



Clinical trial results:

A Randomized, Phase 3, Double-Masked, Parallel Group, Multicenter Study to Compare the Efficacy and Safety of ALT-L9 Versus Eylea® in Patients With Neovascular Age-Related Macular Degeneration (ALTERA) Summary

| | |
|--------------------------|----------------------------|
| EudraCT number | 2021-004530-11 |
| Trial protocol | CZ HU SK LV AT ES BG EE LT |
| Global end of trial date | 20 February 2024 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 07 March 2025 |
| First version publication date | 07 March 2025 |

Trial information

Trial identification

| | |
|-----------------------|-----------|
| Sponsor protocol code | ALT-L9-03 |
|-----------------------|-----------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|-------------------------------------------------------------------------|
| Sponsor organisation name | Altos Biologics Inc. |
| Sponsor organisation address | 8F, 15, Teheran-ro 84-gil, Gangnam-gu, Seoul, Korea, Republic of, 06179 |
| Public contact | SoJin Lee, Altos Biologics Inc., +82 2 2039 9520, sjlee@altosbio.com |
| Scientific contact | SoJin Lee, Altos Biologics Inc., +82 2 2039 9520, sjlee@altosbio.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 | 18 April 2024 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 20 February 2024 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to demonstrate that the biosimilar candidate ALT-L9 2 mg/50 microliter (mcL) was equivalent to Eylea® (aflibercept) in subjects with wet (neovascular) age-related macular degeneration (nAMD) in terms of best-corrected visual acuity (BCVA).

Protection of trial subjects:

This study was conducted in accordance with the accepted version of the Declaration of Helsinki and/or all relevant federal regulations in compliance with the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use good clinical practice (ICH GCP) guidelines, Japanese GCP and Korean GCP, and according to the appropriate regulatory requirements in the countries where the study was conducted.

Background therapy: -

Evidence for comparator: -

| | |
|-----------------------------------------------------------|--------------|
| Actual start date of recruitment | 02 June 2022 |
| 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 | Austria: 7 |
| Country: Number of subjects enrolled | Bulgaria: 16 |
| Country: Number of subjects enrolled | Czechia: 56 |
| Country: Number of subjects enrolled | Estonia: 6 |
| Country: Number of subjects enrolled | Hungary: 97 |
| Country: Number of subjects enrolled | Latvia: 35 |
| Country: Number of subjects enrolled | Lithuania: 9 |
| Country: Number of subjects enrolled | Poland: 92 |
| Country: Number of subjects enrolled | Slovakia: 19 |
| Country: Number of subjects enrolled | Spain: 22 |
| Country: Number of subjects enrolled | Japan: 33 |
| Country: Number of subjects enrolled | Korea, Republic of: 39 |
| Worldwide total number of subjects | 431 |
| EEA total number of subjects | 359 |

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) | 49 |
| From 65 to 84 years | 345 |
| 85 years and over | 37 |

Subject disposition

Recruitment

Recruitment details:

Subjects took part in the study at 79 investigative sites in Japan, Republic of Korea, Austria, Bulgaria, Czech Republic, Estonia, Hungary, Latvia, Lithuania, Poland, Slovakia and Spain from 02 June 2022 to 20 February 2024.

Pre-assignment

Screening details:

A total of 642 subjects with Neovascular Age-Related Macular Degeneration (nAMD) were screened, of which 211 subjects were screen failures and 431 subjects were randomized to receive ALT-L9 or Eylea.

Period 1

| | |
|------------------------------|--------------------------------------------------------|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Data analyst, Assessor |

Arms

| | |
|------------------------------|--------|
| Are arms mutually exclusive? | Yes |
| Arm title | ALT-L9 |

Arm description:

Subjects received single dose of ALT-L9 40 milligrams per milliliter (mg/mL) (2 mg/50 microliter [mcL] aflibercept), ophthalmic intravitreal (IVT) injection, in study eye, once every 4 weeks, for up to Week 8 and once every 8 weeks up to Week 48.

| | |
|----------------------------------------|--------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Aflibercept biosimilar |
| Investigational medicinal product code | ALT-L9 |
| Other name | |
| Pharmaceutical forms | Solution for injection in vial |
| Routes of administration | Intravitreal use |

Dosage and administration details:

ALT-L9 40 mg/mL (2 mg/50 mcL aflibercept), ophthalmic IVT injection, in study eye, once every 4 weeks, for up to Week 8 and once every 8 weeks up to Week 48. The 40 mg/mL concentration of aflibercept was contained in a single vial.

| | |
|------------------|--------|
| Arm title | Eylea® |
|------------------|--------|

Arm description:

Subjects received single dose of Eylea® 40 mg/mL (2 mg/50 mcL aflibercept), ophthalmic IVT injection, in study eye, once every 4 weeks, for up to Week 8 and once every 8 weeks up to Week 48.

| | |
|----------------------------------------|----------------------------------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Eylea® |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Intravitreal use |

Dosage and administration details:

Eylea® 40 mg/mL (2 mg/50 mcL aflibercept), ophthalmic IVT injection, in study eye, once every 4 weeks, for up to Week 8 and once every 8 weeks up to Week 48. The 40 mg/mL concentration of aflibercept was contained in a PFS.

| Number of subjects in period 1 | ALT-L9 | Eylea® |
|---------------------------------------|--------|--------|
| Started | 216 | 215 |
| Completed | 204 | 201 |
| Not completed | 12 | 14 |
| Consent withdrawn by subject | 3 | 4 |
| Physician decision | 1 | - |
| Adverse event, non-fatal | 4 | 8 |
| Death | 1 | - |
| Unspecified | 2 | 1 |
| Lost to follow-up | 1 | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|--------|
| Reporting group title | ALT-L9 |
|-----------------------|--------|

Reporting group description:

Subjects received single dose of ALT-L9 40 milligrams per milliliter (mg/mL) (2 mg/50 microliter [mL] aflibercept), ophthalmic intravitreal (IVT) injection, in study eye, once every 4 weeks, for up to Week 8 and once every 8 weeks up to Week 48.

| | |
|-----------------------|--------|
| Reporting group title | Eylea® |
|-----------------------|--------|

Reporting group description:

Subjects received single dose of Eylea® 40 mg/mL (2 mg/50 mL aflibercept), ophthalmic IVT injection, in study eye, once every 4 weeks, for up to Week 8 and once every 8 weeks up to Week 48.

| Reporting group values | ALT-L9 | Eylea® | Total |
|-------------------------------------------------------------------------|----------------|----------------|-------|
| Number of subjects | 216 | 215 | 431 |
| Age categorical Units: Subjects | | | |
| Age continuous Units: years arithmetic mean standard deviation | 74.4 ± 7.83 | 73.9 ± 7.97 | - |
| Gender categorical Units: Subjects | | | |
| Female | 132 | 126 | 258 |
| Male | 84 | 89 | 173 |

End points

End points reporting groups

| | |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------|
| Reporting group title | ALT-L9 |
| Reporting group description: Subjects received single dose of ALT-L9 40 milligrams per milliliter (mg/mL) (2 mg/50 microliter [mcL] aflibercept), ophthalmic intravitreal (IVT) injection, in study eye, once every 4 weeks, for up to Week 8 and once every 8 weeks up to Week 48. | |
| Reporting group title | Eylea® |
| Reporting group description: Subjects received single dose of Eylea® 40 mg/mL (2 mg/50 mcL aflibercept), ophthalmic IVT injection, in study eye, once every 4 weeks, for up to Week 8 and once every 8 weeks up to Week 48. | |

Primary: Change from Baseline in Best-corrected Visual Acuity (BCVA) at Week 8 as Measured by the Early Treatment Diabetic Retinopathy Study (ETDRS) Letter Score

| | |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Change from Baseline in Best-corrected Visual Acuity (BCVA) at Week 8 as Measured by the Early Treatment Diabetic Retinopathy Study (ETDRS) Letter Score |
| End point description: BCVA was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart. The BCVA letter score ranges from 0 to 100 (best score). A positive change indicates an improvement, and a negative change indicates worsening. The Intent-to-treat (ITT) set included all randomized subjects, irrespective of any deviation from the protocol or premature discontinuation. Here, "n" refers to subjects who were evaluable for this endpoint and for specified estimands. | |
| End point type | Primary |
| End point timeframe: Baseline and at Week 8 | |

| End point values | ALT-L9 | Eylea® | | |
|-------------------------------------|------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 216 | 215 | | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | | | | |
| Primary Estimand (n=216,215) | 5.771 (± 0.5821) | 7.863 (± 0.5888) | | |
| Secondary Estimand (n=216,215) | 6.272 (± 0.6240) | 7.972 (± 0.6248) | | |
| Tertiary Estimand (n=213,214) | 5.782 (± 0.5870) | 7.862 (± 0.5905) | | |

Statistical analyses

| | |
|----------------------------|-----------------------------------|
| Statistical analysis title | Primary Estimand: ALT-L9 vs Eylea |
| Comparison groups | ALT-L9 v Eylea® |

| | |
|-----------------------------------------|------------------------------|
| Number of subjects included in analysis | 431 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence ^[1] |
| Parameter estimate | Least-square Mean Difference |
| Point estimate | -2.092 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.431 |
| upper limit | -0.753 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.6834 |

Notes:

[1] - A predefined margin of ± 3.49 letters was used for analysis.

| | |
|-----------------------------------------|-------------------------------------|
| Statistical analysis title | Secondary Estimand: ALT-L9 vs Eylea |
| Comparison groups | ALT-L9 v Eylea® |
| Number of subjects included in analysis | 431 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence ^[2] |
| Parameter estimate | Least-square Mean Difference |
| Point estimate | -1.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.113 |
| upper limit | -0.287 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.7209 |

Notes:

[2] - A predefined margin of ± 3.49 letters was used for analysis.

| | |
|-----------------------------------------|------------------------------------|
| Statistical analysis title | Tertiary Estimand: ALT-L9 vs Eylea |
| Comparison groups | ALT-L9 v Eylea® |
| Number of subjects included in analysis | 431 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence ^[3] |
| Parameter estimate | Least-square Mean Difference |
| Point estimate | -2.079 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.425 |
| upper limit | -0.734 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.6846 |

Notes:

[3] - A predefined margin of ± 3.49 letters was used for analysis.

Secondary: Proportion of Subjects With a Loss of at Least 5, 10, or 15 Letters in

BCVA Letter Score in the Study Eye Over Time up to Week 52, Compared With Baseline, Using the ETDRS Protocol

| | |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Proportion of Subjects With a Loss of at Least 5, 10, or 15 Letters in BCVA Letter Score in the Study Eye Over Time up to Week 52, Compared With Baseline, Using the ETDRS Protocol |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

BCVA was measured on the ETDRS chart. The BCVA letter score ranges from 0 to 100 (best score). A positive change indicates an improvement, and a negative change indicates worsening. The ITT set included all randomized subjects, irrespective of any deviation from the protocol or premature discontinuation.

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

End point timeframe:

Baseline up to Week 52

| End point values | ALT-L9 | Eylea® | | |
|---------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 216 | 215 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Primary Estimand: ≥ 5 letters | 10.6 | 4.0 | | |
| Secondary Estimand: ≥ 5 letters | 8.1 | 3.7 | | |
| Tertiary Estimand: ≥ 5 letters | 10.3 | 4.0 | | |
| Primary Estimand: ≥ 10 letters | 6.4 | 2.0 | | |
| Secondary Estimand: ≥ 10 letters | 3.5 | 1.5 | | |
| Tertiary Estimand: ≥ 10 letters | 6.4 | 2.0 | | |
| Primary Estimand: ≥ 15 letters | 3.4 | 1.0 | | |
| Secondary Estimand: ≥ 15 letters | 2.0 | 0.6 | | |
| Tertiary Estimand: ≥ 15 letters | 3.4 | 1.0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Subjects With a Gain of at least 5, 10, or 15 Letters in BCVA Letter Score in the Study Eye Over Time up to Week 52, Compared With Baseline, Using the ETDRS Protocol

| | |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Proportion of Subjects With a Gain of at least 5, 10, or 15 Letters in BCVA Letter Score in the Study Eye Over Time up to Week 52, Compared With Baseline, Using the ETDRS Protocol |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

BCVA was measured on the ETDRS chart. The BCVA letter score ranges from 0 to 100 (best score). A positive change indicates an improvement, and a negative change indicates worsening. The ITT set included all randomized subjects, irrespective of any deviation from the protocol or premature discontinuation.

