



Clinical trial results:

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

Summary

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

Results information

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

Trial information

Trial identification

| | |
|-----------------------|-----------|
| Sponsor protocol code | NTMT-03-B |
|-----------------------|-----------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Neurotech Pharmaceuticals Inc |
| Sponsor organisation address | 900 Highland Corporate Drive, Suite 101, Cumberland, United States, |
| Public contact | Kevin Hibbert, Neurotech Pharmaceuticals Inc, k.hibbert@neurotechusa.com |
| Scientific contact | Kevin Hibbert, Neurotech Pharmaceuticals Inc, k.hibbert@neurotechusa.com |

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|-------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 30 November 2023 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 07 September 2022 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

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

Primary objective:

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

Protection of trial subjects:

Ethics committee approval

Background therapy:

None

Evidence for comparator:

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

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

Notes:

Population of trial subjects

Subjects enrolled per country

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

Notes:

Subjects enrolled per age group

| | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |

| | |
|--|----|
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 79 |
| From 65 to 84 years | 40 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Screening period for up to 30 days

Pre-assignment

Screening details:

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

Period 1

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

Blinding implementation details:

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

Arms

| | |
|------------------------------|--------|
| Are arms mutually exclusive? | Yes |
| Arm title | NT-501 |

Arm description:

Test product

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

Dosage and administration details:

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

| | |
|------------------|----------------|
| Arm title | Sham Procedure |
|------------------|----------------|

Arm description:

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

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

Dosage and administration details:

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

Notes:

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

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

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

Baseline characteristics

Reporting groups

| | |
|--------------------------------|---------------|
| Reporting group title | Overall Trial |
| Reporting group description: - | |

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

Subject analysis sets

| | |
|----------------------------|-------------------|
| Subject analysis set title | Safety population |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

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

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

Subject analysis set description:

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

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

Subject analysis set description:

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

| Reporting group values | Safety population | Modified Intention-to-Treat population | Per Protocol Population |
|------------------------|-------------------|--|-------------------------|
| Number of subjects | 113 | 113 | 105 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | 0 |

| | | | |
|---|----|----|----|
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 78 | 78 | 74 |
| From 65-84 years | 35 | 35 | 31 |
| 85 years and over | 0 | 0 | 0 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 82 | 82 | 76 |
| Male | 31 | 31 | 29 |

End points

End points reporting groups

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

Primary: Primary Efficacy Endpoint

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

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

Statistical analyses

| | |
|--|---|
| Statistical analysis title | Statistical Analysis - NT-501 vs Sham Procedure |
| Statistical analysis description: | |
| The efficacy and safety of the NT-501 implant that delivers a daily dose of CNTF in comparison to sham surgery with no implant, in participants with confirmed MacTel. | |
| Comparison groups | Sham Procedure v NT-501 |
| Number of subjects included in analysis | 113 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0186 |
| Method | longitudinal mixed model |
| Parameter estimate | Mean difference (net) |
| Point estimate | -0.049 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.089 |
| upper limit | -0.0082 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.0206 |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

During the Clinical Trial

Adverse event reporting additional description:

Please note that only non-ocular and ocular events in the study eye have been reported.

The Adverse events reported are those that occurred through month 24.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 25.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------|
| Reporting group title | NT-501 |
|-----------------------|--------|

Reporting group description:

Test product

| | |
|-----------------------|----------------|
| Reporting group title | Sham Procedure |
|-----------------------|----------------|

Reporting group description:

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

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

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

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

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 54 (1.85%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Product issues | | | |
| Device extrusion | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 54 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Cellulitis | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 1 / 54 (1.85%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| COVID-19 | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 1 / 54 (1.85%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteomyelitis | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 54 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | NT-501 | Sham Procedure | |
|--|------------------|------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 56 / 59 (94.92%) | 48 / 54 (88.89%) | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Blepharal papilloma | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 0 / 54 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | 1 / 54 (1.85%) | |
| occurrences (all) | 1 | 1 | |
| Melanocytic naevus | | | |

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

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

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported