



Clinical trial results:

A Phase III, Multicenter, Randomised, Double-Masked, Sham-Controlled Study to Assess the Efficacy and Safety of Lampalizumab Administered Intravitreally to Patients with Geographic Atrophy Secondary to Age-Related Macular Degeneration

Summary

EudraCT number	2014-000107-27
Trial protocol	HU DE IT AT DK GB PL NL SK ES BE FR
Global end of trial date	29 January 2018

Results information

Result version number	v1 (current)
This version publication date	07 February 2019
First version publication date	07 February 2019

Trial information

Trial identification

Sponsor protocol code	GX29176
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02247479
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.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	29 January 2018
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	29 January 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to evaluate the efficacy of intravitreal injections of 10-mg lampalizumab administered every 4 weeks (Q4W) or every 6 weeks (Q6W) in complement factor I (CFI)-profile biomarker-positive and CFI-profile biomarker-negative subjects with sham control.

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 September 2014
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	United States: 588
Country: Number of subjects enrolled	Canada: 17
Country: Number of subjects enrolled	Germany: 61
Country: Number of subjects enrolled	Spain: 35
Country: Number of subjects enrolled	France: 31
Country: Number of subjects enrolled	Italy: 17
Country: Number of subjects enrolled	Switzerland: 16
Country: Number of subjects enrolled	Austria: 8
Country: Number of subjects enrolled	Denmark: 5
Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	Netherlands: 2
Country: Number of subjects enrolled	Poland: 35
Country: Number of subjects enrolled	Slovakia: 20
Country: Number of subjects enrolled	Hungary: 12
Country: Number of subjects enrolled	Argentina: 15
Country: Number of subjects enrolled	Mexico: 13
Country: Number of subjects enrolled	Peru: 3
Country: Number of subjects enrolled	Australia: 22
Worldwide total number of subjects	906
EEA total number of subjects	232

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)	52
From 65 to 84 years	634
85 years and over	220

Subject disposition

Recruitment

Recruitment details:

A total of 906 subjects were randomised to the study from 131 investigational sites across 19 countries. The study was terminated early by the Sponsor due to lack of efficacy.

Pre-assignment

Screening details:

This study enrolled subjects with bilateral Geographic Atrophy (GA) secondary to Age-Related Macular Degeneration (AMD) and no signs of prior or active choroidal neovascularisation (CNV), age \geq 50 years with a valid complement factor I (CFI)-profile biomarker result.

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, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Sham Comparator

Arm description:

Subjects received sham comparator Q4W (once in every 4 weeks) or Q6W (once in every 6 weeks) starting at the Day 1 visit.

Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	Lampalizumab Q4W

Arm description:

Subjects received 10 milligrams (mg) dose of lampalizumab administered by intravitreal injections Q4W starting at the Day 1 visit.

Arm type	Experimental
Investigational medicinal product name	Lampalizumab
Investigational medicinal product code	RO5490249
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

Lampalizumab was administered at a dose of 10 milligrams (mg) as an intravitreal injection, starting at the Day 1 visit, Q4W, for a total of 24 injections.

Arm title	Lampalizumab Q6W
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Arm description:

Subjects received 10 mg dose of lampalizumab administered by intravitreal injections Q6W starting at the Day 1 visit.

Arm type	Experimental
Investigational medicinal product name	Lampalizumab
Investigational medicinal product code	RO5490249
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

Lampalizumab was administered at a dose of 10 mg as an intravitreal injection, starting at the Day 1 visit, Q6W, for a total of 16 injections.

Number of subjects in period 1	Sham Comparator	Lampalizumab Q4W	Lampalizumab Q6W
Started	305	298	303
Completed	163	160	165
Not completed	142	138	138
Unspecified Reason	2	5	2
Physician decision	1	-	2
Adverse Event	8	9	8
Death	5	4	6
Non-compliance	-	-	1
Withdrawal by Subject	25	29	24
Study Terminated by Sponsor	98	88	94
Lost to follow-up	3	3	1

Baseline characteristics

Reporting groups

Reporting group title	Sham Comparator
Reporting group description: Subjects received sham comparator Q4W (once in every 4 weeks) or Q6W (once in every 6 weeks) starting at the Day 1 visit.	
Reporting group title	Lampalizumab Q4W
Reporting group description: Subjects received 10 milligrams (mg) dose of lampalizumab administered by intravitreal injections Q4W starting at the Day 1 visit.	
Reporting group title	Lampalizumab Q6W
Reporting group description: Subjects received 10 mg dose of lampalizumab administered by intravitreal injections Q6W starting at the Day 1 visit.	

Reporting group values	Sham Comparator	Lampalizumab Q4W	Lampalizumab Q6W
Number of subjects	305	298	303
Age categorical			
Units: Subjects			

Age Continuous			
Units: years			
arithmetic mean	78.5	77.5	78.3
standard deviation	± 7.8	± 7.9	± 8.5
Sex: Female, Male			
Units: Subjects			
Female	186	182	185
Male	119	116	118
Geographic Atrophy (GA) Area, as Assessed by Fundus Autofluorescence (FAF)			
At baseline the area of GA was assessed by FAF. Intent-to-treat (ITT) population included all the subjects who were randomized to the study. Overall number of baseline subjects for GA area in the reporting groups; Sham Comparator, Lampalizumab Q4W, and Lampalizumab Q6W were 305, 298, and 302, respectively.			
Units: millimetre square (mm ²)			
arithmetic mean	7.953	7.910	8.116
standard deviation	± 3.925	± 3.887	± 4.236
Number of Absolute Scotomatous Points as Assessed by Mesopic Micrometry			
Scotomatous points were testing points on microperimetry examination that were centred on macula and reported a lack of retinal sensitivity within the range tested. The microperimetry analysis population consisted of all subjects who met microperimetry eligibility criteria assessed by reading centre. Overall number of baseline subjects for number of scotomatous points in the reporting groups; Sham Comparator, Lampalizumab Q4W, and Lampalizumab Q6W were 44, 33, and 39, respectively.			
Units: number of absolute scotomatous points			
arithmetic mean	29.1	25.2	20.5
standard deviation	± 16.8	± 13.4	± 13.4
Macular Sensitivity as Assessed by Mesopic Microperimetry			
Mesopic microperimetry was used to assess macular sensitivity. The microperimetry analysis population consisted of all subjects who met the microperimetry eligibility criteria assessed by the reading centre.			