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

End point timeframe:

Baseline up to Week 52

| End point values | ALT-L9 | Eylea® | | |
|---------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 216 | 215 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Primary Estimand: ≥ 5 letters | 68.8 | 72.9 | | |
| Secondary Estimand: ≥ 5 letters | 71.0 | 74.2 | | |
| Tertiary Estimand: ≥ 5 letters | 69.6 | 73.1 | | |
| Primary Estimand: ≥ 10 letters | 41.5 | 44.6 | | |
| Secondary Estimand: ≥ 10 letters | 43.9 | 47.2 | | |
| Tertiary Estimand: ≥ 10 letters | 42.2 | 44.3 | | |
| Primary Estimand: ≥ 15 letters | 19.2 | 21.8 | | |
| Secondary Estimand: ≥ 15 letters | 21.5 | 25.0 | | |
| Tertiary Estimand: ≥ 15 letters | 19.6 | 21.4 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in BCVA Letter Score in The Study Eye Over Time up to Week 52 Using the ETDRS Protocol

| | |
|-----------------|-------------------------------------------------------------------------------------------------------------|
| End point title | Change From Baseline in BCVA Letter Score in The Study Eye Over Time up to Week 52 Using the ETDRS Protocol |
|-----------------|-------------------------------------------------------------------------------------------------------------|

End point description:

BCVA was measured on the ETDRS chart at a starting distance of 4 meters. The BCVA letter score ranges from 0 to 100 (best score). A positive change indicates an improvement, and a negative change indicates worsening. The ITT set included all randomized subjects, irrespective of any deviation from the protocol or premature discontinuation. Here, "n" refers to subjects who were evaluable for specified estimands.

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

End point timeframe:

Baseline up to Week 52

| End point values | ALT-L9 | Eylea® | | |
|-------------------------------------|-----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 216 | 215 | | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | | | | |
| Primary Estimand (n=216, 215) | 7.315 (\pm 0.7871) | 9.259 (\pm 0.8018) | | |
| Secondary Estimand (n=216, 215) | 8.171 (\pm 0.9405) | 9.551 (\pm 0.8940) | | |
| Tertiary Estimand (n=204, 201) | 7.415 (\pm 0.7872) | 9.228 (\pm 0.8014) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Subjects With Existing Intraretinal or Subretinal Fluid in the Study Eye Over Time up to Week 4 and Week 52, Compared With Baseline, as Measured by SD-OCT

| | |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Proportion of Subjects With Existing Intraretinal or Subretinal Fluid in the Study Eye Over Time up to Week 4 and Week 52, Compared With Baseline, as Measured by SD-OCT |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Existing intraretinal or subretinal fluid was measured in the study eye by SD-OCT. The ITT set included all randomized subjects, irrespective of any deviation from the protocol or premature discontinuation.

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

End point timeframe:

Up to Weeks 4 and 52

| End point values | ALT-L9 | Eylea® | | |
|-------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 216 | 215 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Week 4: Primary Estimand | 62.2 | 56.9 | | |
| Week 4: Secondary Estimand | 61.7 | 56.2 | | |
| Week 4: Tertiary Estimand | 62.1 | 56.8 | | |
| Week 52: Primary Estimand | 39.7 | 39.1 | | |
| Week 52: Secondary Estimand | 42.4 | 40.5 | | |
| Week 52: Tertiary Estimand | 38.2 | 37.5 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Central Subfield Thickness (CST) in the Study Eye Up to Week 4 and Week 52 as Measured by Spectral Domain-optical Coherence Tomography (SD-OCT)

| | |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Change From Baseline in Central Subfield Thickness (CST) in the Study Eye Up to Week 4 and Week 52 as Measured by Spectral Domain-optical Coherence Tomography (SD-OCT) |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

CST was measured in the study eye by SD-OCT. The ITT set included all randomized subjects, irrespective of any deviation from the protocol or premature discontinuation. Here, "n" refers to subjects

who were evaluable for specified estimands.

| | |
|--------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, up to Weeks 4 and 52 | |

| End point values | ALT-L9 | Eylea® | | |
|-----------------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 216 | 215 | | |
| Units: microns | | | | |
| least squares mean (standard error) | | | | |
| Week 4: Primary Estimand (n=216,215) | -100.485 (± 6.2919) | -93.569 (± 6.3687) | | |
| Week 4: Secondary Estimand (n=216,215) | -98.250 (± 6.7016) | -93.151 (± 6.8495) | | |
| Week 4: Tertiary Estimand (n=213,213) | -101.102 (± 6.2981) | -93.734 (± 6.3697) | | |
| Week 52: Primary Estimand (n=216,215) | -116.023 (± 7.4471) | -111.281 (± 7.5733) | | |
| Week 52: Secondary Estimand (n=216,215) | -113.450 (± 8.1122) | -111.471 (± 8.2944) | | |
| Week 52: Tertiary Estimand (n=203,195) | -119.154 (± 7.3191) | -108.528 (± 7.4820) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Treatment-related Treatment-emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs) for Systemic and Ocular Category

| | |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Number of Subjects with Treatment-related Treatment-emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs) for Systemic and Ocular Category |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

A treatment-related TEAEs and SAEs were clinical event with plausible time relationship to study drug administration, and that cannot be explained by concurrent disease or other drugs or chemicals. The SAF included all randomized subjects who receive at least 1 administration (full or partial) of the study drug.

| | |
|------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline up to Week 52 | |

| End point values | ALT-L9 | Eylea® | | |
|----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 216 | 215 | | |
| Units: subjects | | | | |
| Systemic Category: Related TEAEs | 0 | 2 | | |
| Systemic Category: Related SAEs | 0 | 2 | | |
| Ocular Category: Related TEAEs | 3 | 3 | | |
| Ocular Category: Related SAEs | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Total Size of the Active Choroidal Neovascularization (CNV) Area in the Study Eye Over Time up to Week 52, as Measured by Fluorescein Angiography (FA)

| | |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Change From Baseline in the Total Size of the Active Choroidal Neovascularization (CNV) Area in the Study Eye Over Time up to Week 52, as Measured by Fluorescein Angiography (FA) |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Active CNV leakage of the study eye was assessed with fluorescein angiography. The active CNV leakage was defined as result of >0 (mm²). ITT set included all randomized subjects, irrespective of any deviation from the protocol or premature discontinuation. Here, "n" refers to subjects who were evaluable for this endpoint and for specified estimands.

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

End point timeframe:

Baseline up to Week 52

| End point values | ALT-L9 | Eylea® | | |
|---------------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 216 | 215 | | |
| Units: square millimeter (mm ²) | | | | |
| least squares mean (standard error) | | | | |
| Primary Estimand (n=216,215) | -1.890 (± 0.4174) | -2.123 (± 0.4188) | | |
| Secondary Estimand (n=216,215) | -1.992 (± 0.5344) | -2.130 (± 0.5201) | | |
| Tertiary Estimand (n=199,194) | -1.857 (± 0.4205) | -2.100 (± 0.4242) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-emergent AEs (TEAEs) and Serious AEs (SAEs) for Systemic and Ocular Category

| | |
|-----------------|----------------------------------------------------------------------------------------------------------------|
| End point title | Number of Subjects With Treatment-emergent AEs (TEAEs) and Serious AEs (SAEs) for Systemic and Ocular Category |
|-----------------|----------------------------------------------------------------------------------------------------------------|

End point description:

A TEAE was defined as any event not present before the initiation of the study treatment or any event already present that worsens in either intensity or frequency following exposure to the treatments. An SAE is any untoward medical occurrence, in the view of either the investigator or Sponsor, that meets one or more of the following criteria: results in death, is life-threatening, results in inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect. The SAF included of all randomized subjects who receive at least 1 administration (full or partial) of the study drug.

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

End point timeframe:

Baseline up to Week 52

| End point values | ALT-L9 | Eylea® | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 216 | 215 | | |
| Units: subjects | | | | |
| Systemic Category: TEAEs | 116 | 112 | | |
| Systemic Category: SAEs | 25 | 25 | | |
| Ocular Category: TEAEs | 90 | 75 | | |
| Ocular Category: SAEs | 1 | 3 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Subjects With Active CNV Leakage in the Study Eye Over Time up to Week 52, Compared With Baseline, as Measured by FA

| | |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Proportion of Subjects With Active CNV Leakage in the Study Eye Over Time up to Week 52, Compared With Baseline, as Measured by FA |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Active CNV leakage of the study eye was assessed with fluorescein angiography. The active CNV leakage was defined as result of >0 (mm²). ITT set included all randomized subjects, irrespective of any deviation from the protocol or premature discontinuation.

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

End point timeframe:

Up to Week 52

| End point values | ALT-L9 | Eylea® | | |
|-------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 216 | 215 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Primary Estimand | 61.7 | 55.1 | | |
| Secodary Estimand | 64.4 | 56.6 | | |
| Tertiary Estimand | 62.3 | 54.9 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to Week 52

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 26.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------|
| Reporting group title | ALT-L9 |
|-----------------------|--------|

Reporting group description:

Subjects received single dose of ALT-L9 40 mg/mL (2 mg/50 mcL aflibercept), ophthalmic IVT injection, in study eye, once every 4 weeks, for up to Week 8 and once every 8 weeks up to Week 48.

| | |
|-----------------------|--------|
| Reporting group title | Eylea® |
|-----------------------|--------|

Reporting group description:

Subjects received single dose of Eylea® 40 mg/mL (2 mg/50 mcL aflibercept), ophthalmic IVT injection, in study eye, once every 4 weeks, for up to Week 8 and once every 8 weeks up to Week 48.

| Serious adverse events | ALT-L9 | Eylea® | |
|---------------------------------------------------------------------|-------------------|-------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 26 / 216 (12.04%) | 28 / 215 (13.02%) | |
| number of deaths (all causes) | 1 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Acute myeloid leukaemia | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bladder transitional cell carcinoma | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Follicular thyroid cancer | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Glioma | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Hormone-dependent prostate cancer | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung adenocarcinoma | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung cancer metastatic | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung neoplasm malignant | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophageal carcinoma | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Polycythaemia vera | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prostate cancer | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Salivary gland neoplasm | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Arteriosclerosis | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 1 / 215 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| 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 | | | |
| Cystocele | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Uterovaginal prolapse | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Anxiety disorder | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Accidental overdose | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Humerus fracture | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rib fracture | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arrhythmia | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocardial ischaemia | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Ischaemic stroke | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 3 / 215 (1.40%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Epilepsy | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhage intracranial | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intracranial aneurysm | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombotic cerebral infarction | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Trigeminal palsy | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood loss anaemia | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ear and labyrinth disorders | | | |
| Vertigo positional | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |
| Blindness | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Gastric ulcer haemorrhage | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ileus | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Inguinal hernia | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|--|
| Pancreatitis acute | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 1 / 215 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Pemphigoid | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Renal colic | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urethral stenosis | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (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 | | | |
| Osteoarthritis | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal stenosis | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| COVID-19 | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 2 / 216 (0.93%) | 0 / 215 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia aspiration | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelonephritis | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urethritis | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vulval abscess | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endophthalmitis | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 2 / 215 (0.93%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | ALT-L9 | Eylea® | |
|---------------------------------------------------------------------|--------------------|--------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 204 / 216 (94.44%) | 180 / 215 (83.72%) | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 2 / 216 (0.93%) | 0 / 215 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Salivary gland neoplasm | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Adenoma benign | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences (all) | 0 | 1 | |
| Bowen's disease | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Glioma | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Laryngeal cancer | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences (all) | 0 | 1 | |
| Metastases to bone | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences (all) | 0 | 1 | |
| Neoplasm | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Oesophageal carcinoma | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Polycythaemia vera | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Vascular disorders | | | |

| | | | |
|------------------------------------------------------|------------------|------------------|--|
| Hypertension | | | |
| subjects affected / exposed | 11 / 216 (5.09%) | 10 / 215 (4.65%) | |
| occurrences (all) | 13 | 11 | |
| Arteriosclerosis | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 1 / 215 (0.47%) | |
| occurrences (all) | 1 | 1 | |
| Blood pressure fluctuation | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 1 / 215 (0.47%) | |
| occurrences (all) | 1 | 1 | |
| Hot flush | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences (all) | 0 | 1 | |
| Hypertensive crisis | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences (all) | 0 | 1 | |
| Subclavian artery stenosis | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Thrombophlebitis | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Venous thrombosis limb | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| White coat hypertension | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 3 / 215 (1.40%) | |
| occurrences (all) | 1 | 3 | |
| Peripheral swelling | | | |
| subjects affected / exposed | 2 / 216 (0.93%) | 1 / 215 (0.47%) | |
| occurrences (all) | 2 | 1 | |
| Pyrexia | | | |

| | | | |
|------------------------------------------------------------------------------------------------------------------------------|----------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 2 / 216 (0.93%) 2 | 0 / 215 (0.00%) 0 | |
| Chest pain subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 1 / 215 (0.47%) 1 | |
| Hernia subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 1 / 215 (0.47%) 1 | |
| Immune system disorders Drug hypersensitivity subjects affected / exposed occurrences (all) | 2 / 216 (0.93%) 2 | 1 / 215 (0.47%) 1 | |
| Contrast media allergy subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 0 / 215 (0.00%) 0 | |
| Reproductive system and breast disorders Benign prostatic hyperplasia subjects affected / exposed occurrences (all) | 2 / 216 (0.93%) 2 | 1 / 215 (0.47%) 1 | |
| Uterine polyp subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 1 / 215 (0.47%) 1 | |
| Cystocele subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 0 / 215 (0.00%) 0 | |
| Endometrial hyperplasia subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 0 / 215 (0.00%) 0 | |
| Uterine prolapse subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 1 / 215 (0.47%) 1 | |
| Uterovaginal prolapse subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 1 / 215 (0.47%) 1 | |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|--------------------------------------|-----------------|-----------------|--|
| Cough | | | |
| subjects affected / exposed | 6 / 216 (2.78%) | 1 / 215 (0.47%) | |
| occurrences (all) | 6 | 1 | |
| Upper respiratory tract inflammation | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 2 / 215 (0.93%) | |
| occurrences (all) | 1 | 2 | |
| Rhinorrhoea | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 1 / 215 (0.47%) | |
| occurrences (all) | 1 | 1 | |
| Lung opacity | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences (all) | 0 | 1 | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Paranasal sinus inflammation | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Rhinitis allergic | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Psychiatric disorders | | | |
| Insomnia | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 3 / 215 (1.40%) | |
| occurrences (all) | 0 | 3 | |
| Anxiety | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Anxiety disorder | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Body dysmorphic disorder | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Delirium | | | |

| | | | |
|------------------------------------------------------------------------------------------------|----------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 0 / 215 (0.00%) 0 | |
| Depression subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 0 / 215 (0.00%) 0 | |
| Sleep disorder subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 0 / 215 (0.00%) 0 | |
| Product issues Device dislocation subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 0 / 215 (0.00%) 0 | |
| Investigations Blood pressure increased subjects affected / exposed occurrences (all) | 4 / 216 (1.85%) 4 | 1 / 215 (0.47%) 1 | |
| Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all) | 3 / 216 (1.39%) 3 | 1 / 215 (0.47%) 1 | |
| Blood triglycerides increased subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 3 / 215 (1.40%) 3 | |
| Blood urea increased subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 2 / 215 (0.93%) 2 | |
| Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 1 / 215 (0.47%) 1 | |
| Blood creatinine increased subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 1 / 215 (0.47%) 1 | |
| Blood glucose increased subjects affected / exposed occurrences (all) | 2 / 216 (0.93%) 2 | 0 / 215 (0.00%) 0 | |
| Alanine aminotransferase increased | | | |

| | | |
|---------------------------------------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Anti-thyroid antibody increased | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Blood alkaline phosphatase increased | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Blood creatine phosphokinase increased | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Blood glucose decreased | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Blood lactate dehydrogenase increased | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Blood phosphorus decreased | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Blood thyroid stimulating hormone increased | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Body temperature increased | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Fibrin D dimer increased | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Glomerular filtration rate decreased | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Influenza A virus test positive | | |

| | | | |
|----------------------------------------------------------------------------------------------|----------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 1 / 215 (0.47%) 1 | |
| Platelet count increased subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 1 / 215 (0.47%) 1 | |
| Ultrasound liver abnormal subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 0 / 215 (0.00%) 0 | |
| Vitamin B12 decreased subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 0 / 215 (0.00%) 0 | |
| Intraocular pressure increased subjects affected / exposed occurrences (all) | 4 / 216 (1.85%) 7 | 3 / 215 (1.40%) 5 | |
| Optical coherence tomography abnormal subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 0 / 215 (0.00%) 0 | |
| Injury, poisoning and procedural complications | | | |
| Fall subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 1 / 215 (0.47%) 1 | |
| Tooth fracture subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 2 / 215 (0.93%) 2 | |
| Rib fracture subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 2 | 0 / 215 (0.00%) 0 | |
| Bone contusion subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 1 / 215 (0.47%) 1 | |
| Contusion subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 1 / 215 (0.47%) 1 | |
| Hand fracture | | | |

| | | |
|-----------------------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Head injury | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Humerus fracture | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Limb injury | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Patella fracture | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Pelvic fracture | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Post-traumatic pain | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Skin wound | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Synovial rupture | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Ulna fracture | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Upper limb fracture | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Wrist fracture | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Corneal abrasion | | |

| | | | |
|------------------------------------------------------------------------------|----------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 0 / 215 (0.00%) 0 | |
| Craniofacial fracture subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 1 / 215 (0.47%) 1 | |
| Injury of conjunctiva subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 1 / 215 (0.47%) 1 | |
| Congenital, familial and genetic disorders | | | |
| Atrial septal defect subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 0 / 215 (0.00%) 0 | |
| Type IIa hyperlipidaemia subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 0 / 215 (0.00%) 0 | |
| Cardiac disorders | | | |
| Cardiac failure chronic subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 2 / 215 (0.93%) 2 | |
| Angina pectoris subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 2 / 215 (0.93%) 2 | |
| Arrhythmia subjects affected / exposed occurrences (all) | 2 / 216 (0.93%) 2 | 0 / 215 (0.00%) 0 | |
| Myocardial ischaemia subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 2 / 215 (0.93%) 2 | |
| Palpitations subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 1 / 215 (0.47%) 1 | |
| Atrial fibrillation subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 1 / 215 (0.47%) 1 | |
| Cardiac asthma | | | |

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|----------------------------------------------------------------------------------|----------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 1 / 215 (0.47%) 1 | |
| Chronic coronary syndrome subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 0 / 215 (0.00%) 0 | |
| Coronary artery disease subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 1 / 215 (0.47%) 1 | |
| Tricuspid valve incompetence subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 1 / 215 (0.47%) 1 | |
| Nervous system disorders | | | |
| Headache subjects affected / exposed occurrences (all) | 7 / 216 (3.24%) 8 | 4 / 215 (1.86%) 5 | |
| Intracranial aneurysm subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 1 / 215 (0.47%) 2 | |
| Lumbar radiculopathy subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 1 / 215 (0.47%) 2 | |
| Cognitive disorder subjects affected / exposed occurrences (all) | 2 / 216 (0.93%) 2 | 0 / 215 (0.00%) 0 | |
| Dizziness subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 1 / 215 (0.47%) 1 | |
| Memory impairment subjects affected / exposed occurrences (all) | 2 / 216 (0.93%) 2 | 0 / 215 (0.00%) 0 | |
| Polyneuropathy subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 2 / 215 (0.93%) 2 | |
| Trigeminal palsy subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 1 / 215 (0.47%) 2 | |

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|------------------------------------|-----------------|-----------------|
| Balance disorder | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Carotid artery stenosis | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Encephalomalacia | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Hypoaesthesia | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Loss of consciousness | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Lumbosacral radiculopathy | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Migraine | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Neuropathy peripheral | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Paresis | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Peripheral sensorimotor neuropathy | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Sciatica | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Spinal cord herniation | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |

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|------------------------------------------------------------------------------------|----------------------|----------------------|--|
| Thrombotic cerebral infarction subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 1 / 215 (0.47%) 1 | |
| Vascular dementia subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 0 / 215 (0.00%) 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia subjects affected / exposed occurrences (all) | 3 / 216 (1.39%) 3 | 0 / 215 (0.00%) 0 | |
| Blood loss anaemia subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 1 / 215 (0.47%) 1 | |
| Leukocytosis subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 0 / 215 (0.00%) 0 | |
| Leukopenia subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 0 / 215 (0.00%) 0 | |
| Ear and labyrinth disorders | | | |
| Vertigo subjects affected / exposed occurrences (all) | 2 / 216 (0.93%) 2 | 0 / 215 (0.00%) 0 | |
| Vertigo positional subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 2 / 215 (0.93%) 2 | |
| Cerumen impaction subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 1 / 215 (0.47%) 1 | |
| Ear pain subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 0 / 215 (0.00%) 0 | |
| Tinnitus subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 1 / 215 (0.47%) 1 | |
| Vestibular disorder | | | |

| | | | |
|----------------------------------------------|-------------------|------------------|--|
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Eye disorders | | | |
| Neovascular age-related macular degeneration | | | |
| subjects affected / exposed | 23 / 216 (10.65%) | 13 / 215 (6.05%) | |
| occurrences (all) | 24 | 13 | |
| Visual acuity reduced | | | |
| subjects affected / exposed | 12 / 216 (5.56%) | 10 / 215 (4.65%) | |
| occurrences (all) | 12 | 11 | |
| Cataract | | | |
| subjects affected / exposed | 8 / 216 (3.70%) | 4 / 215 (1.86%) | |
| occurrences (all) | 8 | 5 | |
| Subretinal fluid | | | |
| subjects affected / exposed | 6 / 216 (2.78%) | 4 / 215 (1.86%) | |
| occurrences (all) | 6 | 4 | |
| Conjunctival haemorrhage | | | |
| subjects affected / exposed | 2 / 216 (0.93%) | 6 / 215 (2.79%) | |
| occurrences (all) | 2 | 6 | |
| Posterior capsule opacification | | | |
| subjects affected / exposed | 3 / 216 (1.39%) | 5 / 215 (2.33%) | |
| occurrences (all) | 3 | 5 | |
| Vitreous floaters | | | |
| subjects affected / exposed | 4 / 216 (1.85%) | 3 / 215 (1.40%) | |
| occurrences (all) | 4 | 3 | |
| Retinal oedema | | | |
| subjects affected / exposed | 3 / 216 (1.39%) | 3 / 215 (1.40%) | |
| occurrences (all) | 3 | 3 | |
| Retinal pigment epithelial tear | | | |
| subjects affected / exposed | 3 / 216 (1.39%) | 3 / 215 (1.40%) | |
| occurrences (all) | 3 | 3 | |
| Macular fibrosis | | | |
| subjects affected / exposed | 2 / 216 (0.93%) | 3 / 215 (1.40%) | |
| occurrences (all) | 2 | 3 | |
| Retinal haemorrhage | | | |

| | | |
|------------------------------|-----------------|-----------------|
| subjects affected / exposed | 2 / 216 (0.93%) | 3 / 215 (1.40%) |
| occurrences (all) | 2 | 3 |
| Vitreous detachment | | |
| subjects affected / exposed | 3 / 216 (1.39%) | 2 / 215 (0.93%) |
| occurrences (all) | 3 | 2 |
| Macular degeneration | | |
| subjects affected / exposed | 3 / 216 (1.39%) | 1 / 215 (0.47%) |
| occurrences (all) | 3 | 1 |
| Visual impairment | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 3 / 215 (1.40%) |
| occurrences (all) | 1 | 3 |
| Eye pain | | |
| subjects affected / exposed | 3 / 216 (1.39%) | 0 / 215 (0.00%) |
| occurrences (all) | 4 | 0 |
| Cataract subcapsular | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 2 / 215 (0.93%) |
| occurrences (all) | 1 | 2 |
| Choroidal neovascularisation | | |
| subjects affected / exposed | 3 / 216 (1.39%) | 0 / 215 (0.00%) |
| occurrences (all) | 3 | 0 |
| Conjunctival hyperaemia | | |
| subjects affected / exposed | 2 / 216 (0.93%) | 1 / 215 (0.47%) |
| occurrences (all) | 2 | 1 |
| Cystoid macular oedema | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 2 / 215 (0.93%) |
| occurrences (all) | 1 | 2 |
| Eye irritation | | |
| subjects affected / exposed | 2 / 216 (0.93%) | 1 / 215 (0.47%) |
| occurrences (all) | 2 | 1 |
| Optic disc haemorrhage | | |
| subjects affected / exposed | 3 / 216 (1.39%) | 0 / 215 (0.00%) |
| occurrences (all) | 3 | 0 |
| Blepharitis | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 1 / 215 (0.47%) |
| occurrences (all) | 1 | 1 |
| Cataract cortical | | |

| | | |
|------------------------------------------|-----------------|-----------------|
| subjects affected / exposed | 2 / 216 (0.93%) | 0 / 215 (0.00%) |
| occurrences (all) | 2 | 0 |
| Chalazion | | |
| subjects affected / exposed | 2 / 216 (0.93%) | 0 / 215 (0.00%) |
| occurrences (all) | 2 | 0 |
| Corneal erosion | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 1 / 215 (0.47%) |
| occurrences (all) | 1 | 1 |
| Detachment of retinal pigment epithelium | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 1 / 215 (0.47%) |
| occurrences (all) | 1 | 1 |
| Lacrimation increased | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 1 / 215 (0.47%) |
| occurrences (all) | 1 | 1 |
| Retinal exudates | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 1 / 215 (0.47%) |
| occurrences (all) | 1 | 1 |
| Vision blurred | | |
| subjects affected / exposed | 2 / 216 (0.93%) | 0 / 215 (0.00%) |
| occurrences (all) | 2 | 0 |
| Vitreous haemorrhage | | |
| subjects affected / exposed | 2 / 216 (0.93%) | 0 / 215 (0.00%) |
| occurrences (all) | 2 | 0 |
| Age-related macular degeneration | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Anterior chamber cell | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Arteriosclerotic retinopathy | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Asthenopia | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |

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|--------------------------------------------------|-----------------|-----------------|
| Conjunctival suffusion | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Cornea verticillata | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Corneal oedema | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Corneal scar | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Dacryostenosis acquired | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Detachment of macular retinal pigment epithelium | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Diplopia | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Dry eye | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Epiretinal membrane | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Eye discharge | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Eye inflammation | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Eye pruritus | | |

| | | |
|--------------------------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Eyelid pain | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Foreign body sensation in eyes | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Macular hole | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Macular oedema | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Macular pseudohole | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Macular scar | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Metamorphopsia | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Optic disc traction syndrome | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Optic nerve sheath haemorrhage | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Photophobia | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Photopsia | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Punctate keratitis | | |

| | | | |
|------------------------------------------------------------------------------------|----------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 1 / 215 (0.47%) 1 | |
| Retinal cyst subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 0 / 215 (0.00%) 0 | |
| Retinal depigmentation subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 0 / 215 (0.00%) 0 | |
| Retinal detachment subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 1 / 215 (0.47%) 1 | |
| Retinal drusen subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 1 / 215 (0.47%) 1 | |
| Retinal pigment epitheliopathy subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 0 / 215 (0.00%) 0 | |
| Retinal vein occlusion subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 1 / 215 (0.47%) 1 | |
| Retinoschisis subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 1 / 215 (0.47%) 1 | |
| Subretinal fibrosis subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 1 / 215 (0.47%) 1 | |
| Visual field defect subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 0 / 215 (0.00%) 0 | |
| Gastrointestinal disorders | | | |
| Diarrhoea subjects affected / exposed occurrences (all) | 2 / 216 (0.93%) 2 | 3 / 215 (1.40%) 3 | |
| Abdominal pain subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 1 / 215 (0.47%) 1 | |

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|--------------------------------------------------------------------------------------|----------------------|----------------------|
| Abdominal pain upper subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 2 / 215 (0.93%) 2 |
| Constipation subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 1 / 215 (0.47%) 1 |
| Nausea subjects affected / exposed occurrences (all) | 2 / 216 (0.93%) 2 | 0 / 215 (0.00%) 0 |
| Abdominal discomfort subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 1 / 215 (0.47%) 1 |
| Dental caries subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 1 / 215 (0.47%) 1 |
| Diverticulum intestinal subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 0 / 215 (0.00%) 0 |
| Gastritis subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 1 / 215 (0.47%) 1 |
| Gastrointestinal disorder subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 0 / 215 (0.00%) 0 |
| Gastrooesophageal reflux disease subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 1 / 215 (0.47%) 1 |
| Haemorrhoids subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 1 / 215 (0.47%) 1 |
| Inguinal hernia subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 0 / 215 (0.00%) 0 |
| Noninfective gingivitis subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 1 / 215 (0.47%) 1 |

| | | | |
|-------------------------------------------------------------------------------|----------------------|----------------------|--|
| Oesophagitis subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 0 / 215 (0.00%) 0 | |
| Hepatobiliary disorders | | | |
| Cholelithiasis subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 2 / 215 (0.93%) 2 | |
| Cholecystitis chronic subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 0 / 215 (0.00%) 0 | |
| Cholestasis subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 1 / 215 (0.47%) 1 | |
| Gallbladder polyp subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 0 / 215 (0.00%) 0 | |
| Hepatic function abnormal subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 0 / 215 (0.00%) 0 | |
| Hepatic steatosis subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 0 / 215 (0.00%) 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Pruritus subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 2 / 215 (0.93%) 2 | |
| Rash subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 2 / 215 (0.93%) 2 | |
| Pemphigoid subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 1 / 215 (0.47%) 3 | |
| Actinic keratosis subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 2 | 0 / 215 (0.00%) 0 | |
| Dermatitis | | | |

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|-----------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences (all) | 0 | 1 | |
| Dermatitis allergic | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences (all) | 0 | 1 | |
| Eczema | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences (all) | 0 | 1 | |
| Pain of skin | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences (all) | 0 | 1 | |
| Rosacea | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Scab | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Skin ulcer | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Urticaria | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Petechiae | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences (all) | 0 | 1 | |
| Renal and urinary disorders | | | |
| Chronic kidney disease | | | |
| subjects affected / exposed | 2 / 216 (0.93%) | 1 / 215 (0.47%) | |
| occurrences (all) | 2 | 1 | |
| Renal cyst | | | |
| subjects affected / exposed | 2 / 216 (0.93%) | 0 / 215 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Renal failure | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 1 / 215 (0.47%) | |
| occurrences (all) | 1 | 1 | |

| | | |
|-----------------------------|-----------------|-----------------|
| Cystitis noninfective | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Haematuria | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Hypertensive nephropathy | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Leukocyturia | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Nephritis | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Nephrolithiasis | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Nephropathy | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Nephropathy toxic | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Renal impairment | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Stress urinary incontinence | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Urethral pain | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Urethral stenosis | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |

| | | | |
|--------------------------------------------------------------------------------|----------------------|----------------------|--|
| Urinary bladder herniation subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 0 / 215 (0.00%) 0 | |
| Urinary tract discomfort subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 0 / 215 (0.00%) 0 | |
| Endocrine disorders | | | |
| Hypothyroidism subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 1 / 215 (0.47%) 1 | |
| Hyperthyroidism subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 1 / 215 (0.47%) 2 | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain subjects affected / exposed occurrences (all) | 4 / 216 (1.85%) 6 | 5 / 215 (2.33%) 5 | |
| Osteoarthritis subjects affected / exposed occurrences (all) | 3 / 216 (1.39%) 3 | 2 / 215 (0.93%) 2 | |
| Pain in extremity subjects affected / exposed occurrences (all) | 3 / 216 (1.39%) 3 | 2 / 215 (0.93%) 2 | |
| Spinal osteoarthritis subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 4 / 215 (1.86%) 7 | |
| Spinal stenosis subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 3 | 2 / 215 (0.93%) 2 | |
| Arthralgia subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 2 / 215 (0.93%) 2 | |
| Muscle spasms subjects affected / exposed occurrences (all) | 1 / 216 (0.46%) 1 | 1 / 215 (0.47%) 1 | |
| Myalgia | | | |

| | | |
|------------------------------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 216 (0.46%) | 1 / 215 (0.47%) |
| occurrences (all) | 1 | 1 |
| Periarthritis | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 1 / 215 (0.47%) |
| occurrences (all) | 1 | 1 |
| Intervertebral disc protrusion | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 3 | 0 |
| Bone pain | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Greater trochanteric pain syndrome | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Intervertebral disc disorder | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Lumbar spinal stenosis | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Musculoskeletal stiffness | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Osteoporotic fracture | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Polymyalgia rheumatica | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Rotator cuff syndrome | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Sacral pain | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Spinal pain | | |

| | | | |
|-----------------------------------------|------------------|------------------|--|
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Spondylolisthesis | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences (all) | 0 | 1 | |
| Sympathetic posterior cervical syndrome | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Tendon disorder | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Tenosynovitis | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences (all) | 0 | 1 | |
| Vertebral foraminal stenosis | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences (all) | 0 | 1 | |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 11 / 216 (5.09%) | 21 / 215 (9.77%) | |
| occurrences (all) | 11 | 23 | |
| COVID-19 | | | |
| subjects affected / exposed | 11 / 216 (5.09%) | 3 / 215 (1.40%) | |
| occurrences (all) | 12 | 3 | |
| Influenza | | | |
| subjects affected / exposed | 2 / 216 (0.93%) | 4 / 215 (1.86%) | |
| occurrences (all) | 2 | 4 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 3 / 216 (1.39%) | 1 / 215 (0.47%) | |
| occurrences (all) | 5 | 1 | |
| Asymptomatic bacteriuria | | | |
| subjects affected / exposed | 2 / 216 (0.93%) | 2 / 215 (0.93%) | |
| occurrences (all) | 2 | 2 | |
| Cystitis | | | |

| | | |
|-----------------------------------|-----------------|-----------------|
| subjects affected / exposed | 2 / 216 (0.93%) | 2 / 215 (0.93%) |
| occurrences (all) | 2 | 2 |
| Upper respiratory tract infection | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 3 / 215 (1.40%) |
| occurrences (all) | 1 | 3 |
| Viral infection | | |
| subjects affected / exposed | 2 / 216 (0.93%) | 2 / 215 (0.93%) |
| occurrences (all) | 2 | 2 |
| Otitis externa | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 2 / 215 (0.93%) |
| occurrences (all) | 1 | 2 |
| Rhinitis | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 2 / 215 (0.93%) |
| occurrences (all) | 1 | 2 |
| Enteritis infectious | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 1 / 215 (0.47%) |
| occurrences (all) | 1 | 1 |
| Gastroenteritis viral | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 1 / 215 (0.47%) |
| occurrences (all) | 1 | 1 |
| Herpes zoster | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 1 / 215 (0.47%) |
| occurrences (all) | 1 | 1 |
| Otitis media | | |
| subjects affected / exposed | 2 / 216 (0.93%) | 0 / 215 (0.00%) |
| occurrences (all) | 2 | 0 |
| Sinusitis | | |
| subjects affected / exposed | 2 / 216 (0.93%) | 0 / 215 (0.00%) |
| occurrences (all) | 2 | 0 |
| Erysipelas | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 2 | 0 |
| Laryngitis | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 2 | 0 |
| Vulval abscess | | |

| | | |
|-----------------------------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 2 | 0 |
| Bronchitis | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Hepatitis C | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Lower respiratory tract infection | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Lyme disease | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Onychomycosis | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Periodontitis | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Pneumonia aspiration | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Pyelonephritis | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Skin infection | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) |
| occurrences (all) | 0 | 1 |
| Tonsillitis | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) |
| occurrences (all) | 1 | 0 |
| Conjunctivitis | | |
| subjects affected / exposed | 6 / 216 (2.78%) | 2 / 215 (0.93%) |
| occurrences (all) | 7 | 2 |
| Hordeolum | | |

| | | | |
|--------------------------------------------------|----------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 0 / 216 (0.00%) 0 | 2 / 215 (0.93%) 2 | |
| Metabolism and nutrition disorders | | | |
| Hypercholesterolaemia | | | |
| subjects affected / exposed | 2 / 216 (0.93%) | 5 / 215 (2.33%) | |
| occurrences (all) | 2 | 5 | |
| Hypertriglyceridaemia | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 4 / 215 (1.86%) | |
| occurrences (all) | 1 | 4 | |
| Diabetes mellitus | | | |
| subjects affected / exposed | 2 / 216 (0.93%) | 1 / 215 (0.47%) | |
| occurrences (all) | 2 | 1 | |
| Dyslipidaemia | | | |
| subjects affected / exposed | 2 / 216 (0.93%) | 1 / 215 (0.47%) | |
| occurrences (all) | 2 | 1 | |
| Hypophosphataemia | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 2 / 215 (0.93%) | |
| occurrences (all) | 0 | 3 | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 2 / 216 (0.93%) | 0 / 215 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Hyperuricaemia | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 1 / 215 (0.47%) | |
| occurrences (all) | 1 | 1 | |
| Glucose tolerance impaired | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences (all) | 0 | 1 | |
| Gout | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences (all) | 0 | 1 | |
| Hyperlipidaemia | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences (all) | 0 | 1 | |

| | | | |
|-----------------------------|-----------------|-----------------|--|
| Hyponatraemia | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Insulin resistance | | | |
| subjects affected / exposed | 0 / 216 (0.00%) | 1 / 215 (0.47%) | |
| occurrences (all) | 0 | 1 | |
| Iron deficiency | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Lipid metabolism disorder | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Type 2 diabetes mellitus | | | |
| subjects affected / exposed | 1 / 216 (0.46%) | 0 / 215 (0.00%) | |
| occurrences (all) | 1 | 0 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 28 September 2022 | Protocol Amendment 1: The primary change of this amendment is the removal of re-randomization at Week 32, which led to adjustments in the sample size and schedule of assessments. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported