



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 standard deviation | 64.9 ± 12.32 | 59.6 ± 13.59 | 62.6 ± 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 standard deviation | 62.1 ± 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 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 \geq 20% Reduction in IOP From Baseline Regardless of Cycle

| | |
|-----------------|--|
| End point title | Percentage of Eyes Achieving \geq 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 population 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 \pm 7 days. Six participants who started treatment received SLT only (1 participant had a planned Stage 1 treatment of Bimatoprost SR 15 μ g; 5 participants had a planned Stage 2 treatment of Bimatoprost SR 10 μ g.)

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 μ g |
|-----------------------|------------------------------------|

Reporting group description:

Sham SLT administered on Day 1 followed by up to three bimatoprost SR 15 μ g 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 μ g |
|-----------------------|------------------------------------|

Reporting group description:

Sham SLT administered on Day 1 followed by up to two bimatoprost SR 10 μ g 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 μ g | 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 | | | |
| 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 |
| 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 |
| 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 |
| 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 |
| 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 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 |
| 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 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 |
| 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 | | | |
| 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 | | |
| 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 | | |
| 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 | | |
| 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 | | |
| 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 THICKENING | | | |
| 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 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 | | |
| 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 occurrences (all) | 4 / 56 (7.14%) 5 | 4 / 55 (7.27%) 5 | 3 / 180 (1.67%) 3 |
| Musculoskeletal and connective tissue disorders OSTEOARTHRITIS subjects affected / exposed occurrences (all) | 3 / 56 (5.36%) 4 | 3 / 55 (5.45%) 4 | 2 / 180 (1.11%) 2 |
| Infections and infestations BRONCHITIS subjects affected / exposed occurrences (all) | 3 / 56 (5.36%) 3 | 3 / 55 (5.45%) 3 | 1 / 180 (0.56%) 1 |
| CONJUNCTIVITIS subjects affected / exposed occurrences (all) | Additional description: ocular event | | |
| COVID-19 subjects affected / exposed occurrences (all) | 0 / 56 (0.00%) 0 | 0 / 55 (0.00%) 0 | 5 / 180 (2.78%) 5 |
| NASOPHARYNGITIS subjects affected / exposed occurrences (all) | 0 / 56 (0.00%) 0 | 0 / 55 (0.00%) 0 | 14 / 180 (7.78%) 15 |
| NASOPHARYNGITIS subjects affected / exposed occurrences (all) | 3 / 56 (5.36%) 5 | 3 / 55 (5.45%) 5 | 8 / 180 (4.44%) 8 |
| Metabolism and nutrition disorders HYPERGLYCAEMIA subjects affected / exposed occurrences (all) | 3 / 56 (5.36%) 3 | 3 / 55 (5.45%) 3 | 0 / 180 (0.00%) 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 subjects affected / exposed occurrences (all) | Additional description: ocular event | | |
| 43 / 175 (24.57%) 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 | 25 / 175 (14.29%) | | |
| occurrences (all) | 34 | | |
| CORNEAL TOUCH | | | |
| subjects affected / exposed | 1 / 175 (0.57%) | | |
| occurrences (all) | 1 | | |
| CORNEAL ENDOTHELIAL CELL LOSS | | | |
| subjects affected / exposed | 11 / 175 (6.29%) | | |
| occurrences (all) | 13 | | |
| CONJUNCTIVAL HYPERAEMIA | | | |
| subjects affected / exposed | 35 / 175 (20.00%) | | |
| occurrences (all) | 48 | | |
| PHOTOPHOBIA | | | |
| subjects affected / exposed | 15 / 175 (8.57%) | | |
| occurrences (all) | 23 | | |
| PUNCTATE KERATITIS | | | |
| subjects affected / exposed | 21 / 175 (12.00%) | | |
| occurrences (all) | 27 | | |
| VISION BLURRED | | | |
| subjects affected / exposed | 6 / 175 (3.43%) | | |
| occurrences (all) | 6 | | |
| VISUAL FIELD DEFECT | | | |
| subjects affected / exposed | 18 / 175 (10.29%) | | |
| occurrences (all) | 20 | | |
| VITREOUS FLOATERS | | | |
| subjects affected / exposed | 2 / 175 (1.14%) | | |
| occurrences (all) | 2 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| COUGH | | | |
| subjects affected / exposed | 3 / 175 (1.71%) | | |
| occurrences (all) | 3 | | |
| Musculoskeletal and connective tissue disorders | | | |
| OSTEOARTHRITIS | | | |
| subjects affected / exposed | 2 / 175 (1.14%) | | |
| occurrences (all) | 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