



## Clinical trial results:

**Phase III, Multinational, Multicenter, Investigator-Masked, Randomised, Active-Controlled Trial, comparing the efficacy and safety of DE-130A with Xalatan® in Patients with Open-Angle Glaucoma or Ocular Hypertension over a 3-Month period, followed by a 12-Month Follow-Up with Open-Label DE-130A Treatment**

### Summary

|                          |                               |
|--------------------------|-------------------------------|
| EudraCT number           | 2017-004262-95                |
| Trial protocol           | FI GB DE EE PL ES BE AT LV IT |
| Global end of trial date | 26 October 2022               |

### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 12 November 2023 |
| First version publication date | 12 November 2023 |

### Trial information

#### Trial identification

|                       |           |
|-----------------------|-----------|
| Sponsor protocol code | 0130A01SA |
|-----------------------|-----------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT04133311 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |                                                                         |
|------------------------------|-------------------------------------------------------------------------|
| Sponsor organisation name    | Santen S.A.S.                                                           |
| Sponsor organisation address | 1 Rue Pierre Fontaine, Genavenir IV, Evry cedex, France, F-91058        |
| Public contact               | Regulatory Affairs EMEA, Santen S.A.S.,<br>regulatoryaffairs@santen.com |
| Scientific contact           | Regulatory Affairs EMEA, Santen S.A.S.,<br>regulatoryaffairs@santen.com |

Notes:

### Paediatric regulatory details

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

Notes:

## Results analysis stage

|                                                      |                  |
|------------------------------------------------------|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 10 November 2022 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 03 February 2022 |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 26 October 2022  |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

To demonstrate that the intraocular pressure (IOP) reducing effect of DE-130A (latanoprost 50 µg/ml preservative-free eye drops emulsion) is non-inferior to that of Xalatan® [latanoprost 50 µg/ml Benzalkonium Chloride (BAK)-preserved eye drops solution] in patients with Open-Angle Glaucoma (OAG) or Ocular Hypertension (OHT) at Week 12 without using any rescue medication(s).

Protection of trial subjects:

This study was conducted in accordance with International Council for Harmonisation (ICH) of Good Clinical Practice (GCP), ethical principles that have their origin in the Declaration of Helsinki as well as other applicable ethical and regulatory requirements.

The final protocol, its amendments, and Informed Consent Form (ICF), relevant supporting information, and patient recruitment information were submitted by the Investigator to an Independent Ethics Committee (IEC) and/or Institutional Review Board (IRB) and approved by the IEC/IRB prior to study initiation.

Background therapy: -

Evidence for comparator: -

|                                                           |                  |
|-----------------------------------------------------------|------------------|
| Actual start date of recruitment                          | 10 April 2019    |
| Long term follow-up planned                               | Yes              |
| Long term follow-up rationale                             | Safety, Efficacy |
| Long term follow-up duration                              | 12 Months        |
| Independent data monitoring committee (IDMC) involvement? | No               |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                         |
|--------------------------------------|-------------------------|
| Country: Number of subjects enrolled | Poland: 9               |
| Country: Number of subjects enrolled | Spain: 43               |
| Country: Number of subjects enrolled | United Kingdom: 13      |
| Country: Number of subjects enrolled | Austria: 7              |
| Country: Number of subjects enrolled | Belgium: 11             |
| Country: Number of subjects enrolled | Estonia: 29             |
| Country: Number of subjects enrolled | Finland: 5              |
| Country: Number of subjects enrolled | France: 4               |
| Country: Number of subjects enrolled | Germany: 15             |
| Country: Number of subjects enrolled | Italy: 37               |
| Country: Number of subjects enrolled | Latvia: 26              |
| Country: Number of subjects enrolled | Russian Federation: 181 |
| Country: Number of subjects enrolled | Korea, Republic of: 6   |

|                                    |     |
|------------------------------------|-----|
| Worldwide total number of subjects | 386 |
| EEA total number of subjects       | 186 |

Notes:

| <b>Subjects enrolled per age group</b>    |     |
|-------------------------------------------|-----|
| 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)                      | 198 |
| From 65 to 84 years                       | 186 |
| 85 years and over                         | 2   |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Out of 488 patients screened, 386 were randomised at Visit 1, n=193 to the DE-130A group and n=193 to the control (Xalatan®) group.

Out of 137 patients who participated in Period 2, 71 had previously been treated with DE-130A and 66 with Xalatan® during Period 1. All 137 subjects were administered at least one dose of DE-130A.

### Period 1

|                              |                                     |
|------------------------------|-------------------------------------|
| Period 1 title               | Double Masked Treatment Period      |
| Is this the baseline period? | Yes                                 |
| Allocation method            | Randomised - controlled             |
| Blinding used                | Double blind <sup>[1]</sup>         |
| Roles blinded                | Investigator, Monitor, Data analyst |

Blinding implementation details:

Instillation of one drop, once daily in the evening (9 pm  $\pm$  1 hour) in the conjunctival sac of the affected eye(s). Both eyes will be treated unless the patient suffers from unilateral OAG/OHT.

DE-130A: Latanoprost 50 microg/ml eye drops emulsion, eye drops emulsion in single-dose containers

### Arms

|                              |                   |
|------------------------------|-------------------|
| Are arms mutually exclusive? | Yes               |
| <b>Arm title</b>             | Period 1: DE-130A |

Arm description:

DE-130A: Latanoprost 50 microg/ml preservative-free eye drops emulsion, eye drops emulsion in single-dose containers.

Instillation of one drop, once daily in the evening (9 pm  $\pm$  1 hour) in the conjunctival sac of the affected eye(s). Both eyes will be treated unless the patient suffers from unilateral OAG/OHT.

|                                        |                     |
|----------------------------------------|---------------------|
| Arm type                               | Experimental        |
| Investigational medicinal product name | DE-130A             |
| Investigational medicinal product code |                     |
| Other name                             |                     |
| Pharmaceutical forms                   | Eye drops, emulsion |
| Routes of administration               | Ophthalmic use      |

Dosage and administration details:

Instillation of one drop, once daily in the evening (9 pm  $\pm$  1 hour) in the conjunctival sac of the affected eye(s).

|                  |                   |
|------------------|-------------------|
| <b>Arm title</b> | Period 1: Xalatan |
|------------------|-------------------|

Arm description:

Xalatan: Latanoprost 50 microg/ml eye drops solution, eye drops in 2.5 ml dropper containers.

Instillation of one drop, once daily in the evening (9 pm  $\pm$  1 hour) in the conjunctival sac of the affected eye(s). Both eyes will be treated unless the patient suffers from unilateral OAG/OH.

|                                        |                     |
|----------------------------------------|---------------------|
| Arm type                               | Active comparator   |
| Investigational medicinal product name | Xalatan             |
| Investigational medicinal product code |                     |
| Other name                             |                     |
| Pharmaceutical forms                   | Eye drops, solution |
| Routes of administration               | Ophthalmic use      |

Dosage and administration details:

Instillation of one drop, once daily in the evening (9 pm  $\pm$  1 hour) in the conjunctival sac of the affected eye(s).

Notes:

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

Justification: The patients did not be explicitly told about the name of the study drug by the drug dispensing staff.

| Number of subjects in period 1         | Period 1: DE-130A | Period 1: Xalatan |
|----------------------------------------|-------------------|-------------------|
| Started                                | 193               | 193               |
| Completed                              | 190               | 190               |
| Not completed                          | 3                 | 3                 |
| Adverse event, serious fatal           | 1                 | -                 |
| Consent withdrawn by subject           | 1                 | 1                 |
| Adverse event, non-fatal               | 1                 | 1                 |
| Sponsor Temporarily Discontinued Study | -                 | 1                 |

## Period 2

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

## Arms

|                              |                           |
|------------------------------|---------------------------|
| Are arms mutually exclusive? | Yes                       |
| <b>Arm title</b>             | Period 2: DE-130A/DE-130A |

Arm description:

DE-130A: Latanoprost 50 microg/ml preservative-free eye drops emulsion, eye drops emulsion in single-dose containers.

After 12 weeks, participants continued to use DE-130A for additional 12 months. Instillation of one drop, once daily in the evening (9 pm  $\pm$ 1 hour) in the conjunctival sac of the affected eye(s). Both eyes will be treated unless the patient suffers from unilateral OAG/OHT.

|                                        |                     |
|----------------------------------------|---------------------|
| Arm type                               | Open-label          |
| Investigational medicinal product name | DE-130A             |
| Investigational medicinal product code |                     |
| Other name                             |                     |
| Pharmaceutical forms                   | Eye drops, emulsion |
| Routes of administration               | Ophthalmic use      |

Dosage and administration details:

Instillation of one drop, once daily in the evening (9 pm  $\pm$ 1 hour) in the conjunctival sac of the affected eye(s).

|                  |                           |
|------------------|---------------------------|
| <b>Arm title</b> | Period 2: Xalatan/DE-130A |
|------------------|---------------------------|

Arm description:

DE-130A: Latanoprost 50 microg/ml preservative-free eye drops emulsion, eye drops emulsion in single-dose containers.

After 12 weeks, participants were converted to use DE-130A instead of Xalatan®. Instillation of one drop, once daily in the evening (9 pm  $\pm$ 1 hour) in the conjunctival sac of the affected eye(s). Both eyes will be treated unless the patient suffers from unilateral OAG/OHT.

|          |            |
|----------|------------|
| Arm type | Open-label |
|----------|------------|

|                                        |                     |
|----------------------------------------|---------------------|
| Investigational medicinal product name | DE-130A             |
| Investigational medicinal product code |                     |
| Other name                             |                     |
| Pharmaceutical forms                   | Eye drops, emulsion |
| Routes of administration               | Ophthalmic use      |

Dosage and administration details:

Instillation of one drop, once daily in the evening (9 pm  $\pm$ 1 hour) in the conjunctival sac of the affected eye(s).

| Number of subjects in period 2 <sup>[2]</sup> | Period 2: DE-130A/DE-130A | Period 2: Xalatan/DE-130A |
|-----------------------------------------------|---------------------------|---------------------------|
|                                               |                           |                           |
| Started                                       | 71                        | 66                        |
| Completed                                     | 67                        | 62                        |
| Not completed                                 | 4                         | 4                         |
| Consent withdrawn by subject                  | 2                         | 2                         |
| Early Terminated                              | 1                         | -                         |
| Adverse event, non-fatal                      | -                         | 2                         |
| Pregnancy                                     | 1                         | -                         |

Notes:

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

Justification: It was defined in protocol as follows, and the number of subjects is as planned. The first 130 patients who completed the week 12 visit and agreed to participate in the open-label period of the study were followed for 12 months from week 12 and received open-label DE-130A treatment.

## Baseline characteristics

### Reporting groups

|                       |                   |
|-----------------------|-------------------|
| Reporting group title | Period 1: DE-130A |
|-----------------------|-------------------|

Reporting group description:

DE-130A: Latanoprost 50 microg/ml preservative-free eye drops emulsion, eye drops emulsion in single-dose containers.

Instillation of one drop, once daily in the evening (9 pm  $\pm$  1 hour) in the conjunctival sac of the affected eye(s). Both eyes will be treated unless the patient suffers from unilateral OAG/OHT.

|                       |                   |
|-----------------------|-------------------|
| Reporting group title | Period 1: Xalatan |
|-----------------------|-------------------|

Reporting group description:

Xalatan: Latanoprost 50 microg/ml eye drops solution, eye drops in 2.5 ml dropper containers.

Instillation of one drop, once daily in the evening (9 pm  $\pm$  1 hour) in the conjunctival sac of the affected eye(s). Both eyes will be treated unless the patient suffers from unilateral OAG/OHT.

| Reporting group values                             | Period 1: DE-130A | Period 1: Xalatan | Total |
|----------------------------------------------------|-------------------|-------------------|-------|
| Number of subjects                                 | 193               | 193               | 386   |
| Age categorical                                    |                   |                   |       |
| Units: Subjects                                    |                   |                   |       |
| In utero                                           | 0                 | 0                 | 0     |
| Preterm newborn infants (gestational age < 37 wks) | 0                 | 0                 | 0     |
| Newborns (0-27 days)                               | 0                 | 0                 | 0     |
| Infants and toddlers (28 days-23 months)           | 0                 | 0                 | 0     |
| Children (2-11 years)                              | 0                 | 0                 | 0     |
| Adolescents (12-17 years)                          | 0                 | 0                 | 0     |
| Adults (18-64 years)                               | 103               | 95                | 198   |
| From 65-84 years                                   | 88                | 98                | 186   |
| 85 years and over                                  | 2                 | 0                 | 2     |
| Age continuous                                     |                   |                   |       |
| Units: years                                       |                   |                   |       |
| arithmetic mean                                    | 62.3              | 63.9              |       |
| standard deviation                                 | $\pm$ 12.04       | $\pm$ 10.13       | -     |
| Gender categorical                                 |                   |                   |       |
| Units: Subjects                                    |                   |                   |       |
| Female                                             | 121               | 117               | 238   |
| Male                                               | 72                | 76                | 148   |

## End points

### End points reporting groups

|                                                                                                                                                                                                                                                                                                                                                                                                                                                |                           |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------|
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                          | Period 1: DE-130A         |
| Reporting group description:<br>DE-130A: Latanoprost 50 microg/ml preservative-free eye drops emulsion, eye drops emulsion in single-dose containers.<br>Instillation of one drop, once daily in the evening (9 pm $\pm$ 1 hour) in the conjunctival sac of the affected eye(s). Both eyes will be treated unless the patient suffers from unilateral OAG/OHT.                                                                                 |                           |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                          | Period 1: Xalatan         |
| Reporting group description:<br>Xalatan: Latanoprost 50 microg/ml eye drops solution, eye drops in 2.5 ml dropper containers.<br>Instillation of one drop, once daily in the evening (9 pm $\pm$ 1 hour) in the conjunctival sac of the affected eye(s). Both eyes will be treated unless the patient suffers from unilateral OAG/OH.                                                                                                          |                           |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                          | Period 2: DE-130A/DE-130A |
| Reporting group description:<br>DE-130A: Latanoprost 50 microg/ml preservative-free eye drops emulsion, eye drops emulsion in single-dose containers.<br>After 12 weeks, participants continued to use DE-130A for additional 12 months. Instillation of one drop, once daily in the evening (9 pm $\pm$ 1 hour) in the conjunctival sac of the affected eye(s). Both eyes will be treated unless the patient suffers from unilateral OAG/OHT. |                           |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                          | Period 2: Xalatan/DE-130A |
| Reporting group description:<br>DE-130A: Latanoprost 50 microg/ml preservative-free eye drops emulsion, eye drops emulsion in single-dose containers.<br>After 12 weeks, participants were converted to use DE-130A instead of Xalatan®. Instillation of one drop, once daily in the evening (9 pm $\pm$ 1 hour) in the conjunctival sac of the affected eye(s). Both eyes will be treated unless the patient suffers from unilateral OAG/OHT. |                           |

### Primary: Intraocular Pressure (IOP) Reduction (mmHg) at Week 12

|                                                                                                                                                                                                                                         |                                                        |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------|
| End point title                                                                                                                                                                                                                         | Intraocular Pressure (IOP) Reduction (mmHg) at Week 12 |
| End point description:<br>The primary efficacy endpoint was the change from baseline in peak (9:00 am $\pm$ 1 hour) and trough (4:00 pm $\pm$ 1 hour) IOPs, respectively, at Week 12 between the two treatment groups in the study eye. |                                                        |
| End point type                                                                                                                                                                                                                          | Primary                                                |
| End point timeframe:<br>Week 12: Peak (9:00 am $\pm$ 1 hour) and trough (4:00 pm $\pm$ 1 hour)                                                                                                                                          |                                                        |

| End point values                    | Period 1: DE-130A  | Period 1: Xalatan  |  |  |
|-------------------------------------|--------------------|--------------------|--|--|
| Subject group type                  | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed         | 188                | 189                |  |  |
| Units: mmHg                         |                    |                    |  |  |
| least squares mean (standard error) |                    |                    |  |  |
| peak (9:00 am $\pm$ 1 hour)         | -8.8 ( $\pm$ 0.25) | -8.2 ( $\pm$ 0.26) |  |  |



## Statistical analyses

|                                                                                                                                                                                                                                                    |                                       |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                                                                                                  | PRIMARY EFFICACY ENDPOINT             |
| Statistical analysis description:                                                                                                                                                                                                                  |                                       |
| The primary efficacy endpoint was change from baseline in peak and trough IOP at Week 12 in the study eye. Non-inferiority was established if the upper limit of the one-sided 97.5% CI is $\leq 1.5$ mmHg at both the peak and trough timepoints. |                                       |
| Comparison groups                                                                                                                                                                                                                                  | Period 1: DE-130A v Period 1: Xalatan |
| Number of subjects included in analysis                                                                                                                                                                                                            | 377                                   |
| Analysis specification                                                                                                                                                                                                                             | Pre-specified                         |
| Analysis type                                                                                                                                                                                                                                      | non-inferiority                       |
| Parameter estimate                                                                                                                                                                                                                                 | Mean difference (final values)        |
| Point estimate                                                                                                                                                                                                                                     | 0                                     |
| Confidence interval                                                                                                                                                                                                                                |                                       |
| level                                                                                                                                                                                                                                              | Other: 97.5 %                         |
| sides                                                                                                                                                                                                                                              | 1-sided                               |
| upper limit                                                                                                                                                                                                                                        | 1.5                                   |
| Variability estimate                                                                                                                                                                                                                               | Standard deviation                    |
| Dispersion value                                                                                                                                                                                                                                   | 4.26                                  |

## Primary: Intraocular Pressure (IOP) Reduction (mmHg) at Week 12

|                                                                                                                                                                                                               |                                                        |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------|
| End point title                                                                                                                                                                                               | Intraocular Pressure (IOP) Reduction (mmHg) at Week 12 |
| End point description:                                                                                                                                                                                        |                                                        |
| The primary efficacy endpoint was the change from baseline in peak (9:00 am $\pm$ 1 hour) and trough (4:00 pm $\pm$ 1 hour) IOPs, respectively, at Week 12 between the two treatment groups in the study eye. |                                                        |
| End point type                                                                                                                                                                                                | Primary                                                |
| End point timeframe:                                                                                                                                                                                          |                                                        |
| Week 12 (16:00) trough timepoint                                                                                                                                                                              |                                                        |

|                                     |                    |                    |  |  |
|-------------------------------------|--------------------|--------------------|--|--|
| <b>End point values</b>             | Period 1: DE-130A  | Period 1: Xalatan  |  |  |
| Subject group type                  | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed         | 186                | 188                |  |  |
| Units: mmHg                         |                    |                    |  |  |
| least squares mean (standard error) |                    |                    |  |  |
| (16:00) trough timepoint            | -8.6 ( $\pm$ 0.24) | -8.1 ( $\pm$ 0.25) |  |  |

## Statistical analyses

|                                                                                                                                                                                                                                                    |                                       |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                                                                                                  | PRIMARY EFFICACY ENDPOINT             |
| Statistical analysis description:                                                                                                                                                                                                                  |                                       |
| The primary efficacy endpoint was change from baseline in peak and trough IOP at Week 12 in the study eye. Non-inferiority was established if the upper limit of the one-sided 97.5% CI is $\leq 1.5$ mmHg at both the peak and trough timepoints. |                                       |
| Comparison groups                                                                                                                                                                                                                                  | Period 1: DE-130A v Period 1: Xalatan |
| Number of subjects included in analysis                                                                                                                                                                                                            | 374                                   |
| Analysis specification                                                                                                                                                                                                                             | Pre-specified                         |
| Analysis type                                                                                                                                                                                                                                      | non-inferiority                       |
| Parameter estimate                                                                                                                                                                                                                                 | Mean difference (final values)        |
| Point estimate                                                                                                                                                                                                                                     | 0                                     |
| Confidence interval                                                                                                                                                                                                                                |                                       |
| level                                                                                                                                                                                                                                              | Other: 97.5 %                         |
| sides                                                                                                                                                                                                                                              | 1-sided                               |
| upper limit                                                                                                                                                                                                                                        | 1.5                                   |
| Variability estimate                                                                                                                                                                                                                               | Standard deviation                    |
| Dispersion value                                                                                                                                                                                                                                   | 4.26                                  |

### Secondary: Corneal Fluorescein Staining (CFS) Change From Baseline (First Key Secondary Endpoint)

|                                                                                       |                                                                                        |
|---------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------|
| End point title                                                                       | Corneal Fluorescein Staining (CFS) Change From Baseline (First Key Secondary Endpoint) |
| End point description:                                                                |                                                                                        |
| CSF Change from baseline in participants with baseline CSF score $\geq 1$ at Week 12. |                                                                                        |
| End point type                                                                        | Secondary                                                                              |
| End point timeframe:                                                                  |                                                                                        |
| At Week 12                                                                            |                                                                                        |

| End point values                    | Period 1: DE-130A    | Period 1: Xalatan    |  |  |
|-------------------------------------|----------------------|----------------------|--|--|
| Subject group type                  | Reporting group      | Reporting group      |  |  |
| Number of subjects analysed         | 80                   | 86                   |  |  |
| Units: Score                        |                      |                      |  |  |
| least squares mean (standard error) | -0.71 ( $\pm$ 0.069) | -0.41 ( $\pm$ 0.077) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Ocular Surface Disease (OSD) Symptoms (Average of 3 Symptoms); Second Key Secondary Endpoint

|                                                                                                   |                                                                                              |
|---------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------|
| End point title                                                                                   | Ocular Surface Disease (OSD) Symptoms (Average of 3 Symptoms); Second Key Secondary Endpoint |
| End point description:                                                                            |                                                                                              |
| Change from baseline in OSD symptom score (average of 3 symptoms: dry eye sensation, blurred/poor |                                                                                              |

vision and burning/stinging/itching) in the study eye at Week 12 in patients with baseline symptom average score>0.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

at Week 12

| End point values                    | Period 1: DE-130A | Period 1: Xalatan |  |  |
|-------------------------------------|-------------------|-------------------|--|--|
| Subject group type                  | Reporting group   | Reporting group   |  |  |
| Number of subjects analysed         | 99                | 104               |  |  |
| Units: Score                        |                   |                   |  |  |
| least squares mean (standard error) | -0.26 (± 0.058)   | -0.17 (± 0.060)   |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Information about AEs were collected from the signing of consent form until the end of the study.

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 23.1 |
|--------------------|------|

### Reporting groups

|                       |         |
|-----------------------|---------|
| Reporting group title | DE-130A |
|-----------------------|---------|

Reporting group description: -

|                       |         |
|-----------------------|---------|
| Reporting group title | Xalatan |
|-----------------------|---------|

Reporting group description: -

|                       |                 |
|-----------------------|-----------------|
| Reporting group title | DE-130A/DE-130A |
|-----------------------|-----------------|

Reporting group description: -

|                       |                 |
|-----------------------|-----------------|
| Reporting group title | Xalatan/DE-130A |
|-----------------------|-----------------|

Reporting group description: -

| Serious adverse events                                              | DE-130A         | Xalatan         | DE-130A/DE-130A |
|---------------------------------------------------------------------|-----------------|-----------------|-----------------|
| Total subjects affected by serious adverse events                   |                 |                 |                 |
| subjects affected / exposed                                         | 1 / 193 (0.52%) | 2 / 193 (1.04%) | 0 / 71 (0.00%)  |
| number of deaths (all causes)                                       | 1               | 0               | 0               |
| number of deaths resulting from adverse events                      | 1               | 0               | 0               |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                 |                 |                 |
| Bladder cancer                                                      |                 |                 |                 |
| subjects affected / exposed                                         | 0 / 193 (0.00%) | 1 / 193 (0.52%) | 0 / 71 (0.00%)  |
| occurrences causally related to treatment / all                     | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0           | 0 / 0           |
| Cardiac disorders                                                   |                 |                 |                 |
| Cardiac failure acute                                               |                 |                 |                 |
| subjects affected / exposed                                         | 1 / 193 (0.52%) | 0 / 193 (0.00%) | 0 / 71 (0.00%)  |
| occurrences causally related to treatment / all                     | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all                          | 0 / 1           | 0 / 0           | 0 / 0           |
| Respiratory, thoracic and mediastinal disorders                     |                 |                 |                 |
| Pulmonary thrombosis                                                |                 |                 |                 |

|                                                 |                 |                 |                |
|-------------------------------------------------|-----------------|-----------------|----------------|
| subjects affected / exposed                     | 0 / 193 (0.00%) | 1 / 193 (0.52%) | 0 / 71 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0          |

|                                                                     |                 |  |  |
|---------------------------------------------------------------------|-----------------|--|--|
| <b>Serious adverse events</b>                                       | Xalatan/DE-130A |  |  |
| Total subjects affected by serious adverse events                   |                 |  |  |
| subjects affected / exposed                                         | 0 / 66 (0.00%)  |  |  |
| number of deaths (all causes)                                       | 0               |  |  |
| number of deaths resulting from adverse events                      | 0               |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                 |  |  |
| Bladder cancer                                                      |                 |  |  |
| subjects affected / exposed                                         | 0 / 66 (0.00%)  |  |  |
| occurrences causally related to treatment / all                     | 0 / 0           |  |  |
| deaths causally related to treatment / all                          | 0 / 0           |  |  |
| Cardiac disorders                                                   |                 |  |  |
| Cardiac failure acute                                               |                 |  |  |
| subjects affected / exposed                                         | 0 / 66 (0.00%)  |  |  |
| occurrences causally related to treatment / all                     | 0 / 0           |  |  |
| deaths causally related to treatment / all                          | 0 / 0           |  |  |
| Respiratory, thoracic and mediastinal disorders                     |                 |  |  |
| Pulmonary thrombosis                                                |                 |  |  |
| subjects affected / exposed                                         | 0 / 66 (0.00%)  |  |  |
| occurrences causally related to treatment / all                     | 0 / 0           |  |  |
| deaths causally related to treatment / all                          | 0 / 0           |  |  |

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

|                                                                     |                   |                   |                  |
|---------------------------------------------------------------------|-------------------|-------------------|------------------|
| <b>Non-serious adverse events</b>                                   | DE-130A           | Xalatan           | DE-130A/DE-130A  |
| Total subjects affected by non-serious adverse events               |                   |                   |                  |
| subjects affected / exposed                                         | 35 / 193 (18.13%) | 42 / 193 (21.76%) | 21 / 71 (29.58%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                   |                   |                  |
| Blepharal papilloma                                                 |                   |                   |                  |
| subjects affected / exposed                                         | 1 / 193 (0.52%)   | 0 / 193 (0.00%)   | 0 / 71 (0.00%)   |
| occurrences (all)                                                   | 1                 | 0                 | 0                |
| Vascular disorders                                                  |                   |                   |                  |

|                                                                                                                              |                      |                      |                     |
|------------------------------------------------------------------------------------------------------------------------------|----------------------|----------------------|---------------------|
| Hypertension<br>subjects affected / exposed<br>occurrences (all)                                                             | 0 / 193 (0.00%)<br>0 | 0 / 193 (0.00%)<br>0 | 1 / 71 (1.41%)<br>1 |
| Surgical and medical procedures<br>Knee arthroplasty<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 193 (0.00%)<br>0 | 1 / 193 (0.52%)<br>1 | 0 / 71 (0.00%)<br>0 |
| Dental implantation<br>subjects affected / exposed<br>occurrences (all)                                                      | 0 / 193 (0.00%)<br>0 | 0 / 193 (0.00%)<br>0 | 0 / 71 (0.00%)<br>0 |
| General disorders and administration<br>site conditions<br>Pyrexia<br>subjects affected / exposed<br>occurrences (all)       | 1 / 193 (0.52%)<br>1 | 0 / 193 (0.00%)<br>0 | 0 / 71 (0.00%)<br>0 |
| Chest pain<br>subjects affected / exposed<br>occurrences (all)                                                               | 0 / 193 (0.00%)<br>0 | 1 / 193 (0.52%)<br>1 | 0 / 71 (0.00%)<br>0 |
| Fatigue<br>subjects affected / exposed<br>occurrences (all)                                                                  | 0 / 193 (0.00%)<br>0 | 1 / 193 (0.52%)<br>1 | 0 / 71 (0.00%)<br>0 |
| Instillation site pain<br>subjects affected / exposed<br>occurrences (all)                                                   | 0 / 193 (0.00%)<br>0 | 3 / 193 (1.55%)<br>3 | 0 / 71 (0.00%)<br>0 |
| Pain<br>subjects affected / exposed<br>occurrences (all)                                                                     | 0 / 193 (0.00%)<br>0 | 0 / 193 (0.00%)<br>0 | 0 / 71 (0.00%)<br>0 |
| Immune system disorders<br>Seasonal allergy<br>subjects affected / exposed<br>occurrences (all)                              | 2 / 193 (1.04%)<br>2 | 0 / 193 (0.00%)<br>0 | 1 / 71 (1.41%)<br>1 |
| Respiratory, thoracic and mediastinal<br>disorders<br>Oropharyngeal pain<br>subjects affected / exposed<br>occurrences (all) | 1 / 193 (0.52%)<br>1 | 0 / 193 (0.00%)<br>0 | 0 / 71 (0.00%)<br>0 |
| Rhinorrhoea                                                                                                                  |                      |                      |                     |

|                                                                                 |                      |                      |                     |
|---------------------------------------------------------------------------------|----------------------|----------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)                                | 1 / 193 (0.52%)<br>1 | 1 / 193 (0.52%)<br>1 | 0 / 71 (0.00%)<br>0 |
| Investigations                                                                  |                      |                      |                     |
| Blood cholesterol increased<br>subjects affected / exposed<br>occurrences (all) | 1 / 193 (0.52%)<br>1 | 0 / 193 (0.00%)<br>0 | 0 / 71 (0.00%)<br>0 |
| Body temperature increased<br>subjects affected / exposed<br>occurrences (all)  | 0 / 193 (0.00%)<br>0 | 2 / 193 (1.04%)<br>2 | 0 / 71 (0.00%)<br>0 |
| Injury, poisoning and procedural complications                                  |                      |                      |                     |
| Tooth fracture<br>subjects affected / exposed<br>occurrences (all)              | 1 / 193 (0.52%)<br>1 | 0 / 193 (0.00%)<br>0 | 0 / 71 (0.00%)<br>0 |
| Contusion<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 193 (0.00%)<br>0 | 1 / 193 (0.52%)<br>1 | 0 / 71 (0.00%)<br>0 |
| Skin laceration<br>subjects affected / exposed<br>occurrences (all)             | 0 / 193 (0.00%)<br>0 | 0 / 193 (0.00%)<br>0 | 1 / 71 (1.41%)<br>1 |
| Cardiac disorders                                                               |                      |                      |                     |
| Angina pectoris<br>subjects affected / exposed<br>occurrences (all)             | 1 / 193 (0.52%)<br>1 | 0 / 193 (0.00%)<br>0 | 0 / 71 (0.00%)<br>0 |
| Atrial fibrillation<br>subjects affected / exposed<br>occurrences (all)         | 0 / 193 (0.00%)<br>0 | 0 / 193 (0.00%)<br>0 | 1 / 71 (1.41%)<br>1 |
| Palpitations<br>subjects affected / exposed<br>occurrences (all)                | 0 / 193 (0.00%)<br>0 | 0 / 193 (0.00%)<br>0 | 1 / 71 (1.41%)<br>1 |
| Nervous system disorders                                                        |                      |                      |                     |
| Dizziness<br>subjects affected / exposed<br>occurrences (all)                   | 2 / 193 (1.04%)<br>2 | 1 / 193 (0.52%)<br>1 | 0 / 71 (0.00%)<br>0 |
| Dysgeusia<br>subjects affected / exposed<br>occurrences (all)                   | 1 / 193 (0.52%)<br>1 | 0 / 193 (0.00%)<br>0 | 0 / 71 (0.00%)<br>0 |

|                             |                 |                 |                |
|-----------------------------|-----------------|-----------------|----------------|
| Eye disorders               |                 |                 |                |
| Ocular hyperaemia           |                 |                 |                |
| subjects affected / exposed | 3 / 193 (1.55%) | 5 / 193 (2.59%) | 2 / 71 (2.82%) |
| occurrences (all)           | 3               | 5               | 2              |
| Conjunctival hyperaemia     |                 |                 |                |
| subjects affected / exposed | 2 / 193 (1.04%) | 3 / 193 (1.55%) | 1 / 71 (1.41%) |
| occurrences (all)           | 2               | 3               | 1              |
| Dry eye                     |                 |                 |                |
| subjects affected / exposed | 2 / 193 (1.04%) | 1 / 193 (0.52%) | 1 / 71 (1.41%) |
| occurrences (all)           | 2               | 1               | 1              |
| Erythema of eyelid          |                 |                 |                |
| subjects affected / exposed | 2 / 193 (1.04%) | 2 / 193 (1.04%) | 0 / 71 (0.00%) |
| occurrences (all)           | 2               | 2               | 0              |
| Keratitis                   |                 |                 |                |
| subjects affected / exposed | 2 / 193 (1.04%) | 0 / 193 (0.00%) | 0 / 71 (0.00%) |
| occurrences (all)           | 2               | 0               | 0              |
| Vision blurred              |                 |                 |                |
| subjects affected / exposed | 2 / 193 (1.04%) | 0 / 193 (0.00%) | 0 / 71 (0.00%) |
| occurrences (all)           | 2               | 0               | 0              |
| Blepharitis                 |                 |                 |                |
| subjects affected / exposed | 1 / 193 (0.52%) | 0 / 193 (0.00%) | 2 / 71 (2.82%) |
| occurrences (all)           | 1               | 0               | 2              |
| Chalazion                   |                 |                 |                |
| subjects affected / exposed | 1 / 193 (0.52%) | 0 / 193 (0.00%) | 1 / 71 (1.41%) |
| occurrences (all)           | 1               | 0               | 1              |
| Conjunctival haemorrhage    |                 |                 |                |
| subjects affected / exposed | 1 / 193 (0.52%) | 1 / 193 (0.52%) | 0 / 71 (0.00%) |
| occurrences (all)           | 1               | 1               | 0              |
| Conjunctival oedema         |                 |                 |                |
| subjects affected / exposed | 1 / 193 (0.52%) | 0 / 193 (0.00%) | 0 / 71 (0.00%) |
| occurrences (all)           | 1               | 0               | 0              |
| Eye pain                    |                 |                 |                |
| subjects affected / exposed | 1 / 193 (0.52%) | 1 / 193 (0.52%) | 1 / 71 (1.41%) |
| occurrences (all)           | 1               | 1               | 1              |
| Eye pruritus                |                 |                 |                |



|                                |                 |                 |                |
|--------------------------------|-----------------|-----------------|----------------|
| subjects affected / exposed    | 1 / 193 (0.52%) | 3 / 193 (1.55%) | 0 / 71 (0.00%) |
| occurrences (all)              | 1               | 3               | 0              |
| Eyelid oedema                  |                 |                 |                |
| subjects affected / exposed    | 1 / 193 (0.52%) | 0 / 193 (0.00%) | 0 / 71 (0.00%) |
| occurrences (all)              | 1               | 0               | 0              |
| Growth of eyelashes            |                 |                 |                |
| subjects affected / exposed    | 1 / 193 (0.52%) | 0 / 193 (0.00%) | 2 / 71 (2.82%) |
| occurrences (all)              | 1               | 0               | 2              |
| Ocular discomfort              |                 |                 |                |
| subjects affected / exposed    | 1 / 193 (0.52%) | 0 / 193 (0.00%) | 0 / 71 (0.00%) |
| occurrences (all)              | 1               | 0               | 0              |
| Swelling of eyelid             |                 |                 |                |
| subjects affected / exposed    | 1 / 193 (0.52%) | 2 / 193 (1.04%) | 1 / 71 (1.41%) |
| occurrences (all)              | 1               | 3               | 1              |
| Abnormal sensation in eye      |                 |                 |                |
| subjects affected / exposed    | 0 / 193 (0.00%) | 4 / 193 (2.07%) | 1 / 71 (1.41%) |
| occurrences (all)              | 0               | 4               | 2              |
| Eye irritation                 |                 |                 |                |
| subjects affected / exposed    | 0 / 193 (0.00%) | 2 / 193 (1.04%) | 0 / 71 (0.00%) |
| occurrences (all)              | 0               | 2               | 0              |
| Foreign body sensation in eyes |                 |                 |                |
| subjects affected / exposed    | 0 / 193 (0.00%) | 3 / 193 (1.55%) | 0 / 71 (0.00%) |
| occurrences (all)              | 0               | 3               | 0              |
| Lacrimal disorder              |                 |                 |                |
| subjects affected / exposed    | 0 / 193 (0.00%) | 1 / 193 (0.52%) | 0 / 71 (0.00%) |
| occurrences (all)              | 0               | 1               | 0              |
| Vitreous detachment            |                 |                 |                |
| subjects affected / exposed    | 0 / 193 (0.00%) | 1 / 193 (0.52%) | 1 / 71 (1.41%) |
| occurrences (all)              | 0               | 1               | 1              |
| Cataract                       |                 |                 |                |
| subjects affected / exposed    | 0 / 193 (0.00%) | 0 / 193 (0.00%) | 1 / 71 (1.41%) |
| occurrences (all)              | 0               | 0               | 2              |
| Eye paraesthesia               |                 |                 |                |
| subjects affected / exposed    | 0 / 193 (0.00%) | 0 / 193 (0.00%) | 1 / 71 (1.41%) |
| occurrences (all)              | 0               | 0               | 1              |
| Retinal haemorrhage            |                 |                 |                |

|                                                                                                                   |                      |                      |                     |
|-------------------------------------------------------------------------------------------------------------------|----------------------|----------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)                                                                  | 0 / 193 (0.00%)<br>0 | 0 / 193 (0.00%)<br>0 | 1 / 71 (1.41%)<br>1 |
| Visual impairment<br>subjects affected / exposed<br>occurrences (all)                                             | 0 / 193 (0.00%)<br>0 | 0 / 193 (0.00%)<br>0 | 1 / 71 (1.41%)<br>1 |
| Vitreous floaters<br>subjects affected / exposed<br>occurrences (all)                                             | 0 / 193 (0.00%)<br>0 | 0 / 193 (0.00%)<br>0 | 1 / 71 (1.41%)<br>1 |
| Macular fibrosis<br>subjects affected / exposed<br>occurrences (all)                                              | 0 / 193 (0.00%)<br>0 | 0 / 193 (0.00%)<br>0 | 0 / 71 (0.00%)<br>0 |
| Photopsia<br>subjects affected / exposed<br>occurrences (all)                                                     | 0 / 193 (0.00%)<br>0 | 0 / 193 (0.00%)<br>0 | 0 / 71 (0.00%)<br>0 |
| Gastrointestinal disorders<br>Burning mouth syndrome<br>subjects affected / exposed<br>occurrences (all)          | 1 / 193 (0.52%)<br>1 | 0 / 193 (0.00%)<br>0 | 0 / 71 (0.00%)<br>0 |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)                                                     | 1 / 193 (0.52%)<br>1 | 0 / 193 (0.00%)<br>0 | 0 / 71 (0.00%)<br>0 |
| Hepatobiliary disorders<br>Cholelithiasis<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 193 (0.00%)<br>0 | 1 / 193 (0.52%)<br>1 | 0 / 71 (0.00%)<br>0 |
| Skin and subcutaneous tissue disorders<br>Hyperkeratosis<br>subjects affected / exposed<br>occurrences (all)      | 0 / 193 (0.00%)<br>0 | 0 / 193 (0.00%)<br>0 | 1 / 71 (1.41%)<br>1 |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all) | 3 / 193 (1.55%)<br>3 | 1 / 193 (0.52%)<br>1 | 0 / 71 (0.00%)<br>0 |
| Musculoskeletal chest pain<br>subjects affected / exposed<br>occurrences (all)                                    | 1 / 193 (0.52%)<br>1 | 0 / 193 (0.00%)<br>0 | 1 / 71 (1.41%)<br>1 |

|                                                                        |                      |                      |                     |
|------------------------------------------------------------------------|----------------------|----------------------|---------------------|
| Pain in extremity<br>subjects affected / exposed<br>occurrences (all)  | 1 / 193 (0.52%)<br>1 | 0 / 193 (0.00%)<br>0 | 0 / 71 (0.00%)<br>0 |
| Back pain<br>subjects affected / exposed<br>occurrences (all)          | 0 / 193 (0.00%)<br>0 | 3 / 193 (1.55%)<br>3 | 0 / 71 (0.00%)<br>0 |
| Mobility decreased<br>subjects affected / exposed<br>occurrences (all) | 0 / 193 (0.00%)<br>0 | 1 / 193 (0.52%)<br>1 | 0 / 71 (0.00%)<br>0 |
| Osteoarthritis<br>subjects affected / exposed<br>occurrences (all)     | 0 / 193 (0.00%)<br>0 | 1 / 193 (0.52%)<br>1 | 1 / 71 (1.41%)<br>1 |
| Plantar fasciitis<br>subjects affected / exposed<br>occurrences (all)  | 0 / 193 (0.00%)<br>0 | 0 / 193 (0.00%)<br>0 | 1 / 71 (1.41%)<br>1 |
| Tendon disorder<br>subjects affected / exposed<br>occurrences (all)    | 0 / 193 (0.00%)<br>0 | 0 / 193 (0.00%)<br>0 | 1 / 71 (1.41%)<br>1 |
| Spinal pain<br>subjects affected / exposed<br>occurrences (all)        | 0 / 193 (0.00%)<br>0 | 0 / 193 (0.00%)<br>0 | 0 / 71 (0.00%)<br>0 |
| Infections and infestations                                            |                      |                      |                     |
| Bronchitis<br>subjects affected / exposed<br>occurrences (all)         | 1 / 193 (0.52%)<br>1 | 0 / 193 (0.00%)<br>0 | 0 / 71 (0.00%)<br>0 |
| COVID-19<br>subjects affected / exposed<br>occurrences (all)           | 1 / 193 (0.52%)<br>1 | 2 / 193 (1.04%)<br>2 | 0 / 71 (0.00%)<br>0 |
| Influenza<br>subjects affected / exposed<br>occurrences (all)          | 1 / 193 (0.52%)<br>1 | 0 / 193 (0.00%)<br>0 | 1 / 71 (1.41%)<br>1 |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)    | 1 / 193 (0.52%)<br>1 | 2 / 193 (1.04%)<br>2 | 0 / 71 (0.00%)<br>0 |
| Subcutaneous abscess                                                   |                      |                      |                     |

|                                   |                 |                 |                |
|-----------------------------------|-----------------|-----------------|----------------|
| subjects affected / exposed       | 1 / 193 (0.52%) | 0 / 193 (0.00%) | 0 / 71 (0.00%) |
| occurrences (all)                 | 1               | 0               | 0              |
| Tooth infection                   |                 |                 |                |
| subjects affected / exposed       | 1 / 193 (0.52%) | 0 / 193 (0.00%) | 0 / 71 (0.00%) |
| occurrences (all)                 | 1               | 0               | 0              |
| Cystitis                          |                 |                 |                |
| subjects affected / exposed       | 0 / 193 (0.00%) | 1 / 193 (0.52%) | 0 / 71 (0.00%) |
| occurrences (all)                 | 0               | 1               | 0              |
| Genital infection                 |                 |                 |                |
| subjects affected / exposed       | 0 / 193 (0.00%) | 1 / 193 (0.52%) | 0 / 71 (0.00%) |
| occurrences (all)                 | 0               | 1               | 0              |
| Labyrinthitis                     |                 |                 |                |
| subjects affected / exposed       | 0 / 193 (0.00%) | 1 / 193 (0.52%) | 0 / 71 (0.00%) |
| occurrences (all)                 | 0               | 1               | 0              |
| Lower respiratory tract infection |                 |                 |                |
| subjects affected / exposed       | 0 / 193 (0.00%) | 1 / 193 (0.52%) | 0 / 71 (0.00%) |
| occurrences (all)                 | 0               | 1               | 0              |
| Respiratory tract infection viral |                 |                 |                |
| subjects affected / exposed       | 0 / 193 (0.00%) | 1 / 193 (0.52%) | 0 / 71 (0.00%) |
| occurrences (all)                 | 0               | 1               | 0              |
| Conjunctivitis                    |                 |                 |                |
| subjects affected / exposed       | 0 / 193 (0.00%) | 0 / 193 (0.00%) | 1 / 71 (1.41%) |
| occurrences (all)                 | 0               | 0               | 1              |
| Conjunctivitis viral              |                 |                 |                |
| subjects affected / exposed       | 0 / 193 (0.00%) | 0 / 193 (0.00%) | 1 / 71 (1.41%) |
| occurrences (all)                 | 0               | 0               | 1              |
| Ear infection                     |                 |                 |                |
| subjects affected / exposed       | 0 / 193 (0.00%) | 0 / 193 (0.00%) | 1 / 71 (1.41%) |
| occurrences (all)                 | 0               | 0               | 1              |
| Herpes simplex                    |                 |                 |                |
| subjects affected / exposed       | 0 / 193 (0.00%) | 0 / 193 (0.00%) | 1 / 71 (1.41%) |
| occurrences (all)                 | 0               | 0               | 1              |
| Hordeolum                         |                 |                 |                |
| subjects affected / exposed       | 0 / 193 (0.00%) | 0 / 193 (0.00%) | 1 / 71 (1.41%) |
| occurrences (all)                 | 0               | 0               | 1              |
| Rhinitis                          |                 |                 |                |

|                                                                                                |                      |                      |                     |
|------------------------------------------------------------------------------------------------|----------------------|----------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)                                               | 0 / 193 (0.00%)<br>0 | 0 / 193 (0.00%)<br>0 | 1 / 71 (1.41%)<br>1 |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)          | 0 / 193 (0.00%)<br>0 | 0 / 193 (0.00%)<br>0 | 1 / 71 (1.41%)<br>1 |
| Coronavirus infection<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 193 (0.00%)<br>0 | 0 / 193 (0.00%)<br>0 | 0 / 71 (0.00%)<br>0 |
| Metabolism and nutrition disorders<br>Gout<br>subjects affected / exposed<br>occurrences (all) | 0 / 193 (0.00%)<br>0 | 0 / 193 (0.00%)<br>0 | 1 / 71 (1.41%)<br>1 |

|                                                                                                                                                                                         |                                                |  |  |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------|--|--|
| <b>Non-serious adverse events</b>                                                                                                                                                       | Xalatan/DE-130A                                |  |  |
| Total subjects affected by non-serious adverse events<br>subjects affected / exposed                                                                                                    | 21 / 66 (31.82%)                               |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps)<br>Blepharal papilloma<br>subjects affected / exposed<br>occurrences (all)                                          | 0 / 66 (0.00%)<br>0                            |  |  |
| Vascular disorders<br>Hypertension<br>subjects affected / exposed<br>occurrences (all)                                                                                                  | 0 / 66 (0.00%)<br>0                            |  |  |
| Surgical and medical procedures<br>Knee arthroplasty<br>subjects affected / exposed<br>occurrences (all)<br><br>Dental implantation<br>subjects affected / exposed<br>occurrences (all) | 0 / 66 (0.00%)<br>0<br><br>1 / 66 (1.52%)<br>1 |  |  |
| General disorders and administration site conditions<br>Pyrexia<br>subjects affected / exposed<br>occurrences (all)<br><br>Chest pain                                                   | 0 / 66 (0.00%)<br>0                            |  |  |

|                                                                                                                                                                                                                                                                                                          |                                                                                                                             |  |  |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Fatigue</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Instillation site pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 66 (0.00%)</p> <p>0</p> <p>0 / 66 (0.00%)</p> <p>0</p> <p>1 / 66 (1.52%)</p> <p>1</p> <p>1 / 66 (1.52%)</p> <p>1</p> |  |  |
| <p>Immune system disorders</p> <p>Seasonal allergy</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                                                                                                                                       | <p>0 / 66 (0.00%)</p> <p>0</p>                                                                                              |  |  |
| <p>Respiratory, thoracic and mediastinal disorders</p> <p>Oropharyngeal pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Rhinorrhoea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                              | <p>0 / 66 (0.00%)</p> <p>0</p> <p>0 / 66 (0.00%)</p> <p>0</p>                                                               |  |  |
| <p>Investigations</p> <p>Blood cholesterol increased</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Body temperature increased</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                                       | <p>0 / 66 (0.00%)</p> <p>0</p> <p>0 / 66 (0.00%)</p> <p>0</p>                                                               |  |  |
| <p>Injury, poisoning and procedural complications</p> <p>Tooth fracture</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Contusion</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                                     | <p>0 / 66 (0.00%)</p> <p>0</p> <p>0 / 66 (0.00%)</p> <p>0</p>                                                               |  |  |

|                                                                                           |                     |  |  |
|-------------------------------------------------------------------------------------------|---------------------|--|--|
| Skin laceration<br>subjects affected / exposed<br>occurrences (all)                       | 0 / 66 (0.00%)<br>0 |  |  |
| Cardiac disorders<br>Angina pectoris<br>subjects affected / exposed<br>occurrences (all)  | 0 / 66 (0.00%)<br>0 |  |  |
| Atrial fibrillation<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 66 (0.00%)<br>0 |  |  |
| Palpitations<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 66 (0.00%)<br>0 |  |  |
| Nervous system disorders<br>Dizziness<br>subjects affected / exposed<br>occurrences (all) | 0 / 66 (0.00%)<br>0 |  |  |
| Dysgeusia<br>subjects affected / exposed<br>occurrences (all)                             | 0 / 66 (0.00%)<br>0 |  |  |
| Eye disorders<br>Ocular hyperaemia<br>subjects affected / exposed<br>occurrences (all)    | 2 / 66 (3.03%)<br>2 |  |  |
| Conjunctival hyperaemia<br>subjects affected / exposed<br>occurrences (all)               | 1 / 66 (1.52%)<br>1 |  |  |
| Dry eye<br>subjects affected / exposed<br>occurrences (all)                               | 0 / 66 (0.00%)<br>0 |  |  |
| Erythema of eyelid<br>subjects affected / exposed<br>occurrences (all)                    | 1 / 66 (1.52%)<br>1 |  |  |
| Keratitis<br>subjects affected / exposed<br>occurrences (all)                             | 0 / 66 (0.00%)<br>0 |  |  |
| Vision blurred                                                                            |                     |  |  |

|                             |                |  |  |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 66 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Blepharitis                 |                |  |  |
| subjects affected / exposed | 1 / 66 (1.52%) |  |  |
| occurrences (all)           | 1              |  |  |
| Chalazion                   |                |  |  |
| subjects affected / exposed | 0 / 66 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Conjunctival haemorrhage    |                |  |  |
| subjects affected / exposed | 0 / 66 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Conjunctival oedema         |                |  |  |
| subjects affected / exposed | 0 / 66 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Eye pain                    |                |  |  |
| subjects affected / exposed | 1 / 66 (1.52%) |  |  |
| occurrences (all)           | 2              |  |  |
| Eye pruritus                |                |  |  |
| subjects affected / exposed | 1 / 66 (1.52%) |  |  |
| occurrences (all)           | 1              |  |  |
| Eyelid oedema               |                |  |  |
| subjects affected / exposed | 0 / 66 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Growth of eyelashes         |                |  |  |
| subjects affected / exposed | 2 / 66 (3.03%) |  |  |
| occurrences (all)           | 2              |  |  |
| Ocular discomfort           |                |  |  |
| subjects affected / exposed | 0 / 66 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Swelling of eyelid          |                |  |  |
| subjects affected / exposed | 2 / 66 (3.03%) |  |  |
| occurrences (all)           | 3              |  |  |
| Abnormal sensation in eye   |                |  |  |
| subjects affected / exposed | 4 / 66 (6.06%) |  |  |
| occurrences (all)           | 4              |  |  |
| Eye irritation              |                |  |  |



|                                |                |  |  |
|--------------------------------|----------------|--|--|
| subjects affected / exposed    | 0 / 66 (0.00%) |  |  |
| occurrences (all)              | 0              |  |  |
| Foreign body sensation in eyes |                |  |  |
| subjects affected / exposed    | 1 / 66 (1.52%) |  |  |
| occurrences (all)              | 1              |  |  |
| Lacrimonal disorder            |                |  |  |
| subjects affected / exposed    | 0 / 66 (0.00%) |  |  |
| occurrences (all)              | 0              |  |  |
| Vitreous detachment            |                |  |  |
| subjects affected / exposed    | 0 / 66 (0.00%) |  |  |
| occurrences (all)              | 0              |  |  |
| Cataract                       |                |  |  |
| subjects affected / exposed    | 0 / 66 (0.00%) |  |  |
| occurrences (all)              | 0              |  |  |
| Eye paraesthesia               |                |  |  |
| subjects affected / exposed    | 0 / 66 (0.00%) |  |  |
| occurrences (all)              | 0              |  |  |
| Retinal haemorrhage            |                |  |  |
| subjects affected / exposed    | 0 / 66 (0.00%) |  |  |
| occurrences (all)              | 0              |  |  |
| Visual impairment              |                |  |  |
| subjects affected / exposed    | 0 / 66 (0.00%) |  |  |
| occurrences (all)              | 0              |  |  |
| Vitreous floaters              |                |  |  |
| subjects affected / exposed    | 0 / 66 (0.00%) |  |  |
| occurrences (all)              | 0              |  |  |
| Macular fibrosis               |                |  |  |
| subjects affected / exposed    | 1 / 66 (1.52%) |  |  |
| occurrences (all)              | 1              |  |  |
| Photopsia                      |                |  |  |
| subjects affected / exposed    | 1 / 66 (1.52%) |  |  |
| occurrences (all)              | 1              |  |  |
| Gastrointestinal disorders     |                |  |  |
| Burning mouth syndrome         |                |  |  |
| subjects affected / exposed    | 0 / 66 (0.00%) |  |  |
| occurrences (all)              | 0              |  |  |

|                                                                                                                   |                     |  |  |
|-------------------------------------------------------------------------------------------------------------------|---------------------|--|--|
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)                                                     | 0 / 66 (0.00%)<br>0 |  |  |
| Hepatobiliary disorders<br>Cholelithiasis<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 66 (0.00%)<br>0 |  |  |
| Skin and subcutaneous tissue disorders<br>Hyperkeratosis<br>subjects affected / exposed<br>occurrences (all)      | 0 / 66 (0.00%)<br>0 |  |  |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all) | 1 / 66 (1.52%)<br>1 |  |  |
| Musculoskeletal chest pain<br>subjects affected / exposed<br>occurrences (all)                                    | 0 / 66 (0.00%)<br>0 |  |  |
| Pain in extremity<br>subjects affected / exposed<br>occurrences (all)                                             | 0 / 66 (0.00%)<br>0 |  |  |
| Back pain<br>subjects affected / exposed<br>occurrences (all)                                                     | 2 / 66 (3.03%)<br>2 |  |  |
| Mobility decreased<br>subjects affected / exposed<br>occurrences (all)                                            | 1 / 66 (1.52%)<br>1 |  |  |
| Osteoarthritis<br>subjects affected / exposed<br>occurrences (all)                                                | 1 / 66 (1.52%)<br>1 |  |  |
| Plantar fasciitis<br>subjects affected / exposed<br>occurrences (all)                                             | 0 / 66 (0.00%)<br>0 |  |  |
| Tendon disorder<br>subjects affected / exposed<br>occurrences (all)                                               | 0 / 66 (0.00%)<br>0 |  |  |

|                                   |                |  |  |
|-----------------------------------|----------------|--|--|
| Spinal pain                       |                |  |  |
| subjects affected / exposed       | 1 / 66 (1.52%) |  |  |
| occurrences (all)                 | 1              |  |  |
| Infections and infestations       |                |  |  |
| Bronchitis                        |                |  |  |
| subjects affected / exposed       | 0 / 66 (0.00%) |  |  |
| occurrences (all)                 | 0              |  |  |
| COVID-19                          |                |  |  |
| subjects affected / exposed       | 4 / 66 (6.06%) |  |  |
| occurrences (all)                 | 4              |  |  |
| Influenza                         |                |  |  |
| subjects affected / exposed       | 0 / 66 (0.00%) |  |  |
| occurrences (all)                 | 0              |  |  |
| Nasopharyngitis                   |                |  |  |
| subjects affected / exposed       | 0 / 66 (0.00%) |  |  |
| occurrences (all)                 | 0              |  |  |
| Subcutaneous abscess              |                |  |  |
| subjects affected / exposed       | 0 / 66 (0.00%) |  |  |
| occurrences (all)                 | 0              |  |  |
| Tooth infection                   |                |  |  |
| subjects affected / exposed       | 0 / 66 (0.00%) |  |  |
| occurrences (all)                 | 0              |  |  |
| Cystitis                          |                |  |  |
| subjects affected / exposed       | 0 / 66 (0.00%) |  |  |
| occurrences (all)                 | 0              |  |  |
| Genital infection                 |                |  |  |
| subjects affected / exposed       | 0 / 66 (0.00%) |  |  |
| occurrences (all)                 | 0              |  |  |
| Labyrinthitis                     |                |  |  |
| subjects affected / exposed       | 0 / 66 (0.00%) |  |  |
| occurrences (all)                 | 0              |  |  |
| Lower respiratory tract infection |                |  |  |
| subjects affected / exposed       | 0 / 66 (0.00%) |  |  |
| occurrences (all)                 | 0              |  |  |
| Respiratory tract infection viral |                |  |  |

|                                    |                |  |  |
|------------------------------------|----------------|--|--|
| subjects affected / exposed        | 0 / 66 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |
| Conjunctivitis                     |                |  |  |
| subjects affected / exposed        | 0 / 66 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |
| Conjunctivitis viral               |                |  |  |
| subjects affected / exposed        | 0 / 66 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |
| Ear infection                      |                |  |  |
| subjects affected / exposed        | 0 / 66 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |
| Herpes simplex                     |                |  |  |
| subjects affected / exposed        | 0 / 66 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |
| Hordeolum                          |                |  |  |
| subjects affected / exposed        | 0 / 66 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |
| Rhinitis                           |                |  |  |
| subjects affected / exposed        | 1 / 66 (1.52%) |  |  |
| occurrences (all)                  | 1              |  |  |
| Upper respiratory tract infection  |                |  |  |
| subjects affected / exposed        | 0 / 66 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |
| Coronavirus infection              |                |  |  |
| subjects affected / exposed        | 1 / 66 (1.52%) |  |  |
| occurrences (all)                  | 1              |  |  |
| Metabolism and nutrition disorders |                |  |  |
| Gout                               |                |  |  |
| subjects affected / exposed        | 0 / 66 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported