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 [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.	

Reporting group values	ALT-L9	Eylea®	Total
Number of subjects	216	215	431
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	74.4	73.9	
standard deviation	± 7.83	± 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 (± 0.7871)	9.259 (± 0.8018)		
Secondary Estimand (n=216, 215)	8.171 (± 0.9405)	9.551 (± 0.8940)		
Tertiary Estimand (n=204, 201)	7.415 (± 0.7872)	9.228 (± 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 (mm^2). 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 (mm^2). 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	2 / 216 (0.93%)	0 / 215 (0.00%)	
occurrences (all)	2	0	
Chest pain			
subjects affected / exposed	0 / 216 (0.00%)	1 / 215 (0.47%)	
occurrences (all)	0	1	
Hernia			
subjects affected / exposed	0 / 216 (0.00%)	1 / 215 (0.47%)	
occurrences (all)	0	1	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	2 / 216 (0.93%)	1 / 215 (0.47%)	
occurrences (all)	2	1	
Contrast media allergy			
subjects affected / exposed	1 / 216 (0.46%)	0 / 215 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	2 / 216 (0.93%)	1 / 215 (0.47%)	
occurrences (all)	2	1	
Uterine polyp			
subjects affected / exposed	1 / 216 (0.46%)	1 / 215 (0.47%)	
occurrences (all)	1	1	
Cystocele			
subjects affected / exposed	1 / 216 (0.46%)	0 / 215 (0.00%)	
occurrences (all)	1	0	
Endometrial hyperplasia			
subjects affected / exposed	1 / 216 (0.46%)	0 / 215 (0.00%)	
occurrences (all)	1	0	
Uterine prolapse			
subjects affected / exposed	0 / 216 (0.00%)	1 / 215 (0.47%)	
occurrences (all)	0	1	
Uterovaginal prolapse			
subjects affected / exposed	0 / 216 (0.00%)	1 / 215 (0.47%)	
occurrences (all)	0	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	1 / 216 (0.46%)	0 / 215 (0.00%)	
occurrences (all)	1	0	
Depression			
subjects affected / exposed	1 / 216 (0.46%)	0 / 215 (0.00%)	
occurrences (all)	1	0	
Sleep disorder			
subjects affected / exposed	1 / 216 (0.46%)	0 / 215 (0.00%)	
occurrences (all)	1	0	
Product issues			
Device dislocation			
subjects affected / exposed	1 / 216 (0.46%)	0 / 215 (0.00%)	
occurrences (all)	1	0	
Investigations			
Blood pressure increased			
subjects affected / exposed	4 / 216 (1.85%)	1 / 215 (0.47%)	
occurrences (all)	4	1	
Gamma-glutamyltransferase increased			
subjects affected / exposed	3 / 216 (1.39%)	1 / 215 (0.47%)	
occurrences (all)	3	1	
Blood triglycerides increased			
subjects affected / exposed	0 / 216 (0.00%)	3 / 215 (1.40%)	
occurrences (all)	0	3	
Blood urea increased			
subjects affected / exposed	1 / 216 (0.46%)	2 / 215 (0.93%)	
occurrences (all)	1	2	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 216 (0.46%)	1 / 215 (0.47%)	
occurrences (all)	1	1	
Blood creatinine increased			
subjects affected / exposed	1 / 216 (0.46%)	1 / 215 (0.47%)	
occurrences (all)	1	1	
Blood glucose increased			
subjects affected / exposed	2 / 216 (0.93%)	0 / 215 (0.00%)	
occurrences (all)	2	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	0 / 216 (0.00%)	1 / 215 (0.47%)	
occurrences (all)	0	1	
Platelet count increased			
subjects affected / exposed	0 / 216 (0.00%)	1 / 215 (0.47%)	
occurrences (all)	0	1	
Ultrasound liver abnormal			
subjects affected / exposed	1 / 216 (0.46%)	0 / 215 (0.00%)	
occurrences (all)	1	0	
Vitamin B12 decreased			
subjects affected / exposed	1 / 216 (0.46%)	0 / 215 (0.00%)	
occurrences (all)	1	0	
Intraocular pressure increased			
subjects affected / exposed	4 / 216 (1.85%)	3 / 215 (1.40%)	
occurrences (all)	7	5	
Optical coherence tomography abnormal			
subjects affected / exposed	1 / 216 (0.46%)	0 / 215 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 216 (0.46%)	1 / 215 (0.47%)	
occurrences (all)	1	1	
Tooth fracture			
subjects affected / exposed	0 / 216 (0.00%)	2 / 215 (0.93%)	
occurrences (all)	0	2	
Rib fracture			
subjects affected / exposed	1 / 216 (0.46%)	0 / 215 (0.00%)	
occurrences (all)	2	0	
Bone contusion			
subjects affected / exposed	0 / 216 (0.00%)	1 / 215 (0.47%)	
occurrences (all)	0	1	
Contusion			
subjects affected / exposed	0 / 216 (0.00%)	1 / 215 (0.47%)	
occurrences (all)	0	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	1 / 216 (0.46%)	0 / 215 (0.00%)	
occurrences (all)	1	0	
Craniofacial fracture			
subjects affected / exposed	1 / 216 (0.46%)	1 / 215 (0.47%)	
occurrences (all)	1	1	
Injury of conjunctiva			
subjects affected / exposed	0 / 216 (0.00%)	1 / 215 (0.47%)	
occurrences (all)	0	1	
Congenital, familial and genetic disorders			
Atrial septal defect			
subjects affected / exposed	1 / 216 (0.46%)	0 / 215 (0.00%)	
occurrences (all)	1	0	
Type IIa hyperlipidaemia			
subjects affected / exposed	1 / 216 (0.46%)	0 / 215 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Cardiac failure chronic			
subjects affected / exposed	1 / 216 (0.46%)	2 / 215 (0.93%)	
occurrences (all)	1	2	
Angina pectoris			
subjects affected / exposed	0 / 216 (0.00%)	2 / 215 (0.93%)	
occurrences (all)	0	2	
Arrhythmia			
subjects affected / exposed	2 / 216 (0.93%)	0 / 215 (0.00%)	
occurrences (all)	2	0	
Myocardial ischaemia			
subjects affected / exposed	0 / 216 (0.00%)	2 / 215 (0.93%)	
occurrences (all)	0	2	
Palpitations			
subjects affected / exposed	1 / 216 (0.46%)	1 / 215 (0.47%)	
occurrences (all)	1	1	
Atrial fibrillation			
subjects affected / exposed	0 / 216 (0.00%)	1 / 215 (0.47%)	
occurrences (all)	0	1	
Cardiac asthma			

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

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	

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

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

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

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

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