Overall number of baseline subjects for macular sensitivity in the reporting groups; Sham Comparator, Lampalizumab Q4W, and Lampalizumab Q6W were 44, 33, and 39, respectively.			
Units: decibel (dB)			
arithmetic mean	5.40	6.37	7.38
standard deviation	± 3.37	± 4.02	± 3.40
Best Corrected Visual Acuity (BCVA) Score as Assessed by Early Treatment Diabetic Retinopathy Study			
BCVA score was based on number of letters read correctly on ETDRS visual acuity chart assessed at starting distance of 4 metres. BCVA score testing was performed prior to dilating the eyes. BCVA score ranges from 0 to 100 letters in the study eye. The lower the number of letters read correctly on the eye chart, the worse the vision (or visual acuity). ITT population included all the subjects who were randomized to the study. Overall number of baseline subjects for BCVA score in the reporting groups; Sham Comparator, Lampalizumab Q4W, and Lampalizumab Q6W were 301, 295, and 301, respectively.			
Units: letters			
arithmetic mean	65.9	66.1	66.4
standard deviation	± 9.9	± 10.0	± 10.1
Low Luminance Visual Acuity (LLVA) as Assessed by ETDRS Chart Under Low Luminance Conditions			
The low luminance visual acuity was measured by placing a 2.0-log-unit neutral density filter over the best correction for that eye and having the subject read the normally illuminated ETDRS chart. The assessment was performed prior to dilating the eyes. ITT population included all the subjects who were randomized to the study. Overall number of baseline subjects for LLVA score in the reporting groups; Sham Comparator, Lampalizumab Q4W, and Lampalizumab Q6W were 299, 287, and 293, respectively.			
Units: letters			
arithmetic mean	36.0	36.9	36.2
standard deviation	± 15.7	± 17.8	± 16.7
Binocular Reading Speed as Assessed by Minnesota Low-Vision Reading Test or Radner Reading Charts			
MNRead acuity cards were suitable for measuring reading speed of normal and low-vision subjects. Sentences that could not be read should be recorded as 0 for time and 10 for errors. Radner Reading Cards were suitable for measuring reading speed, visual acuity, and critical print size. Test stopped when reading time was longer than 20 seconds. ITT population included all subjects who were randomized to the study. Overall number of baseline subjects for binocular reading speed in the reporting groups; Sham Comparator, Lampalizumab Q4W, and Lampalizumab Q6W were 278, 262, and 269, respectively.			
Units: words per minute (wpm)			
arithmetic mean	106.89	109.18	104.22
standard deviation	± 57.98	± 60.14	± 62.37
National Eye Institute Visual Functioning Questionnaire 25-item (NEI VFQ-25) Version Composite Score			
It included 25 items based on which overall composite VFQ score and 12 subscales (general vision, near vision, distance vision, ocular pain, social functioning, mental health, roll difficulties, dependency, driving, color vision and peripheral vision) were derived. For each subscale and total score, score range is 0 to 100, higher score represents better functioning. ITT population included all subjects who were randomized to study. Overall number of baseline subjects for NEI-VFQ-25 score in reporting groups; Sham Comparator, Lampalizumab Q4W, and Lampalizumab Q6W were 276, 275, and			
Units: score on a scale			
arithmetic mean	66.16	64.80	65.19
standard deviation	± 17.33	± 16.12	± 17.27
Mean Functional Reading Independence (FRI) Index			
FRI was an interviewer-administered questionnaire with 7 items on functional reading activities most relevant to GA AMD subjects. It has one total index score. For each reading activity performed in the past 7 days, subjects were asked about the extent to which they required vision aids, adjustments in activity, or help from another subject. ITT population included all subjects who were randomized to the study. Overall number of baseline subjects for FRI index in the reporting groups; Sham Comparator, Lampalizumab Q4W, and Lampalizumab Q6W were 276, 273, and 282, respectively.			
Units: scores on a scale			

arithmetic mean	2.69	2.71	2.70
standard deviation	± 0.83	± 0.79	± 0.82
NEI VFQ-25 Near Activity Subscale Score			
NEI-VFQ-25 questionnaire included 25 items based on which near activities were measured. Near activities are defined as reading ordinary print in newspapers, performing work requiring near vision, or finding something on crowded shelf. Response to each question converted to 0-100 score. Higher score represents better functioning. ITT population included all subjects who were randomized to study. Overall number of baseline subjects for NEI VFQ-25 near activity subscale score in reporting groups; Sham Comparator, Lampalizumab Q4W, and Lampalizumab Q6W were 276, 275, and 282, respectively.			
Units: score on a scale			
arithmetic mean	54.98	53.78	53.67
standard deviation	± 20.98	± 20.56	± 22.21
NEI VFQ-25 Distance Activity Subscale Score			
NEI-VFQ-25 questionnaire included 25 items based on which distance activities was measured. Distance activities are defined as reading street signs or names on stores, and going down stairs, steps, or curbs. Response to each question converted to 0-100 score. A higher score represents better functioning. ITT population included all subjects who were randomized to the study. Overall number of baseline subjects for NEI VFQ-25 distance activity subscale score in the reporting groups; Sham Comparator, Lampalizumab Q4W, and Lampalizumab Q6W were 276, 275, and 282, respectively.			
Units: score on a scale			
arithmetic mean	62.86	60.97	62.10
standard deviation	± 21.46	± 20.48	± 22.16
Monocular Maximum Reading Speed as Assessed by MNRead Charts or Radner Reading Charts			
MNRead acuity cards were suitable for measuring reading speed of normal and low-vision subjects. Sentences that could not be read should be recorded as 0 for time and 10 for errors. Radner Reading Cards were suitable for measuring reading speed, visual acuity, and critical print size. Test stopped when reading time was longer than 20 seconds. ITT population included all subjects who were randomized to the study. Overall number of baseline subjects for monocular reading speed in the reporting groups; Sham Comparator, Lampalizumab Q4W, and Lampalizumab Q6W were 278, 265, and 271, respectively.			
Units: wpm			
arithmetic mean	80.89	85.18	79.49
standard deviation	± 52.95	± 54.55	± 54.23
GA Area in Complement Factor I (CFI) Positive Subjects			
For CFI profile, positive biomarker status refers to the presence (carrier) of the risk allele at CFI and at least one risk allele at complement factor H (CFH) or risk locus containing both complement component 2 and complement factor B (C2/CFB). ITT population included all subjects who were randomized to study. Overall number of baseline CFI positive subjects for GA area in reporting groups; Sham Comparator, Lampalizumab Q4W, and Lampalizumab Q6W were 181, 176, and 177, respectively.			
Units: mm ²			
arithmetic mean	8.015	8.152	8.406
standard deviation	± 3.915	± 4.118	± 4.399
GA Area in CFI Negative Subjects			
For CFI profile, negative biomarker status refers to the absence of the risk allele at CFI and at least one risk allele at CFH or risk locus containing both C2/CFB. ITT population included all subjects who were randomized to study. Overall number of baseline CFI negative subjects for GA area in reporting groups; Sham Comparator, Lampalizumab Q4W, and Lampalizumab Q6W were 124, 122, and 125, respectively.			
Units: mm ²			
arithmetic mean	7.864	7.560	7.705
standard deviation	± 3.952	± 3.515	± 3.975
Reporting group values	Total		
Number of subjects	906		

Age categorical Units: Subjects			
Age Continuous Units: years arithmetic mean standard deviation	-		
Sex: Female, Male Units: Subjects			
Female	553		
Male	353		
Geographic Atrophy (GA) Area, as Assessed by Fundus Autofluorescence (FAF)			
At baseline the area of GA was assessed by FAF. Intent-to-treat (ITT) population included all the subjects who were randomized to the study. Overall number of baseline subjects for GA area in the reporting groups; Sham Comparator, Lampalizumab Q4W, and Lampalizumab Q6W were 305, 298, and 302, respectively.			
Units: millimetre square (mm ²) arithmetic mean standard deviation	-		
Number of Absolute Scotomatous Points as Assessed by Mesopic Micrometry			
Scotomatous points were testing points on microperimetry examination that were centred on macula and reported a lack of retinal sensitivity within the range tested. The microperimetry analysis population consisted of all subjects who met microperimetry eligibility criteria assessed by reading centre. Overall number of baseline subjects for number of scotomatous points in the reporting groups; Sham Comparator, Lampalizumab Q4W, and Lampalizumab Q6W were 44, 33, and 39, respectively.			
Units: number of absolute scotomatous points arithmetic mean standard deviation	-		
Macular Sensitivity as Assessed by Mesopic Microperimetry			
Mesopic microperimetry was used to assess macular sensitivity. The microperimetry analysis population consisted of all subjects who met the microperimetry eligibility criteria assessed by the reading centre. Overall number of baseline subjects for macular sensitivity in the reporting groups; Sham Comparator, Lampalizumab Q4W, and Lampalizumab Q6W were 44, 33, and 39, respectively.			
Units: decibel (dB) arithmetic mean standard deviation	-		
Best Corrected Visual Acuity (BCVA) Score as Assessed by Early Treatment Diabetic Retinopathy Study			
BCVA score was based on number of letters read correctly on ETDRS visual acuity chart assessed at starting distance of 4 metres. BCVA score testing was performed prior to dilating the eyes. BCVA score ranges from 0 to 100 letters in the study eye. The lower the number of letters read correctly on the eye chart, the worse the vision (or visual acuity). ITT population included all the subjects who were randomized to the study. Overall number of baseline subjects for BCVA score in the reporting groups; Sham Comparator, Lampalizumab Q4W, and Lampalizumab Q6W were 301, 295, and 301, respectively.			
Units: letters arithmetic mean standard deviation	-		
Low Luminance Visual Acuity (LLVA) as Assessed by ETDRS Chart Under Low Luminance Conditions			
The low luminance visual acuity was measured by placing a 2.0-log-unit neutral density filter over the best correction for that eye and having the subject read the normally illuminated ETDRS chart. The assessment was performed prior to dilating the eyes. ITT population included all the subjects who were			

randomized to the study. Overall number of baseline subjects for LLVA score in the reporting groups; Sham Comparator, Lampalizumab Q4W, and Lampalizumab Q6W were 299, 287, and 293, respectively.			
Units: letters arithmetic mean standard deviation		-	
Binocular Reading Speed as Assessed by Minnesota Low-Vision Reading Test or Radner Reading Charts			
MNRead acuity cards were suitable for measuring reading speed of normal and low-vision subjects. Sentences that could not be read should be recorded as 0 for time and 10 for errors. Radner Reading Cards were suitable for measuring reading speed, visual acuity, and critical print size. Test stopped when reading time was longer than 20 seconds. ITT population included all subjects who were randomized to the study. Overall number of baseline subjects for binocular reading speed in the reporting groups; Sham Comparator, Lampalizumab Q4W, and Lampalizumab Q6W were 278, 262, and 269, respectively.			
Units: words per minute (wpm) arithmetic mean standard deviation		-	
National Eye Institute Visual Functioning Questionnaire 25-item (NEI VFQ-25) Version Composite Score			
It included 25 items based on which overall composite VFQ score and 12 subscales (general vision,near vision,distance vision,ocular pain,social functioning,mental health,roll difficulties,dependency,driving,color vision and peripheral vision) were derived. For each subscale and total score, score range is 0 to 100, higher score represents better functioning. ITT population included all subjects who were randomized to study. Overall number of baseline subjects for NEI-VFQ-25 score in reporting groups; Sham Comparator, Lampalizumab Q4W, and Lampalizumab Q6W were 276, 275, and			
Units: score on a scale arithmetic mean standard deviation		-	
Mean Functional Reading Independence (FRI) Index			
FRI was an interviewer-administered questionnaire with 7 items on functional reading activities most relevant to GA AMD subjects. It has one total index score. For each reading activity performed in the past 7 days, subjects were asked about the extent to which they required vision aids, adjustments in activity, or help from another subject. ITT population included all subjects who were randomized to the study. Overall number of baseline subjects for FRI index in the reporting groups; Sham Comparator, Lampalizumab Q4W, and Lampalizumab Q6W were 276, 273, and 282, respectively.			
Units: scores on a scale arithmetic mean standard deviation		-	
NEI VFQ-25 Near Activity Subscale Score			
NEI-VFQ-25 questionnaire included 25 items based on which near activities were measured. Near activities are defined as reading ordinary print in newspapers, performing work requiring near vision, or finding something on crowded shelf. Response to each question converted to 0-100 score. Higher score represents better functioning. ITT population included all subjects who were randomized to study. Overall number of baseline subjects for NEI VFQ-25 near activity subscale score in reporting groups; Sham Comparator, Lampalizumab Q4W, and Lampalizumab Q6W were 276, 275, and 282, respectively.			
Units: score on a scale arithmetic mean standard deviation		-	
NEI VFQ-25 Distance Activity Subscale Score			
NEI-VFQ-25 questionnaire included 25 items based on which distance activities was measured. Distance activities are defined as reading street signs or names on stores, and going down stairs, steps, or curbs. Response to each question converted to 0-100 score. A higher score represents better functioning. ITT population included all subjects who were randomized to the study. Overall number of baseline subjects for NEI VFQ-25 distance activity subscale score in the reporting groups; Sham Comparator, Lampalizumab Q4W, and Lampalizumab Q6W were 276, 275, and 282, respectively.			
Units: score on a scale			

arithmetic mean			
standard deviation	-		
Monocular Maximum Reading Speed as Assessed by MNRead Charts or Radner Reading Charts			
MNRead acuity cards were suitable for measuring reading speed of normal and low-vision subjects. Sentences that could not be read should be recorded as 0 for time and 10 for errors. Radner Reading Cards were suitable for measuring reading speed, visual acuity, and critical print size. Test stopped when reading time was longer than 20 seconds. ITT population included all subjects who were randomized to the study. Overall number of baseline subjects for monocular reading speed in the reporting groups; Sham Comparator, Lampalizumab Q4W, and Lampalizumab Q6W were 278, 265, and 271, respectively.			
Units: wpm			
arithmetic mean			
standard deviation	-		
GA Area in Complement Factor I (CFI) Positive Subjects			
For CFI profile, positive biomarker status refers to the presence (carrier) of the risk allele at CFI and at least one risk allele at complement factor H (CFH) or risk locus containing both complement component 2 and complement factor B (C2/CFB). ITT population included all subjects who were randomized to study. Overall number of baseline CFI positive subjects for GA area in reporting groups; Sham Comparator, Lampalizumab Q4W, and Lampalizumab Q6W were 181, 176, and 177, respectively.			
Units: mm ²			
arithmetic mean			
standard deviation	-		
GA Area in CFI Negative Subjects			
For CFI profile, negative biomarker status refers to the absence of the risk allele at CFI and at least one risk allele at CFH or risk locus containing both C2/CFB. ITT population included all subjects who were randomized to study. Overall number of baseline CFI negative subjects for GA area in reporting groups; Sham Comparator, Lampalizumab Q4W, and Lampalizumab Q6W were 124, 122, and 125, respectively.			
Units: mm ²			
arithmetic mean			
standard deviation	-		

End points

End points reporting groups

Reporting group title	Sham Comparator
Reporting group description: Subjects received sham comparator Q4W (once in every 4 weeks) or Q6W (once in every 6 weeks) starting at the Day 1 visit.	
Reporting group title	Lampalizumab Q4W
Reporting group description: Subjects received 10 milligrams (mg) dose of lampalizumab administered by intravitreal injections Q4W starting at the Day 1 visit.	
Reporting group title	Lampalizumab Q6W
Reporting group description: Subjects received 10 mg dose of lampalizumab administered by intravitreal injections Q6W starting at the Day 1 visit.	

Primary: Change From Baseline in Geographic Atrophy (GA) Area, as Assessed by Fundus Autofluorescence (FAF) at Week 48

End point title	Change From Baseline in Geographic Atrophy (GA) Area, as Assessed by Fundus Autofluorescence (FAF) at Week 48
End point description: The change in GA lesion area was measured by FAF and analysis of FAF images was performed by the central reading centre. A positive change from baseline indicates an increase in size of GA lesion area (worsening; disease progression). Intent-to-treat (ITT) population included all the subjects who were randomised to the study. Number of subjects analysed in this end point were included in Mixed-effect model repeated measures (MMRM analysis).	
End point type	Primary
End point timeframe: Baseline, Week 48	

End point values	Sham Comparator	Lampalizumab Q4W	Lampalizumab Q6W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	274	259	270	
Units: millimetre square(mm^2)				
arithmetic mean (standard error)	2.035 (± 0.066)	2.016 (± 0.068)	2.086 (± 0.067)	

Statistical analyses

Statistical analysis title	Lampalizumab Q4W vs Sham Comparator
Statistical analysis description: Week 48: MMRM analysis uses change as response variable and included treatment group, visit, treatment-by-visit interaction, baseline GA area, lesion location, contiguity, biomarker status, modified baseline BCVA and sex.	
Comparison groups	Sham Comparator v Lampalizumab Q4W

Number of subjects included in analysis	533
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8381
Method	MMRM
Parameter estimate	Difference in Adjusted Means
Point estimate	-0.019
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.206
upper limit	0.167

Statistical analysis title	Lampalizumab Q6W vs Sham Comparator
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Statistical analysis description:

Week 48: MMRM analysis uses change as response variable and included treatment group, visit, treatment-by-visit interaction, baseline GA area, lesion location, contiguity, biomarker status, modified baseline BCVA and sex.

Comparison groups	Sham Comparator v Lampalizumab Q6W
Number of subjects included in analysis	544
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5901
Method	MMRM
Parameter estimate	Difference in Adjusted Means
Point estimate	0.051
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.134
upper limit	0.236

Primary: Change From Baseline in GA Area in Complement Factor I (CFI) Positive and Negative Subjects at Week 48

End point title	Change From Baseline in GA Area in Complement Factor I (CFI) Positive and Negative Subjects at Week 48
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End point description:

For CFI profile, positive or negative biomarker status refers to the presence (carrier) or absence of the risk allele at CFI and at least one risk allele at complement factor H (CFH) or risk locus containing both complement component 2 and complement factor B (C2/CFB). The change in GA lesion area was measured by FAF and analysis of FAF images was performed by the central reading centre. A positive change from baseline indicates an increase in size of GA lesion area (worsening; disease progression). ITT population included all the subjects who were randomised to the study. Reported here are data for CFI-positive and CFI-negative subjects within the ITT population. Here, "n" is the number of subjects who were analysed for this endpoint.

End point type	Primary
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End point timeframe:

Baseline, Week 48

End point values	Sham Comparator	Lampalizumab Q4W	Lampalizumab Q6W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	305	298	303	
Units: mm ²				
arithmetic mean (standard error)				
CFI-Positive Subjects (n= 162, 152, 160)	2.067 (± 0.086)	2.045 (± 0.089)	2.144 (± 0.087)	
CFI-Negative Subjects (n= 112, 107, 110)	2.006 (± 0.103)	1.974 (± 0.105)	2.012 (± 0.104)	

Statistical analyses

Statistical analysis title	Lampalizumab Q4W vs Sham Comparator
Statistical analysis description:	
CFI Positive: MMRM analysis uses change as response variable and included treatment group, visit, treatment-by-visit interaction, baseline GA area, lesion location, contiguity, biomarker status, modified baseline BCVA and sex.	
Comparison groups	Sham Comparator v Lampalizumab Q4W
Number of subjects included in analysis	603
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8612
Method	MMRM
Parameter estimate	Difference in Adjusted Means
Point estimate	-0.022
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.266
upper limit	0.223

Statistical analysis title	Lampalizumab Q6W vs Sham Comparator
Statistical analysis description:	
CFI Positive: MMRM analysis uses change as response variable and included treatment group, visit, treatment-by-visit interaction, baseline GA area, lesion location, contiguity, biomarker status, modified baseline BCVA and sex.	
Comparison groups	Sham Comparator v Lampalizumab Q6W
Number of subjects included in analysis	608
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5317
Method	MMRM
Parameter estimate	Difference in Adjusted Means
Point estimate	0.077

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.165
upper limit	0.319

Statistical analysis title	Lampalizumab Q4W vs Sham Comparator
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Statistical analysis description:

CFI Negative: MMRM analysis uses change as response variable and included treatment group, visit, treatment-by-visit interaction, baseline GA area, lesion location, contiguity, biomarker status, modified baseline BCVA and sex.

Comparison groups	Sham Comparator v Lampalizumab Q4W
Number of subjects included in analysis	603
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.824
Method	MMRM
Parameter estimate	Difference in Adjusted Means
Point estimate	-0.033
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.322
upper limit	0.257

Statistical analysis title	Lampalizumab Q6W vs Sham Comparator
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Statistical analysis description:

CFI Negative: MMRM analysis uses change as response variable and included treatment group, visit, treatment-by-visit interaction, baseline GA area, lesion location, contiguity, biomarker status, modified baseline BCVA and sex.

Comparison groups	Sham Comparator v Lampalizumab Q6W
Number of subjects included in analysis	608
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9676
Method	MMRM
Parameter estimate	Difference in Adjusted Means
Point estimate	0.006
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.283
upper limit	0.294

Secondary: Change From Baseline in Number of Absolute Scotomatous Points as

Assessed by Mesopic Micrometry at Week 48

End point title	Change From Baseline in Number of Absolute Scotomatous Points as Assessed by Mesopic Micrometry at Week 48
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End point description:

Scotomatous points were the testing points on microperimetry examination that were centered on the macula and reported a lack of retinal sensitivity within the range tested. Mesopic microperimetry assessments were performed post-dilation on the study eye only, and the data was forwarded to the central reading centre. A positive change from baseline indicates an increase in the number of absolute scotomatous points (more lack of retinal sensitivity); disease worsening. The microperimetry analysis population consisted of all subjects who met the microperimetry eligibility criteria assessed by the reading centre (subjects at selected sites only; subjects grouped according to treatment assigned at randomisation). Number of subjects analysed in this end point were included in MMRM analysis. The data was collected up to Week 48 instead of Week 96, due to early termination of the study.

End point type	Secondary
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End point timeframe:

Baseline, Week 48

End point values	Sham Comparator	Lampalizumab Q4W	Lampalizumab Q6W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	30	26	26	
Units: number of absolute scotomatous points				
arithmetic mean (standard error)	8.3 (± 1.7)	8.1 (± 1.8)	8.3 (± 1.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Mean Macular Sensitivity as Assessed by Mesopic Microperimetry at Week 48

End point title	Change From Baseline in Mean Macular Sensitivity as Assessed by Mesopic Microperimetry at Week 48
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End point description:

Mesopic microperimetry was used to assess macular sensitivity and assessments were performed post-dilation on the study eye only, and the data was forwarded to the central reading centre. A negative change from baseline indicates a decrease in the mean macular sensitivity; disease worsening. The microperimetry analysis population consisted of all subjects who met the microperimetry eligibility criteria assessed by the reading centre (subjects at selected sites only; subjects grouped according to treatment assigned at randomisation). Number of subjects analysed in this end point were included in MMRM analysis. The data was collected up to Week 48 instead of Week 96, due to early termination of the study.

End point type	Secondary
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End point timeframe:

Baseline, Week 48

End point values	Sham Comparator	Lampalizumab Q4W	Lampalizumab Q6W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	30	26	26	
Units: decibel (dB)				
arithmetic mean (standard error)	-1.61 (± 0.33)	-1.33 (± 0.34)	-2.24 (± 0.35)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Best Corrected Visual Acuity (BCVA) Score as Assessed by Early Treatment Diabetic Retinopathy Study (ETDRS) Chart at Week 48

End point title	Change From Baseline in Best Corrected Visual Acuity (BCVA) Score as Assessed by Early Treatment Diabetic Retinopathy Study (ETDRS) Chart at Week 48
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End point description:

BCVA score was based on the number of letters read correctly on the ETDRS visual acuity chart assessed at a starting distance of 4 metres (m). BCVA score testing was performed prior to dilating the eyes. BCVA score ranges from 0 to 100 letters in the study eye. The lower the number of letters read correctly on the eye chart, the worse the vision (or visual acuity). A negative change from baseline indicates a decrease in the visual acuity; disease worsening. ITT population included all the subjects who were randomized to the study. Number of subjects analysed in this end point were included in MMRM analysis. The data was collected up to Week 48 instead of Week 96, due to early termination of the study.

End point type	Secondary
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End point timeframe:

Baseline, Week 48

End point values	Sham Comparator	Lampalizumab Q4W	Lampalizumab Q6W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	267	259	261	
Units: letters				
arithmetic mean (standard error)	-4.5 (± 0.6)	-3.4 (± 0.6)	-4.6 (± 0.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Less Than 15 Letters Loss From Baseline in BCVA Score at Week 48

End point title	Percentage of Subjects with Less Than 15 Letters Loss From Baseline in BCVA Score at Week 48
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End point description:

Loss of less than 15 letters from baseline was assessed by the ETDRS chart at a starting distance of 4 m. BCVA was measured using an eye chart and was reported as the number of letters read correctly (ranging from 0 to 100 letters). The lower the number of letters read correctly on the eye chart, the

worse the vision (or visual acuity). ITT population included all the subjects who were randomized to the study. The data was collected up to Week 48 instead of Week 96, due to early termination of the study.

End point type	Secondary
End point timeframe:	
Baseline, Week 48	

End point values	Sham Comparator	Lampalizumab Q4W	Lampalizumab Q6W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	267	259	262	
Units: percentage of subjects				
number (confidence interval 95%)	85.8 (81.6 to 90.0)	88.8 (85.0 to 92.6)	87.0 (83.0 to 91.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Low Luminance Visual Acuity (LLVA) as Assessed by ETDRS Chart Under Low Luminance Conditions at Week 48

End point title	Change From Baseline in Low Luminance Visual Acuity (LLVA) as Assessed by ETDRS Chart Under Low Luminance Conditions at Week 48
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End point description:

The LLVA was measured by placing a 2.0-log-unit neutral density filter over the best correction for that eye and having the subject read the normally illuminated ETDRS chart. The assessment was performed prior to dilating the eyes. A negative change from baseline indicates a decrease in the visual acuity; disease worsening. ITT population included all the subjects who were randomized to the study. Number of subjects analysed in this end point were included in MMRM analysis. The data was collected up to Week 48 instead of Week 96, due to early termination of the study.

End point type	Secondary
End point timeframe:	
Baseline, Week 48	

End point values	Sham Comparator	Lampalizumab Q4W	Lampalizumab Q6W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	265	251	252	
Units: letters				
arithmetic mean (standard error)	-3.0 (± 0.7)	-2.4 (± 0.7)	-2.7 (± 0.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Less Than 15 Letters Loss From Baseline in LLVA Score at Week 48

End point title	Percentage of Subjects with Less Than 15 Letters Loss From Baseline in LLVA Score at Week 48
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End point description:

Loss of less than 15 letters from baseline was assessed by the ETDRS chart at a starting distance of 4 m. ITT population included all the subjects who were randomized to the study. The data was collected up to Week 48 instead of Week 96, due to early termination of the study.

End point type	Secondary
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End point timeframe:

Week 48

End point values	Sham Comparator	Lampalizumab Q4W	Lampalizumab Q6W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	265	251	253	
Units: percentage of subjects				
number (confidence interval 95%)	86.8 (82.7 to 90.9)	85.3 (80.9 to 89.6)	86.6 (82.4 to 90.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Binocular Reading Speed as Assessed by Minnesota Low-Vision Reading Test (MNRead) Charts or Radner Reading Charts at Week 48

End point title	Change From Baseline in Binocular Reading Speed as Assessed by Minnesota Low-Vision Reading Test (MNRead) Charts or Radner Reading Charts at Week 48
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End point description:

MNRead acuity cards were continuous-text reading-acuity cards suitable for measuring the reading acuity and reading speed of normal and low-vision subjects. The MNRead acuity cards consisted of single, simple sentences with equal numbers of characters. A stopwatch was used to record time to a tenth of a second. Sentences that could not be read or were not attempted due to vision should be recorded as 0 for time and 10 for errors. The Radner Reading Cards were suitable for measuring reading speed, reading visual acuity, and critical print size. The reading test was stopped when the reading time was longer than 20 seconds or when the subject was making severe errors. A negative change from baseline indicates a decrease in the binocular reading speed; disease worsening. Reported here is the ITT population included in MMRM analysis. The data was collected up to Week 48 instead of Week 96, due to early termination of the study.

End point type	Secondary
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End point timeframe:

Baseline, Week 48

End point values	Sham Comparator	Lampalizumab Q4W	Lampalizumab Q6W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	242	223	229	
Units: words per minute (wpm)				
arithmetic mean (standard error)	-18.97 (\pm 2.37)	-13.32 (\pm 2.47)	-19.96 (\pm 2.44)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Monocular Maximum Reading Speed as Assessed by MNRead Charts or Radner Reading Charts at Week 48

End point title	Change From Baseline in Monocular Maximum Reading Speed as Assessed by MNRead Charts or Radner Reading Charts at Week 48
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End point description:

MNRead acuity cards were continuous-text reading-acuity cards suitable for measuring the reading acuity and reading speed of normal and low-vision subjects. The MNRead acuity cards consisted of single, simple sentences with equal numbers of characters. A stopwatch was used to record time to a tenth of a second. Sentences that could not be read or were not attempted due to vision should be recorded as 0 for time and 10 for errors. The Radner Reading Cards were suitable for measuring reading speed, reading visual acuity, and critical print size. The reading test was stopped when the reading time was longer than 20 seconds or when the subject was making severe errors. A negative change from baseline indicates a decrease in the monocular reading speed; disease worsening. Reported here is the ITT population included in MMRM analysis. The data was collected up to Week 48 instead of Week 96, due to early termination of the study.

End point type	Secondary
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End point timeframe:

Baseline, Week 48

End point values	Sham Comparator	Lampalizumab Q4W	Lampalizumab Q6W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	243	229	233	
Units: wpm				
arithmetic mean (standard error)	-19.63 (\pm 2.41)	-17.91 (\pm 2.49)	-18.16 (\pm 2.47)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in National Eye Institute Visual Functioning Questionnaire 25-item (NEI VFQ-25) Version Composite Score at Week 48

End point title	Change From Baseline in National Eye Institute Visual Functioning Questionnaire 25-item (NEI VFQ-25) Version Composite Score at Week 48
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End point description:

NEI-VFQ-25 questionnaire included 25 items based on which overall composite VFQ score and 12 subscales were derived: near activities, distance activities, general health, general vision, ocular pain, vision-specific social functioning, vision-specific mental health, vision-specific role difficulties, vision-specific dependency, driving, color vision and peripheral vision. Response to each question converted to 0-100 score. Each subscale, total score=average of items contributing to score. For each subscale and total score, score range: 0 to 100, a higher score represents better functioning. A negative change from baseline indicates a decrease in the visual functioning; disease worsening. ITT population included all the subjects who were randomized to the study. Number of subjects analysed in this end point were included in MMRM analysis. The data was collected up to Week 48 instead of Week 96, due to early termination of the study.

End point type	Secondary
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End point timeframe:

Baseline, Week 48

End point values	Sham Comparator	Lampalizumab Q4W	Lampalizumab Q6W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	239	234	248	
Units: score on a scale				
arithmetic mean (standard error)	-1.31 (± 0.71)	-1.66 (± 0.72)	-2.87 (± 0.70)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in NEI VFQ-25 Near Activity Subscale Score at Week 48

End point title	Change From Baseline in NEI VFQ-25 Near Activity Subscale Score at Week 48
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End point description:

NEI-VFQ-25 questionnaire included 25 items based on which near activities were measured. Near activities are defined as reading ordinary print in newspapers, performing work or hobbies requiring near vision, or finding something on a crowded shelf. Response to each question converted to 0-100 score. A higher score represents better functioning. A negative change from baseline indicates a decrease in the near visual activities; disease worsening. ITT population included all the subjects who were randomized to the study. Number of subjects analysed in this end point were included in MMRM analysis. The data was collected up to Week 48 instead of Week 96, due to early termination of the study.

End point type	Secondary
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End point timeframe:

Baseline, Week 48

End point values	Sham Comparator	Lampalizumab Q4W	Lampalizumab Q6W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	239	234	248	
Units: score on a scale				
arithmetic mean (standard error)	-2.12 (± 0.93)	-2.35 (± 0.94)	-4.06 (± 0.92)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in NEI VFQ-25 Distance Activity Subscale Score at Week 48

End point title	Change From Baseline in NEI VFQ-25 Distance Activity Subscale Score at Week 48
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End point description:

NEI-VFQ-25 questionnaire included 25 items based on which distance activities were measured. Distance activities are defined as reading street signs or names on stores, and going down stairs, steps, or curbs. Response to each question converted to 0-100 score. A higher score represents better functioning. A negative change from baseline indicates a decrease in the distance visual activities; disease worsening. ITT population included all the subjects who were randomized to the study. Number of subjects analysed in this end point were included in MMRM analysis. The data was collected up to Week 48 instead of Week 96, due to early termination of the study.

End point type	Secondary
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End point timeframe:

Baseline, Week 48

End point values	Sham Comparator	Lampalizumab Q4W	Lampalizumab Q6W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	239	234	248	
Units: score on a scale				
arithmetic mean (standard error)	-2.03 (\pm 0.99)	-1.04 (\pm 1.00)	-3.62 (\pm 0.97)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Mean Functional Reading Independence (FRI) Index at Week 48

End point title	Change From Baseline in Mean Functional Reading Independence (FRI) Index at Week 48
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End point description:

The FRI was an interviewer-administered questionnaire with 7 items on functional reading activities most relevant to GA AMD subjects. It has one total index score. The index score is an ordinal scale with higher levels representing higher FRI. For each FRI Index reading activity performed in the past 7 days, subjects were asked about the extent to which they required vision aids, adjustments in the activity, or help from another subject. A negative change from baseline indicates a decrease in the FRI; disease worsening. ITT population included all the subjects who were randomized to the study. Number of subjects analysed in this end point were included in MMRM analysis. The data was collected up to Week 48 instead of Week 96, due to early termination of the study.

End point type	Secondary
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End point timeframe:

Baseline, Week 48

End point values	Sham Comparator	Lampalizumab Q4W	Lampalizumab Q6W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	237	230	244	
Units: score on a scale				
arithmetic mean (standard error)	-0.06 (± 0.04)	-0.13 (± 0.04)	-0.15 (± 0.04)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to approximately 2 years

Adverse event reporting additional description:

Safety population included all subjects who received at least one dose of study drug.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.1
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Reporting groups

Reporting group title	Sham Comparator
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Reporting group description:

Subjects received sham comparator Q4W (once in every 4 weeks) or Q6W (once in every 6 weeks) for approximately 96 weeks.

Reporting group title	Lampalizumab Q4W
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Reporting group description:

Subjects received 10 milligrams (mg) dose of lampalizumab administered by intravitreal injections Q4W for approximately 96 weeks.

Reporting group title	Lampalizumab Q6W
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Reporting group description:

Subjects received 10 mg dose of lampalizumab administered by intravitreal injections Q6W for approximately 96 weeks.

Serious adverse events	Sham Comparator	Lampalizumab Q4W	Lampalizumab Q6W
Total subjects affected by serious adverse events			
subjects affected / exposed	97 / 300 (32.33%)	118 / 298 (39.60%)	108 / 303 (35.64%)
number of deaths (all causes)	6	5	6
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign neoplasm of ureter			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder cancer			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	2 / 303 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			

subjects affected / exposed	2 / 300 (0.67%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchial carcinoma			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangiocarcinoma			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometrial cancer			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung adenocarcinoma			
subjects affected / exposed	0 / 300 (0.00%)	3 / 298 (1.01%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung cancer metastatic			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm malignant			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	2 / 303 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant melanoma			
subjects affected / exposed	2 / 300 (0.67%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant melanoma stage IV			

subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant pleural effusion			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningioma			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelodysplastic syndrome			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myxofibrosarcoma			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasm skin			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuroendocrine carcinoma			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non–small cell lung cancer metastatic			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal carcinoma			

subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cancer			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cancer metastatic			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic carcinoma			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Plasma cell myeloma			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	1 / 300 (0.33%)	2 / 298 (0.67%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer metastatic			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	2 / 303 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin cancer			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma			

subjects affected / exposed	0 / 300 (0.00%)	2 / 298 (0.67%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder neoplasm			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipoma			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urethral cancer			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Aortic stenosis			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood pressure inadequately controlled			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			

subjects affected / exposed	1 / 300 (0.33%)	2 / 298 (0.67%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	2 / 303 (0.66%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
May–Thurner syndrome			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral embolism			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombophlebitis			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orthostatic hypotension			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Cardiac pacemaker battery replacement			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			

Chest pain			
subjects affected / exposed	1 / 300 (0.33%)	1 / 298 (0.34%)	2 / 303 (0.66%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impaired healing			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Postmenopausal haemorrhage			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterovaginal prolapse			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			

subjects affected / exposed	0 / 300 (0.00%)	3 / 298 (1.01%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	2 / 303 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchial hyperreactivity			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 300 (0.00%)	3 / 298 (1.01%)	5 / 303 (1.65%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 300 (0.33%)	1 / 298 (0.34%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epiglottic cyst			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			

subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	2 / 303 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax spontaneous			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary air leakage			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 300 (0.00%)	2 / 298 (0.67%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	1 / 300 (0.33%)	1 / 298 (0.34%)	2 / 303 (0.66%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			

Blood pressure increased			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Heart rate irregular			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial necrosis marker increased			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostatic specific antigen increased			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Troponin increased			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intraocular pressure increased			
subjects affected / exposed	0 / 300 (0.00%)	16 / 298 (5.37%)	14 / 303 (4.62%)
occurrences causally related to treatment / all	0 / 0	11 / 29	8 / 27
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acetabulum fracture			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Ankle fracture			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Comminuted fracture			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Contusion			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Craniocerebral injury			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dislocation of vertebra			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	5 / 300 (1.67%)	2 / 298 (0.67%)	4 / 303 (1.32%)
occurrences causally related to treatment / all	0 / 5	0 / 2	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	1 / 300 (0.33%)	4 / 298 (1.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fibula fracture			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Forearm fracture			

subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	3 / 300 (1.00%)	3 / 298 (1.01%)	3 / 303 (0.99%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	0 / 300 (0.00%)	2 / 298 (0.67%)	2 / 303 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Internal injury			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower limb fracture			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar vertebral fracture			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle rupture			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic fracture			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			

subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	2 / 300 (0.67%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	2 / 300 (0.67%)	2 / 298 (0.67%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal fracture			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sternal fracture			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper limb fracture			

subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	2 / 303 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Corneal abrasion			
subjects affected / exposed	1 / 300 (0.33%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial bones fracture			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyphaema			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical vertebral fracture			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foreign body in eye			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic intracranial haemorrhage			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Atrial septal defect			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			

Acute myocardial infarction			
subjects affected / exposed	1 / 300 (0.33%)	3 / 298 (1.01%)	3 / 303 (0.99%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arrhythmia			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	3 / 300 (1.00%)	4 / 298 (1.34%)	3 / 303 (0.99%)
occurrences causally related to treatment / all	0 / 4	0 / 4	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block first degree			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			

subjects affected / exposed	2 / 300 (0.67%)	0 / 298 (0.00%)	2 / 303 (0.66%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	1 / 300 (0.33%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	1 / 300 (0.33%)	3 / 298 (1.01%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	2 / 300 (0.67%)	3 / 298 (1.01%)	6 / 303 (1.98%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	4 / 300 (1.33%)	1 / 298 (0.34%)	2 / 303 (0.66%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	2 / 303 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Palpitations			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia			

subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular fibrillation			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Amyotrophic lateral sclerosis			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carotid artery stenosis			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haematoma			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	2 / 303 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral microangiopathy			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	3 / 300 (1.00%)	3 / 298 (1.01%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervicogenic vertigo			

subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dementia			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dementia Alzheimer's type			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dural arteriovenous fistula			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised tonic-clonic seizure			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic stroke			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			

subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiparesis			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	1 / 300 (0.33%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lacunar infarction			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar radiculopathy			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraesthesia			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	0 / 300 (0.00%)	2 / 298 (0.67%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Senile dementia			

subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	1 / 300 (0.33%)	4 / 298 (1.34%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vertigo CNS origin			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	2 / 300 (0.67%)	2 / 298 (0.67%)	2 / 303 (0.66%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aphasia			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cognitive disorder			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolic stroke			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 300 (0.33%)	2 / 298 (0.67%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic anaemia			

subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 300 (0.33%)	1 / 298 (0.34%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Blindness transient			
subjects affected / exposed	0 / 300 (0.00%)	2 / 298 (0.67%)	2 / 303 (0.66%)
occurrences causally related to treatment / all	0 / 0	1 / 9	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Borderline glaucoma			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Choroidal neovascularisation			
subjects affected / exposed	2 / 300 (0.67%)	2 / 298 (0.67%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iritis			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neovascular age-related macular degeneration			
subjects affected / exposed	3 / 300 (1.00%)	3 / 298 (1.01%)	3 / 303 (0.99%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Open angle glaucoma			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Retinal artery occlusion			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal detachment			
subjects affected / exposed	1 / 300 (0.33%)	2 / 298 (0.67%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal neovascularisation			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal tear			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Visual acuity reduced			
subjects affected / exposed	10 / 300 (3.33%)	12 / 298 (4.03%)	8 / 303 (2.64%)
occurrences causally related to treatment / all	0 / 13	0 / 12	0 / 10
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Visual acuity reduced transiently			
subjects affected / exposed	0 / 300 (0.00%)	2 / 298 (0.67%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	1 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vitreous haemorrhage			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vitritis			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dry age-related macular degeneration			

subjects affected / exposed	2 / 300 (0.67%)	0 / 298 (0.00%)	2 / 303 (0.66%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cataract			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis ischaemic			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticular hernia			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulum intestinal			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspepsia			

subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Flatulence			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric volvulus			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroduodenitis			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	2 / 303 (0.66%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 300 (0.00%)	2 / 298 (0.67%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			

subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophagitis ulcerative			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	2 / 303 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal ulcer			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	2 / 300 (0.67%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 300 (0.33%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal angiectasia			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstructive pancreatitis			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			

subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bladder cyst			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic kidney disease			
subjects affected / exposed	0 / 300 (0.00%)	2 / 298 (0.67%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysuria			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydronephrosis			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	1 / 300 (0.33%)	3 / 298 (1.01%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oliguria			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	0 / 300 (0.00%)	2 / 298 (0.67%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			

subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary bladder polyp			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 300 (0.33%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemarthrosis			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuropathic arthropathy			

subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	2 / 300 (0.67%)	3 / 298 (1.01%)	2 / 303 (0.66%)
occurrences causally related to treatment / all	0 / 2	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator cuff syndrome			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal column stenosis			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal osteoarthritis			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal pain			
subjects affected / exposed	0 / 300 (0.00%)	2 / 298 (0.67%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abdominal sepsis			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			

subjects affected / exposed	0 / 300 (0.00%)	3 / 298 (1.01%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Campylobacter infection			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	2 / 303 (0.66%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	2 / 300 (0.67%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocarditis			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	2 / 300 (0.67%)	1 / 298 (0.34%)	2 / 303 (0.66%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			

subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious pleural effusion			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 300 (0.00%)	2 / 298 (0.67%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perihepatic abscess			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	9 / 300 (3.00%)	11 / 298 (3.69%)	5 / 303 (1.65%)
occurrences causally related to treatment / all	0 / 9	0 / 12	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	3 / 300 (1.00%)	3 / 298 (1.01%)	2 / 303 (0.66%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal sepsis			

subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	2 / 300 (0.67%)	3 / 298 (1.01%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Conjunctivitis			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endophthalmitis			
subjects affected / exposed	0 / 300 (0.00%)	2 / 298 (0.67%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	2 / 300 (0.67%)	2 / 298 (0.67%)	2 / 303 (0.66%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gout			
subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			

subjects affected / exposed	0 / 300 (0.00%)	1 / 298 (0.34%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	1 / 300 (0.33%)	2 / 298 (0.67%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iron deficiency			
subjects affected / exposed	0 / 300 (0.00%)	0 / 298 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malnutrition			
subjects affected / exposed	1 / 300 (0.33%)	0 / 298 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Sham Comparator	Lampalizumab Q4W	Lampalizumab Q6W
Total subjects affected by non-serious adverse events			
subjects affected / exposed	221 / 300 (73.67%)	239 / 298 (80.20%)	232 / 303 (76.57%)
Investigations			
Intraocular pressure increased			
subjects affected / exposed	9 / 300 (3.00%)	42 / 298 (14.09%)	27 / 303 (8.91%)
occurrences (all)	13	102	55
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	36 / 300 (12.00%)	29 / 298 (9.73%)	34 / 303 (11.22%)
occurrences (all)	41	39	43
Vascular disorders			

Hypertension subjects affected / exposed occurrences (all)	14 / 300 (4.67%) 14	16 / 298 (5.37%) 16	13 / 303 (4.29%) 13
Nervous system disorders Headache subjects affected / exposed occurrences (all)	7 / 300 (2.33%) 7	20 / 298 (6.71%) 26	13 / 303 (4.29%) 13
Eye disorders Conjunctival haemorrhage subjects affected / exposed occurrences (all)	84 / 300 (28.00%) 186	111 / 298 (37.25%) 343	93 / 303 (30.69%) 199
Eye pain subjects affected / exposed occurrences (all)	20 / 300 (6.67%) 31	39 / 298 (13.09%) 65	33 / 303 (10.89%) 57
Vitreous floaters subjects affected / exposed occurrences (all)	16 / 300 (5.33%) 22	41 / 298 (13.76%) 53	25 / 303 (8.25%) 35
Vitreous detachment subjects affected / exposed occurrences (all)	24 / 300 (8.00%) 31	22 / 298 (7.38%) 27	24 / 303 (7.92%) 33
Dry eye subjects affected / exposed occurrences (all)	25 / 300 (8.33%) 43	23 / 298 (7.72%) 40	14 / 303 (4.62%) 27
Cataract subjects affected / exposed occurrences (all)	12 / 300 (4.00%) 19	22 / 298 (7.38%) 33	15 / 303 (4.95%) 22
Posterior capsule opacification subjects affected / exposed occurrences (all)	14 / 300 (4.67%) 15	21 / 298 (7.05%) 27	13 / 303 (4.29%) 17
Retinal haemorrhage subjects affected / exposed occurrences (all)	20 / 300 (6.67%) 25	14 / 298 (4.70%) 16	17 / 303 (5.61%) 21
Punctate keratitis subjects affected / exposed occurrences (all)	15 / 300 (5.00%) 30	16 / 298 (5.37%) 27	16 / 303 (5.28%) 24
Gastrointestinal disorders			

Nausea subjects affected / exposed occurrences (all)	15 / 300 (5.00%) 15	10 / 298 (3.36%) 11	7 / 303 (2.31%) 7
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	9 / 300 (3.00%) 9	16 / 298 (5.37%) 17	13 / 303 (4.29%) 14
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all)	25 / 300 (8.33%) 25 11 / 300 (3.67%) 13	20 / 298 (6.71%) 20 21 / 298 (7.05%) 26	14 / 303 (4.62%) 16 15 / 303 (4.95%) 17
Infections and infestations Bronchitis subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) Influenza subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all)	22 / 300 (7.33%) 28 25 / 300 (8.33%) 32 17 / 300 (5.67%) 18 12 / 300 (4.00%) 14 27 / 300 (9.00%) 33	29 / 298 (9.73%) 36 26 / 298 (8.72%) 35 14 / 298 (4.70%) 14 14 / 298 (4.70%) 17 45 / 298 (15.10%) 59	26 / 303 (8.58%) 27 21 / 303 (6.93%) 39 11 / 303 (3.63%) 11 16 / 303 (5.28%) 18 34 / 303 (11.22%) 40

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 August 2014	Protocol was amended to allow investigator site staff to perform telephone administration of the patient-reported outcome (PRO) assessments on the study subjects in countries where law and/or regulation prohibit the use of a third-party Sponsor contracted call centre to perform the telephone administration of the PRO assessments.
04 September 2014	Protocol was amended to reflect that the microperimetry assessment should be performed post-dilation.
18 November 2014	Protocol was amended to include additional inclusion/exclusion criteria to enhance subject safety and to comply with health authority requests, enabling the protocol to be conducted globally.
06 March 2015	Protocol was amended to change the telephone-based collection of patient-reported outcome questionnaires (National Eye Institute Visual Functioning Questionnaire 25-item Version and Functional Reading Independence Index) to an on-site, in-person administration format. The screening period was extended from 21 days to 28 days. To reduce the chance of user error, the sham vial appropriate handling was clarified. This amendment included small revisions and clarifications to the inclusion and exclusion criteria. The protocol expanded on use of Lucentis (at the discretion of the investigator) in either eye for any ocular condition for which it was approved in a country.
24 September 2015	Planned total sample size was updated to provide a more accurate number of planned global sites. Section Subjects included guidance regarding the procedure for handling subjects who needed an extended screening period to prevent unnecessary re-screening. In the inclusion criteria contraceptive methods for women of childbearing potential and men as well as definition of women of childbearing potential were harmonised with current international recommendations. In the exclusion criteria concurrent systemic conditions were updated to include treatment for localised in addition to systemic infection. Ongoing prophylactic use of antimicrobial therapy should be discussed with Medical Monitor. Additional details regarding the masked and unmasked roles were added. In Permitted Therapy, updated instructions were given in the event that Lucentis treatment was given at the same visit as a study eye treatment with lamplelizumab/sham to help ensure subject safety. Safety Plan was updated to include transient vision loss as a potential ocular safety issue currently thought to be associated with the route of administration to help ensure subject safety. More detailed guidance was provided for the assessment of causality of adverse events. Clarified the pre-treatment procedures for subjects undergoing treatment or sham injections to help ensure subject safety. Preparation and administration of lamplelizumab injection was revised to include equivalent study treatment supplies (needles) available outside of the United States and to further clarify the steps required to prepare and administer a lamplelizumab injection to help ensure subject safety.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
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29 January 2018	The study was terminated early by the Sponsor due to lack of efficacy of the compound.	-
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Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

This study was terminated early by the Sponsor because the compound had demonstrated lack of efficacy. Thus, not all subjects in this study completed the full duration of treatment.

Notes: