chamber.

Arm title	Stage 1: Bimatoprost SR 15 µg (PR Eye) / SLT (CL Eye)

Arm description:

Participants enrolled prior to implementation of Protocol Amendment 3 received the following treatment in each eye:
Assigned PR Eye: Sham SLT administered on Day 1 followed by up to three bimatoprost SR 15 µg administrations.
CL Eye: SLT administered on Day 1 followed by up to three sham bimatoprost SR administrations.

Bimatoprost SR/sham bimatoprost SR was administered on Day 4 (Cycle 1) and at Week 16 (Cycle 2) and Week 32 (Cycle 3; participants who reached Week 32 prior to implementation of Protocol Amendment 3 only).

Arm type	Experimental
Investigational medicinal product name	Bimatoprost SR
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Implant
Routes of administration	Intracameral use

Dosage and administration details:

Bimatoprost SR is a biodegradable, sustained-release, preservative free bimatoprost implant, preloaded in an applicator for administration. The Bimatoprost SR implant is administered into the anterior chamber via the corneal limbus using the prefilled applicator.

Investigational medicinal product name	Sham Bimatoprost
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Implant
Routes of administration	Intracameral use

Dosage and administration details:

Sham bimatoprost SR performed using the same procedure as for Bimatoprost SR using an needleless applicator that touches the eye at the area of insertion but does not deliver an implant into the anterior chamber.

Arm title	Stage 2: SLT (PR Eye) / Bimatoprost SR 10 µg (CL Eye)

Arm description:

Participants enrolled after implementation of Protocol Amendment 3 received the following treatment in each eye:
Assigned PR Eye: SLT administered on Day 1 followed by up to two sham bimatoprost SR administrations.
CL Eye: Sham SLT administered on Day 1 followed by up to two bimatoprost SR 10 µg administrations.

Bimatoprost SR/sham bimatoprost SR was administered on Day 4 (Cycle 1) and at Week 16 (Cycle 2). After implementation of Protocol Amendment 6, Cycle 2 retreatment could have occurred after Week 16 and prior to Month 12 based on when retreatment criteria were met.

Arm type	Experimental
Investigational medicinal product name	Bimatoprost SR
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Implant
Routes of administration	Intracameral use

Dosage and administration details:

Bimatoprost SR is a biodegradable, sustained-release, preservative free bimatoprost implant, preloaded in an applicator for administration. The Bimatoprost SR implant is administered into the anterior chamber via the corneal limbus using the prefilled applicator.

Investigational medicinal product name	Sham Bimatoprost
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Implant
Routes of administration	Intracameral use

Dosage and administration details:

Sham bimatoprost SR performed using the same procedure as for Bimatoprost SR using an needleless applicator that touches the eye at the area of insertion but does not deliver an implant into the anterior chamber.

Arm title	Stage 2: Bimatoprost SR 10 µg (PR Eye) / SLT (CL Eye)

Arm description:

Participants enrolled after implementation of Protocol Amendment 3 received the following treatment in each eye:
Assigned PR Eye: Sham SLT administered on Day 1 followed by up to two bimatoprost SR 10 µg administrations.
CL Eye: SLT administered on Day 1 followed by up to two sham bimatoprost SR administrations.

Bimatoprost SR/sham bimatoprost SR was administered on Day 4 (Cycle 1) and at Week 16 (Cycle 2). After implementation of Protocol Amendment 6, Cycle 2 retreatment could have occurred after Week 16 and prior to Month 12 based on when retreatment criteria were met.

Arm type	Experimental
Investigational medicinal product name	Bimatoprost SR
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Implant
Routes of administration	Intracameral use

Dosage and administration details:

Bimatoprost SR is a biodegradable, sustained-release, preservative free bimatoprost implant, preloaded in an applicator for administration. The Bimatoprost SR implant is administered into the anterior chamber via the corneal limbus using the prefilled applicator.

Investigational medicinal product name	Sham Bimatoprost
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Implant
Routes of administration	Intracameral use

Dosage and administration details:

Sham bimatoprost SR performed using the same procedure as for Bimatoprost SR using an needleless applicator that touches the eye at the area of insertion but does not deliver an implant into the anterior chamber.

Notes:

[1] - The roles blinded appear to be inconsistent with a double blind trial.

Justification: The correct roles blinded are specified.

Number of subjects in period 1	Stage 1: SLT (PR Eye)/Bimatoprost SR 15 µg (CL Eye)	Stage 1: Bimatoprost SR 15 µg (PR Eye) / SLT (CL Eye)	Stage 2: SLT (PR Eye) / Bimatoprost SR 10 µg (CL Eye)
Started	29	28	92
Received Treatment	29	27	90
Completed	24	22	77
Not completed	5	6	15
Consent withdrawn by subject	1	4	6
Other, not specified	-	-	2
Adverse event	3	2	2

Screen failure	-	-	1
Lost to follow-up	-	-	2
Protocol deviation	1	-	2

Number of subjects in period 1	Stage 2: Bimatoprost SR 10 µg (PR Eye) / SLT (CL Eye)
Started	91
Received Treatment	90
Completed	78
Not completed	13
Consent withdrawn by subject	6
Other, not specified	4
Adverse event	2
Screen failure	-
Lost to follow-up	1
Protocol deviation	-

Baseline characteristics

Reporting groups

Reporting group title	Stage 1: SLT (PR Eye)/Bimatoprost SR 15 µg (CL Eye)

Reporting group description:

Participants enrolled prior to implementation of Protocol Amendment 3 received the following treatment in each eye:
Assigned PR Eye: SLT administered on Day 1 followed by up to three sham bimatoprost SR administrations.
CL Eye: Sham SLT administered on Day 1 followed by up to three bimatoprost SR 15 µg administrations.

Bimatoprost SR/sham bimatoprost SR was administered on Day 4 (Cycle 1) and at Week 16 (Cycle 2) and Week 32 (Cycle 3; participants who reached Week 32 prior to implementation of Protocol Amendment 3 only).

Reporting group title	Stage 1: Bimatoprost SR 15 µg (PR Eye) / SLT (CL Eye)

Reporting group description:

Participants enrolled prior to implementation of Protocol Amendment 3 received the following treatment in each eye:
Assigned PR Eye: Sham SLT administered on Day 1 followed by up to three bimatoprost SR 15 µg administrations.
CL Eye: SLT administered on Day 1 followed by up to three sham bimatoprost SR administrations.

Bimatoprost SR/sham bimatoprost SR was administered on Day 4 (Cycle 1) and at Week 16 (Cycle 2) and Week 32 (Cycle 3; participants who reached Week 32 prior to implementation of Protocol Amendment 3 only).

Reporting group title	Stage 2: SLT (PR Eye) / Bimatoprost SR 10 µg (CL Eye)

Reporting group description:

Participants enrolled after implementation of Protocol Amendment 3 received the following treatment in each eye:
Assigned PR Eye: SLT administered on Day 1 followed by up to two sham bimatoprost SR administrations.
CL Eye: Sham SLT administered on Day 1 followed by up to two bimatoprost SR 10 µg administrations.

Bimatoprost SR/sham bimatoprost SR was administered on Day 4 (Cycle 1) and at Week 16 (Cycle 2). After implementation of Protocol Amendment 6, Cycle 2 retreatment could have occurred after Week 16 and prior to Month 12 based on when retreatment criteria were met.

Reporting group title	Stage 2: Bimatoprost SR 10 µg (PR Eye) / SLT (CL Eye)

Reporting group description:

Participants enrolled after implementation of Protocol Amendment 3 received the following treatment in each eye:
Assigned PR Eye: Sham SLT administered on Day 1 followed by up to two bimatoprost SR 10 µg administrations.
CL Eye: SLT administered on Day 1 followed by up to two sham bimatoprost SR administrations.

Bimatoprost SR/sham bimatoprost SR was administered on Day 4 (Cycle 1) and at Week 16 (Cycle 2). After implementation of Protocol Amendment 6, Cycle 2 retreatment could have occurred after Week 16 and prior to Month 12 based on when retreatment criteria were met.

Reporting group values	Stage 1: SLT (PR Eye)/Bimatoprost SR 15 µg (CL Eye)	Stage 1: Bimatoprost SR 15 µg (PR Eye) / SLT (CL Eye)	Stage 2: SLT (PR Eye) / Bimatoprost SR 10 µg (CL Eye)
Number of subjects	29	28	92
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	64.9	59.6	62.6
standard deviation	± 12.32	± 13.59	± 11.61
Gender categorical Units: Subjects			
Female	16	12	46
Male	13	16	46
Race Units: Subjects			
White	25	23	58
Black or African American	1	2	27
Asian	3	3	4
American Indian or Alaska Native	0	0	0
Not Reported	0	0	3
Ethnicity Units: Subjects			
Hispanic or Latino	1	4	6
Not Hispanic or Latino	28	24	86
Unknown or Not Reported	0	0	0

Reporting group values	Stage 2: Bimatoprost SR 10 µg (PR Eye) / SLT (CL Eye)	Total	
Number of subjects	91	240	
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	62.1		
standard deviation	± 10.74	-	
Gender categorical Units: Subjects			
Female	48	122	
Male	43	118	
Race Units: Subjects			
White	69	175	
Black or African American	14	44	
Asian	6	16	
American Indian or Alaska Native	2	2	
Not Reported	0	3	
Ethnicity Units: Subjects			
Hispanic or Latino	10	21	
Not Hispanic or Latino	81	219	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	Stage 1: SLT (PR Eye)/Bimatoprost SR 15 µg (CL Eye)

Reporting group description:

Participants enrolled prior to implementation of Protocol Amendment 3 received the following treatment in each eye:
Assigned PR Eye: SLT administered on Day 1 followed by up to three sham bimatoprost SR administrations.
CL Eye: Sham SLT administered on Day 1 followed by up to three bimatoprost SR 15 µg administrations.

Bimatoprost SR/sham bimatoprost SR was administered on Day 4 (Cycle 1) and at Week 16 (Cycle 2) and Week 32 (Cycle 3; participants who reached Week 32 prior to implementation of Protocol Amendment 3 only).

Reporting group title	Stage 1: Bimatoprost SR 15 µg (PR Eye) / SLT (CL Eye)

Reporting group description:

Participants enrolled prior to implementation of Protocol Amendment 3 received the following treatment in each eye:
Assigned PR Eye: Sham SLT administered on Day 1 followed by up to three bimatoprost SR 15 µg administrations.
CL Eye: SLT administered on Day 1 followed by up to three sham bimatoprost SR administrations.

Bimatoprost SR/sham bimatoprost SR was administered on Day 4 (Cycle 1) and at Week 16 (Cycle 2) and Week 32 (Cycle 3; participants who reached Week 32 prior to implementation of Protocol Amendment 3 only).

Reporting group title	Stage 2: SLT (PR Eye) / Bimatoprost SR 10 µg (CL Eye)

Reporting group description:

Participants enrolled after implementation of Protocol Amendment 3 received the following treatment in each eye:
Assigned PR Eye: SLT administered on Day 1 followed by up to two sham bimatoprost SR administrations.
CL Eye: Sham SLT administered on Day 1 followed by up to two bimatoprost SR 10 µg administrations.

Bimatoprost SR/sham bimatoprost SR was administered on Day 4 (Cycle 1) and at Week 16 (Cycle 2). After implementation of Protocol Amendment 6, Cycle 2 retreatment could have occurred after Week 16 and prior to Month 12 based on when retreatment criteria were met.

Reporting group title	Stage 2: Bimatoprost SR 10 µg (PR Eye) / SLT (CL Eye)

Reporting group description:

Participants enrolled after implementation of Protocol Amendment 3 received the following treatment in each eye:
Assigned PR Eye: Sham SLT administered on Day 1 followed by up to two bimatoprost SR 10 µg administrations.
CL Eye: SLT administered on Day 1 followed by up to two sham bimatoprost SR administrations.

Bimatoprost SR/sham bimatoprost SR was administered on Day 4 (Cycle 1) and at Week 16 (Cycle 2). After implementation of Protocol Amendment 6, Cycle 2 retreatment could have occurred after Week 16 and prior to Month 12 based on when retreatment criteria were met.

Subject analysis set title	Stage 2: SLT
Subject analysis set type	Intention-to-treat

Subject analysis set description:

One 360° administration of SLT on Day 1 followed by up to two sham bimatoprost SR administrations.

Subject analysis set title	Stage 2: Bimatoprost SR 10 µg
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Sham SLT on Day 1 followed by bimatoprost SR 10 µg administered on Day 4 with repeat administration at Week 16 or after Week 16 and prior to Month 12 depending on when retreatment criteria were met.

Primary: Change From Baseline in Intraocular Pressure at Week 4

End point title	Change From Baseline in Intraocular Pressure at Week 4[1]

End point description:

Intraocular pressure was measured at 8 am (Hour 0) at each visit in each eye using the Goldmann applanation tonometer. A negative change from Baseline indicates a decrease (improvement) in intraocular pressure. A mixed-effects model with repeated measures (MMRM) was used for the analysis. IOP measurements obtained after initiation of non-study IOP-lowering treatment in an eye were excluded from the analysis.

The intent-to-treat (ITT) population is defined as all randomized participants. Primary efficacy analysis was performed for participants enrolled in Stage 2. Overall Number of Participants / Units Analyzed reflects the number of participants and eyes with data available for the analysis.

End point type	Primary

End point timeframe:

Baseline and Week 4

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: Descriptive statistics are presented per protocol.

End point values	Stage 2: SLT	Stage 2: Bimatoprost SR 10 µg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	168[2]	170[3]		
Units: mmHg				
least squares mean (standard error)	-6.2 (± 0.28)	-6.8 (± 0.28)		

Notes:

[2] - 168 eyes

[3] - 170 eyes

Attachments (see zip file)	Statistical Analysis Week 4.docx

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Intraocular Pressure at Week 12

End point title	Change From Baseline in Intraocular Pressure at Week 12[4]

End point description:

Intraocular pressure was measured at 8 am (Hour 0) at each visit in each eye using the Goldmann applanation tonometer. A negative change from Baseline indicates a decrease (improvement) in intraocular pressure. An MMRM was used for the analysis. IOP measurements obtained after initiation of non-study IOP-lowering treatment in an eye were excluded from the analysis.

The ITT population is defined as all randomized participants. Primary efficacy analysis was performed for participants enrolled in Stage 2. Overall Number of Participants / Units Analyzed reflects the number of participants and eyes with data available for the analysis.

End point type	Primary

End point timeframe:

Baseline and Week 12

Notes:

[4] - 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: Descriptive statistics are presented per protocol.

End point values	Stage 2: SLT	Stage 2: Bimatoprost SR 10 µg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	149[5]	156[6]		
Units: mmHg				
least squares mean (standard error)	-6.4 (± 0.30)	-6.9 (± 0.30)		

Notes:

[5] - 149 eyes

[6] - 156 eyes

Attachments (see zip file)	Statistical Analysis Week 12.docx

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Intraocular Pressure at Week 24

End point title	Change From Baseline in Intraocular Pressure at Week 24[7]

End point description:

Intraocular pressure was measured at 8 am (Hour 0) at each visit in each eye using the Goldmann applanation tonometer. A negative change from Baseline indicates a decrease (improvement) in intraocular pressure. An MMRM was used for the analysis. IOP measurements obtained after initiation of non-study IOP-lowering treatment in an eye were excluded from the analysis.

The ITT population is defined as all randomized participants. Primary efficacy analysis was performed for participants enrolled in Stage 2. Overall Number of Participants / Units Analyzed reflects the number of participants and eyes with data available for the analysis.

End point type	Primary

End point timeframe:

Baseline and Week 24

Notes:

[7] - 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: Descriptive statistics are presented per protocol.

End point values	Stage 2: SLT	Stage 2: Bimatoprost SR 10 µg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	138[8]	145[9]		
Units: mmHg				
least squares mean (standard error)	-6.5 (± 0.28)	-6.9 (± 0.27)		

Notes:

[8] - 138 eyes

[9] - 145 eyes

Attachments (see zip file)	Statistical Analysis Week 24.docx

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Initial Use of Non-study IOP-lowering Treatment

End point title	Time to Initial Use of Non-study IOP-lowering Treatment

End point description:

The time from the date of initial treatment to the date date of first use of non-study IOP-lowering treatment (rescue) was analyzed using the Kaplan-Meier method.
If a participant did not use any non-study IOP-lowering treatment in an eye, then the event (initial use of non-study IOP lowering treatment) time was censored at the study exit date or the last visit date if the study exit date was not available.

Participants in the ITT population enrolled in Stage 2; eyes that received study treatment are included in the analysis.

End point type	Secondary

End point timeframe:

From first administration of study treatment to the end of study; overall median follow-up time of 728 days.

End point values	Stage 2: SLT	Stage 2: Bimatoprost SR 10 µg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	180[10]	175[11]		
Units: days				
median (confidence interval 95%)				
25% percentile	263 (167.0 to 329.0)	276 (217.0 to 323.0)		
50% percentile	99999 (736.0 to 99999)	732 (496.0 to 99999)		
75% percentile	99999 (99999 to 99999)	99999 (99999 to 99999)		

Notes:

[10] - 180 eyes
99999=NA (Data could not be estimated due to the low number of events.)
[11] - 175 eyes
99999=NA (Data could not be estimated due to the low number of events.)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Eyes Achieving ≥ 20% Reduction in IOP From Baseline Regardless of Cycle

End point title	Percentage of Eyes Achieving ≥ 20% Reduction in IOP From Baseline Regardless of Cycle

End point description:

Intraocular pressure was measured at 8 am (Hour 0) at each visit in each eye using the Goldmann applanation tonometer.
For by-cycle analyses, cycle number refers to the administration cycle for bimatoprost SR, or sham bimatoprost SR administration in SLT-treated eyes. For SLT-treated eyes cycle number does not refer to SLT administrations, because SLT was only performed once (Day 1). The Day/Week number refers to the number of days/weeks after bimatoprost SR/sham bimatoprost SR administration.
IOP measurements obtained after initiation of non-study IOP-lowering treatment in an eye were excluded from the analysis.

Participants/eyes enrolled in Stage 2 with available IOP data at Baseline and each time point; participants who received retreatment with bimatoprost SR/sham bimatoprost SR at or after Week 16 are not included in Cycle 1 time points from the date of retreatment.

End point type	Secondary

End point timeframe:

Baseline, Cycle 1: Day 2, Weeks 4, 8, 12, 15, 20, 24, 28, 31, 36, 40, 44, 47, 52, Months 13, 14, 15, 16, 18, 20, 22, 24

End point values	Stage 2: SLT	Stage 2: Bimatoprost SR 10 µg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	183[12]	183[13]		
Units: percentage of eyes				
number (not applicable)				
Day 2; n=171, 172	59.1	86.6		
Week 4; n=168, 170	68.5	71.2		
Week 8; n=164, 166	64.0	75.3		
Week 12; n=149, 156	71.1	71.8		
Week 15; n=147, 152	65.3	61.2		
Week 20; n=145, 150	62.8	67.3		
Week 24; n=138, 145	73.2	75.2		
Week 28; n=129, 133	72.1	71.4		
Week 31; n=126, 132	67.5	62.1		
Week 36; n=126, 128	68.3	55.5		
Week 40; n=122, 121	72.1	62.0		
Week 44; n=116, 114	65.5	57.9		
Week 47; n=114, 110	83.3	70.9		
Week 52; n=111, 110	78.4	66.4		
Month 13; n=78, 70	73.1	65.7		
Month 14; n=79, 72	73.4	56.9		
Month 15; n=75, 67	72.0	61.2		
Month 16; n=82, 72	76.8	70.8		
Month 18; n=72, 63	75.0	60.3		
Month 20; n=73, 61	79.5	62.3		
Month 22; n=70, 55	78.6	69.1		
Month 24; n=71, 57	73.2	66.7		

Notes:

[12] - n=number of eyes at given time point

[13] - n=number of eyes at given time point

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Intraocular Pressure at Weeks 8, 15, and 20

End point title	Change From Baseline in Intraocular Pressure at Weeks 8, 15, and 20

End point description:

Intraocular pressure was measured at 8 am (Hour 0) at each visit in each eye using the Goldmann applanation tonometer. A negative change from Baseline indicates a decrease (improvement) in intraocular pressure. IOP measurements obtained after initiation of non-study IOP-lowering treatment in an eye were excluded from the analysis.

Intent-to-treat poulation participants enrolled in Stage 2 with available IOP data at each time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 8, 15, and 20

End point values	Stage 2: SLT	Stage 2: Bimatoprost SR 10 µg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	183	183		
Units: mmHg				
arithmetic mean (standard deviation)				
Baseline; n=183, 183 eyes/subjects	25.1 (± 3.00)	25.2 (± 2.99)		
Week 8; n=164, 166 eyes/subjects	-6.1 (± 3.52)	-6.8 (± 3.96)		
Week 15; n=147, 152 eyes/subjects	-6.0 (± 3.58)	-6.0 (± 4.36)		
Week 20; n=145, 150 eyes/subjects	-5.9 (± 3.44)	-6.4 (± 3.97)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug up to Month 24 ±7 days. Six participants who started treatment received SLT only (1 participant had a planned Stage 1 treatment of Bimatoprost SR 15 µg; 5 participants had a planned Stage 2 treatment of Bimatoprost SR 10 µg.)

Adverse event reporting additional description:

Ocular AEs (i.e., those reported for the system organ class 'eye disorders' plus those footnoted as 'ocular events') are reported for the eye that received the treatment specified. Because this is a paired-eye study, and both eyes belong to a single participant, non-ocular AEs affect both reporting groups, and are reported under both interventions.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Stage 1: SLT

Reporting group description:

Selective laser trabeculoplasty (SLT) administered on Day 1 followed by up to three sham bimatoprost SR administrations.
Sham bimatoprost SR was administered on Day 4 (Cycle 1) and at Week 16 (Cycle 2) and Week 32 (Cycle 3; participants who reached Week 32 prior to implementation of Protocol Amendment 3 only).

Reporting group title	Stage 1: Bimatoprost SR 15 µg

Reporting group description:

Sham SLT administered on Day 1 followed by up to three bimatoprost SR 15 µg administrations.
Bimatoprost SR was administered on Day 4 (Cycle 1) and at Week 16 (Cycle 2) and Week 32 (Cycle 3; participants who reached Week 32 prior to implementation of Protocol Amendment 3 only).

Reporting group title	Stage 2: SLT

Reporting group description:

SLT administered on Day 1 followed by up to two sham bimatoprost SR administrations.
Sham bimatoprost SR was administered on Day 4 (Cycle 1) and at Week 16 (Cycle 2). After implementation of Protocol Amendment 6, Cycle 2 retreatment could have occurred after Week 16 and prior to Month 12 based on when retreatment criteria were met.

Reporting group title	Stage 2: Bimatoprost SR 10 µg

Reporting group description:

Sham SLT administered on Day 1 followed by up to two bimatoprost SR 10 µg administrations.
Bimatoprost SR was administered on Day 4 (Cycle 1) and at Week 16 (Cycle 2). After implementation of Protocol Amendment 6, Cycle 2 retreatment could have occurred after Week 16 and prior to Month 12 based on when retreatment criteria were met.

Serious adverse events	Stage 1: SLT	Stage 1: Bimatoprost SR 15 µg	Stage 2: SLT
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 56 (5.36%)	3 / 55 (5.45%)	18 / 180 (10.00%)
number of deaths (all causes)	0	0	2
number of deaths resulting from adverse events	0	0	2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
GASTRIC CANCER			

subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	1 / 180 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BLADDER CANCER			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	1 / 180 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
ADENOCARCINOMA OF COLON			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	1 / 180 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OESOPHAGEAL CANCER METASTATIC			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	1 / 180 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
PROSTATE CANCER			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	1 / 180 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PROSTATE CANCER STAGE I			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	1 / 180 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RENAL CELL CARCINOMA			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	1 / 180 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
ACCELERATED HYPERTENSION			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	1 / 180 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERTENSION			

subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	1 / 180 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	2 / 180 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIAC FAILURE CONGESTIVE			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	1 / 180 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CORONARY ARTERY DISEASE			
subjects affected / exposed	1 / 56 (1.79%)	1 / 55 (1.82%)	0 / 180 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ARTERIOSCLEROSIS CORONARY ARTERY			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	1 / 180 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
MYELOPATHY			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	1 / 180 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
APHASIA			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	1 / 180 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
NON-CARDIAC CHEST PAIN			

subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	1 / 180 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
EPISCLERITIS			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	0 / 180 (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
PHOTOPHOBIA			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	0 / 180 (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
RETINAL VEIN OCCLUSION			
subjects affected / exposed	1 / 56 (1.79%)	0 / 55 (0.00%)	0 / 180 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VISION BLURRED			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	0 / 180 (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
CORNEAL OEDEMA			
subjects affected / exposed	0 / 56 (0.00%)	1 / 55 (1.82%)	0 / 180 (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
CORNEAL ENDOTHELIAL CELL LOSS			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	0 / 180 (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
CATARACT SUBCAPSULAR			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	0 / 180 (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
CORNEAL THICKENING			

subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	0 / 180 (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
Gastrointestinal disorders			
GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	1 / 180 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTESTINAL OBSTRUCTION			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	1 / 180 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
VOCAL CORD DISORDER			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	1 / 180 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
SKIN ULCER			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	1 / 180 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	1 / 180 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	1 / 180 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SPINAL OSTEOARTHRITIS			

subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	1 / 180 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OSTEOARTHRITIS			
subjects affected / exposed	1 / 56 (1.79%)	1 / 55 (1.82%)	1 / 180 (0.56%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MUSCULAR WEAKNESS			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	1 / 180 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CERVICAL SPINAL STENOSIS			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	1 / 180 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
PNEUMONIA			
subjects affected / exposed	1 / 56 (1.79%)	1 / 55 (1.82%)	0 / 180 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	1 / 180 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
BURSITIS INFECTIVE			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	1 / 180 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Stage 2: Bimatoprost SR 10 µg		
Total subjects affected by serious adverse events			
subjects affected / exposed	22 / 175 (12.57%)		
number of deaths (all causes)	2		
number of deaths resulting from	2		

adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
GASTRIC CANCER			
subjects affected / exposed	1 / 175 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
BLADDER CANCER			
subjects affected / exposed	1 / 175 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
ADENOCARCINOMA OF COLON			
subjects affected / exposed	1 / 175 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
OESOPHAGEAL CANCER METASTATIC			
subjects affected / exposed	1 / 175 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
PROSTATE CANCER			
subjects affected / exposed	1 / 175 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PROSTATE CANCER STAGE I			
subjects affected / exposed	1 / 175 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
RENAL CELL CARCINOMA			
subjects affected / exposed	1 / 175 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
ACCELERATED HYPERTENSION			

subjects affected / exposed	1 / 175 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
HYPERTENSION				
subjects affected / exposed	1 / 175 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
ATRIAL FIBRILLATION				
subjects affected / exposed	2 / 175 (1.14%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
CARDIAC FAILURE CONGESTIVE				
subjects affected / exposed	1 / 175 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
CORONARY ARTERY DISEASE				
subjects affected / exposed	0 / 175 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ARTERIOSCLEROSIS CORONARY ARTERY				
subjects affected / exposed	1 / 175 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
MYELOPATHY				
subjects affected / exposed	1 / 175 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
APHASIA				
subjects affected / exposed	1 / 175 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

General disorders and administration site conditions			
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	1 / 175 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
EPISCLERITIS			
subjects affected / exposed	1 / 175 (0.57%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
PHOTOPHOBIA			
subjects affected / exposed	1 / 175 (0.57%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
RETINAL VEIN OCCLUSION			
subjects affected / exposed	0 / 175 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
VISION BLURRED			
subjects affected / exposed	1 / 175 (0.57%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
CORNEAL OEDEMA			
subjects affected / exposed	1 / 175 (0.57%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
CORNEAL ENDOTHELIAL CELL LOSS			
subjects affected / exposed	1 / 175 (0.57%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
CATARACT SUBCAPSULAR			
subjects affected / exposed	1 / 175 (0.57%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

CORNEAL THICKENING			
subjects affected / exposed	1 / 175 (0.57%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	1 / 175 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
INTESTINAL OBSTRUCTION			
subjects affected / exposed	1 / 175 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
VOCAL CORD DISORDER			
subjects affected / exposed	1 / 175 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
SKIN ULCER			
subjects affected / exposed	1 / 175 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	1 / 175 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	1 / 175 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
SPINAL OSTEOARTHRITIS			

subjects affected / exposed	1 / 175 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
OSTEOARTHRITIS			
subjects affected / exposed	1 / 175 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
MUSCULAR WEAKNESS			
subjects affected / exposed	1 / 175 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
CERVICAL SPINAL STENOSIS			
subjects affected / exposed	1 / 175 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
PNEUMONIA			
subjects affected / exposed	0 / 175 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
COVID-19			
subjects affected / exposed	1 / 175 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
BURSITIS INFECTIVE			
subjects affected / exposed	1 / 175 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Stage 1: SLT	Stage 1: Bimatoprost SR 15 µg	Stage 2: SLT
Total subjects affected by non-serious adverse events			
subjects affected / exposed	41 / 56 (73.21%)	49 / 55 (89.09%)	107 / 180 (59.44%)
Investigations			
INTRAOCULAR PRESSURE INCREASED	Additional description: ocular event		
subjects affected / exposed	5 / 56 (8.93%)	8 / 55 (14.55%)	33 / 180 (18.33%)
occurrences (all)	6	8	41
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	4 / 56 (7.14%)	4 / 55 (7.27%)	15 / 180 (8.33%)
occurrences (all)	4	4	16
Nervous system disorders			
HEADACHE	Additional description: Stage 1 arms = ocular event		
subjects affected / exposed	1 / 56 (1.79%)	2 / 55 (3.64%)	10 / 180 (5.56%)
occurrences (all)	1	2	10
Eye disorders			
ANTERIOR CHAMBER CELL			
subjects affected / exposed	4 / 56 (7.14%)	6 / 55 (10.91%)	10 / 180 (5.56%)
occurrences (all)	4	8	10
CONJUNCTIVAL HAEMORRHAGE			
subjects affected / exposed	6 / 56 (10.71%)	10 / 55 (18.18%)	2 / 180 (1.11%)
occurrences (all)	6	11	2
BLEPHARITIS			
subjects affected / exposed	3 / 56 (5.36%)	2 / 55 (3.64%)	4 / 180 (2.22%)
occurrences (all)	3	2	4
ANTERIOR CHAMBER FLARE			
subjects affected / exposed	2 / 56 (3.57%)	4 / 55 (7.27%)	1 / 180 (0.56%)
occurrences (all)	2	4	1
EYE IRRITATION			
subjects affected / exposed	4 / 56 (7.14%)	6 / 55 (10.91%)	2 / 180 (1.11%)
occurrences (all)	4	6	2
EYE PAIN			
subjects affected / exposed	6 / 56 (10.71%)	6 / 55 (10.91%)	4 / 180 (2.22%)
occurrences (all)	7	11	5
FOREIGN BODY SENSATION IN EYES			

subjects affected / exposed	1 / 56 (1.79%)	5 / 55 (9.09%)	2 / 180 (1.11%)
occurrences (all)	1	5	2
IRITIS			
subjects affected / exposed	0 / 56 (0.00%)	4 / 55 (7.27%)	0 / 180 (0.00%)
occurrences (all)	0	4	0
LACRIMATION INCREASED			
subjects affected / exposed	3 / 56 (5.36%)	1 / 55 (1.82%)	3 / 180 (1.67%)
occurrences (all)	3	1	3
DRY EYE			
subjects affected / exposed	5 / 56 (8.93%)	7 / 55 (12.73%)	22 / 180 (12.22%)
occurrences (all)	7	10	25
CORNEAL TOUCH			
subjects affected / exposed	0 / 56 (0.00%)	3 / 55 (5.45%)	0 / 180 (0.00%)
occurrences (all)	0	3	0
CORNEAL ENDOTHELIAL CELL LOSS			
subjects affected / exposed	4 / 56 (7.14%)	6 / 55 (10.91%)	6 / 180 (3.33%)
occurrences (all)	4	6	6
CONJUNCTIVAL HYPERAEMIA			
subjects affected / exposed	13 / 56 (23.21%)	21 / 55 (38.18%)	22 / 180 (12.22%)
occurrences (all)	22	47	23
PHOTOPHOBIA			
subjects affected / exposed	1 / 56 (1.79%)	5 / 55 (9.09%)	2 / 180 (1.11%)
occurrences (all)	1	8	2
PUNCTATE KERATITIS			
subjects affected / exposed	5 / 56 (8.93%)	7 / 55 (12.73%)	19 / 180 (10.56%)
occurrences (all)	5	9	25
VISION BLURRED			
subjects affected / exposed	3 / 56 (5.36%)	4 / 55 (7.27%)	4 / 180 (2.22%)
occurrences (all)	3	4	4
VISUAL FIELD DEFECT			
subjects affected / exposed	0 / 56 (0.00%)	2 / 55 (3.64%)	18 / 180 (10.00%)
occurrences (all)	0	2	22
VITREOUS FLOATERS			
subjects affected / exposed	1 / 56 (1.79%)	3 / 55 (5.45%)	1 / 180 (0.56%)
occurrences (all)	1	3	1
Respiratory, thoracic and mediastinal			

disorders			
COUGH			
subjects affected / exposed	4 / 56 (7.14%)	4 / 55 (7.27%)	3 / 180 (1.67%)
occurrences (all)	5	5	3
Musculoskeletal and connective tissue disorders			
OSTEOARTHRITIS			
subjects affected / exposed	3 / 56 (5.36%)	3 / 55 (5.45%)	2 / 180 (1.11%)
occurrences (all)	4	4	2
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	3 / 56 (5.36%)	3 / 55 (5.45%)	1 / 180 (0.56%)
occurrences (all)	3	3	1
CONJUNCTIVITIS	Additional description: ocular event		
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	5 / 180 (2.78%)
occurrences (all)	0	0	5
COVID-19			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	14 / 180 (7.78%)
occurrences (all)	0	0	15
NASOPHARYNGITIS			
subjects affected / exposed	3 / 56 (5.36%)	3 / 55 (5.45%)	8 / 180 (4.44%)
occurrences (all)	5	5	8
Metabolism and nutrition disorders			
HYPERGLYCAEMIA			
subjects affected / exposed	3 / 56 (5.36%)	3 / 55 (5.45%)	0 / 180 (0.00%)
occurrences (all)	3	3	0

Non-serious adverse events	Stage 2: Bimatoprost SR 10 µg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	121 / 175 (69.14%)		
Investigations			
INTRAOCULAR PRESSURE INCREASED	Additional description: ocular event		
subjects affected / exposed	43 / 175 (24.57%)		
occurrences (all)	55		
Vascular disorders			
HYPERTENSION			

subjects affected / exposed	15 / 175 (8.57%)		
occurrences (all)	16		
Nervous system disorders			
HEADACHE	Additional description: Stage 1 arms = ocular event		
subjects affected / exposed	10 / 175 (5.71%)		
occurrences (all)	10		
Eye disorders			
ANTERIOR CHAMBER CELL			
subjects affected / exposed	7 / 175 (4.00%)		
occurrences (all)	12		
CONJUNCTIVAL HAEMORRHAGE			
subjects affected / exposed	9 / 175 (5.14%)		
occurrences (all)	9		
BLEPHARITIS			
subjects affected / exposed	3 / 175 (1.71%)		
occurrences (all)	3		
ANTERIOR CHAMBER FLARE			
subjects affected / exposed	3 / 175 (1.71%)		
occurrences (all)	4		
EYE IRRITATION			
subjects affected / exposed	4 / 175 (2.29%)		
occurrences (all)	4		
EYE PAIN			
subjects affected / exposed	15 / 175 (8.57%)		
occurrences (all)	19		
FOREIGN BODY SENSATION IN EYES			
subjects affected / exposed	12 / 175 (6.86%)		
occurrences (all)	14		
IRITIS			
subjects affected / exposed	5 / 175 (2.86%)		
occurrences (all)	7		
LACRIMATION INCREASED			
subjects affected / exposed	4 / 175 (2.29%)		
occurrences (all)	5		
DRY EYE			

subjects affected / exposed occurrences (all) CORNEAL TOUCH subjects affected / exposed occurrences (all) CORNEAL ENDOTHELIAL CELL LOSS subjects affected / exposed occurrences (all) CONJUNCTIVAL HYPERAEMIA subjects affected / exposed occurrences (all) PHOTOPHOBIA subjects affected / exposed occurrences (all) PUNCTATE KERATITIS subjects affected / exposed occurrences (all) VISION BLURRED subjects affected / exposed occurrences (all) VISUAL FIELD DEFECT subjects affected / exposed occurrences (all) VITREOUS FLOATERS subjects affected / exposed occurrences (all)	25 / 175 (14.29%) 34 1 / 175 (0.57%) 1 11 / 175 (6.29%) 13 35 / 175 (20.00%) 48 15 / 175 (8.57%) 23 21 / 175 (12.00%) 27 6 / 175 (3.43%) 6 18 / 175 (10.29%) 20 2 / 175 (1.14%) 2		
Respiratory, thoracic and mediastinal disorders COUGH subjects affected / exposed occurrences (all)	 3 / 175 (1.71%) 3		
Musculoskeletal and connective tissue disorders OSTEOARTHRITIS subjects affected / exposed occurrences (all)	 2 / 175 (1.14%) 2		
Infections and infestations			

BRONCHITIS			
subjects affected / exposed	1 / 175 (0.57%)		
occurrences (all)	1		
CONJUNCTIVITIS	Additional description: ocular event		
subjects affected / exposed	9 / 175 (5.14%)		
occurrences (all)	10		
COVID-19			
subjects affected / exposed	14 / 175 (8.00%)		
occurrences (all)	15		
NASOPHARYNGITIS			
subjects affected / exposed	8 / 175 (4.57%)		
occurrences (all)	8		
Metabolism and nutrition disorders			
HYPERGLYCAEMIA			
subjects affected / exposed	0 / 175 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 October 2015	This protocol was amended to clarify some sections, to modify the inclusion/exclusion criteria, and to remove the LUMIGAN challenge.
01 May 2017	This protocol was amended to change the screening requirement for angle eligibility confirmation, modify/clarify the inclusion/exclusion criteria, and change additional procedures for patients with sickle cell disease from required to optional.
05 September 2018	This protocol was amended to change the Bimatoprost SR dose strength under study from 15 µg to 10 µg, and to reduce the number of administration cycles from 3 to 2.
31 January 2020	This protocol was amended to extend the washout period and update the list of medications requiring washout, allow patients enrolled in the 192024-091/092 studies who were randomized to the control treatment and never received an implant to be considered for enrollment at the investigator's discretion, and revise the statistical methods.
21 April 2020	This protocol was amended to add additional detail regarding Bimatoprost SR retreatment criteria.
28 August 2020	This protocol was amended to lengthen the study duration, to update retreatment criteria, and to add flexibility in the timing of Cycle 2 Bimatoprost SR administration for patients not meeting the retreatment criteria at Week 16.
29 September 2021	This protocol was amended to update the covariates in the primary analysis model, add a subgroup analyses for the flexible administration and clarify the differences in the analyses to be done for Bimatoprost SR 10 µg and Bimatoprost SR 15 µg.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported