



Clinical trial results:

A Multicenter, Open-Label Extension Study to Evaluate the Long-Term Safety and Tolerability of Lampalizumab in Patients with Geographic Atrophy Secondary to Age-Related Macular Degeneration who have Completed a Roche-Sponsored Study

Summary

EudraCT number	2016-000423-13
Trial protocol	GB PT HU DK AT SE DE PL ES SK BE FR NL IT
Global end of trial date	31 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	GX30191
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02745119
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	31 January 2018
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	31 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 long-term safety and tolerability of intravitreal (ITV) injections of lapanizumab, 10 milligrams (mg) administered to subjects with geographic atrophy (GA) secondary to age-related macular degeneration (AMD).

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	21 July 2016
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: 576
Country: Number of subjects enrolled	Spain: 40
Country: Number of subjects enrolled	United Kingdom: 20
Country: Number of subjects enrolled	Italy: 10
Country: Number of subjects enrolled	Switzerland: 13
Country: Number of subjects enrolled	Denmark: 6
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Portugal: 3
Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Poland: 27
Country: Number of subjects enrolled	Hungary: 18
Country: Number of subjects enrolled	Slovakia: 8
Country: Number of subjects enrolled	Australia: 23
Country: Number of subjects enrolled	Germany: 39
Country: Number of subjects enrolled	France: 30
Country: Number of subjects enrolled	Austria: 26
Worldwide total number of subjects	842
EEA total number of subjects	230

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)	36
From 65 to 84 years	569
85 years and over	237

Subject disposition

Recruitment

Recruitment details:

A total of 994 subjects were enrolled in the study at 202 investigational sites across 19 countries. The study was terminated early by the Sponsor due to lack of efficacy.

Pre-assignment

Screening details:

Eligible subjects were those who enrolled in Studies GX29176 (NCT02247479) and GX29185 (NCT02247531) and had completed the 96-week treatment period without early treatment discontinuation or study discontinuation.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Lampalizumab Q4W - Treatment-Naive

Arm description:

Subjects who received sham comparator every 4 weeks in one of the parent studies and completed the Week 96 visit received lampalizumab, 10 milligrams (mg), by intravitreal (ITV) injection, administered every 4 weeks.

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:

Subjects who received sham comparator every 4 weeks in one of the parent studies and completed the Week 96 visit received lampalizumab, 10 mg, by intravitreal (ITV) injection, administered every 4 weeks.

Arm title	Lampalizumab Q4W – Previously Treated
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Arm description:

Subjects who received lampalizumab every 4 weeks in one of the parent studies and completed the Week 96 visit received lampalizumab, 10 mg, by ITV injection, administered every 4 weeks.

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:

Subjects who received lampalizumab every 4 weeks in one of the parent studies and completed the Week 96 visit received lampalizumab, 10 mg, by ITV injection, administered every 4 weeks.

Arm title	Lampalizumab Q6W - Treatment-Naive
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Arm description:

Subjects who received sham comparator every 6 weeks in one of the parent studies and completed the Week 96 visit received lampalizumab, 10 mg, by ITV injection, administered every 6 weeks.

Arm type	Experimental
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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:

Subjects who received sham comparator every 6 weeks in one of the parent studies and completed the Week 96 visit received lampalizumab, 10 mg, by ITV injection, administered every 6 weeks.

Arm title	Lampalizumab Q6W – Previously Treated
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Arm description:

Subjects who received lampalizumab every 6 weeks in one of the parent studies and completed the Week 96 visit received lampalizumab, 10 mg, by ITV injection, administered every 6 weeks.

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:

Subjects who received lampalizumab every 6 weeks in one of the parent studies and completed the Week 96 visit received lampalizumab, 10 mg, by ITV injection, administered every 6 weeks.

Number of subjects in period 1	Lampalizumab Q4W - Treatment-Naive	Lampalizumab Q4W - Previously Treated	Lampalizumab Q6W - Treatment-Naive
Started	145	274	146
Completed	0	0	0
Not completed	145	274	146
Consent withdrawn by subject	7	15	8
Physician decision	-	2	2
Protocol Deviation	-	-	-
Death	3	3	-
Reason Not Specified	-	2	-
Adverse event	1	-	1
Study Terminated by Sponsor	134	252	135
Lost to follow-up	-	-	-

Number of subjects in period 1	Lampalizumab Q6W - Previously Treated
Started	277
Completed	0
Not completed	277
Consent withdrawn by subject	14
Physician decision	2
Protocol Deviation	1
Death	4
Reason Not Specified	1

Adverse event	3
Study Terminated by Sponsor	251
Lost to follow-up	1

Baseline characteristics

Reporting groups

Reporting group title	Lampalizumab Q4W - Treatment-Naive
Reporting group description: Subjects who received sham comparator every 4 weeks in one of the parent studies and completed the Week 96 visit received lampalizumab, 10 milligrams (mg), by intravitreal (ITV) injection, administered every 4 weeks.	
Reporting group title	Lampalizumab Q4W – Previously Treated
Reporting group description: Subjects who received lampalizumab every 4 weeks in one of the parent studies and completed the Week 96 visit received lampalizumab, 10 mg, by ITV injection, administered every 4 weeks.	
Reporting group title	Lampalizumab Q6W - Treatment-Naive
Reporting group description: Subjects who received sham comparator every 6 weeks in one of the parent studies and completed the Week 96 visit received lampalizumab, 10 mg, by ITV injection, administered every 6 weeks.	
Reporting group title	Lampalizumab Q6W – Previously Treated
Reporting group description: Subjects who received lampalizumab every 6 weeks in one of the parent studies and completed the Week 96 visit received lampalizumab, 10 mg, by ITV injection, administered every 6 weeks.	

Reporting group values	Lampalizumab Q4W - Treatment-Naive	Lampalizumab Q4W - Previously Treated	Lampalizumab Q6W - Treatment-Naive
Number of subjects	145	274	146
Age categorical			
Units: Subjects			

Age Continuous			
Units: years			
arithmetic mean	79.0	78.7	79.2
standard deviation	± 8.2	± 7.8	± 8.6
Sex: Female, Male			
Units: Subjects			
Female	82	167	79
Male	63	107	67

Reporting group values	Lampalizumab Q6W - Previously Treated	Total	
Number of subjects	277	842	
Age categorical			
Units: Subjects			

Age Continuous			
Units: years			
arithmetic mean	80.2		
standard deviation	± 7.9	-	
Sex: Female, Male			
Units: Subjects			
Female	164	492	
Male	113	350	

End points

End points reporting groups

Reporting group title	Lampalizumab Q4W - Treatment-Naive
Reporting group description: Subjects who received sham comparator every 4 weeks in one of the parent studies and completed the Week 96 visit received lampalizumab, 10 milligrams (mg), by intravitreal (ITV) injection, administered every 4 weeks.	
Reporting group title	Lampalizumab Q4W – Previously Treated
Reporting group description: Subjects who received lampalizumab every 4 weeks in one of the parent studies and completed the Week 96 visit received lampalizumab, 10 mg, by ITV injection, administered every 4 weeks.	
Reporting group title	Lampalizumab Q6W - Treatment-Naive
Reporting group description: Subjects who received sham comparator every 6 weeks in one of the parent studies and completed the Week 96 visit received lampalizumab, 10 mg, by ITV injection, administered every 6 weeks.	
Reporting group title	Lampalizumab Q6W – Previously Treated
Reporting group description: Subjects who received lampalizumab every 6 weeks in one of the parent studies and completed the Week 96 visit received lampalizumab, 10 mg, by ITV injection, administered every 6 weeks.	
Subject analysis set title	All Subjects
Subject analysis set type	Sub-group analysis
Subject analysis set description: All subjects in the study received lampalizumab 10 mg, ITV, Q4W or Q6W.	

Primary: Percentage of Subjects with Ocular Adverse Events (AEs) by Severity

End point title	Percentage of Subjects with Ocular Adverse Events (AEs) by Severity ^[1]
End point description: An AE was defined as any unfavourable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product, whether considered related to the medicinal product, any new disease or exacerbation of an existing disease, recurrence of an intermittent medical condition, or any deterioration in a laboratory value or other clinical test. Ocular AEs are the events which are localized in the ocular region. The safety-evaluable population included all subjects who enrolled in the extension study and received at least one lampalizumab injection in the extension study.	
End point type	Primary
End point timeframe: Up to approximately one year	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics only

End point values	Lampalizumab Q4W - Treatment-Naive	Lampalizumab Q4W – Previously Treated	Lampalizumab Q6W - Treatment-Naive	Lampalizumab Q6W – Previously Treated
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	145	274	146	277
Units: percentage of subjects				
number (not applicable)				
Any severity	37.2	40.1	24.7	33.2
Mild	25.5	26.6	16.4	21.7
Moderate	9.7	11.3	8.2	10.1
Severe	2.1	2.2	0	1.4

End point values	All Subjects			
Subject group type	Subject analysis set			
Number of subjects analysed	842			
Units: percentage of subjects				
number (not applicable)				
Any severity	34.7			
Mild	23.0			
Moderate	10.1			
Severe	1.5			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Systemic (Non-Ocular) AEs by Severity

End point title	Percentage of Subjects with Systemic (Non-Ocular) AEs by Severity ^[2]
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End point description:

An AE was defined as any unfavourable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product, whether considered related to the medicinal product, any new disease or exacerbation of an existing disease, recurrence of an intermittent medical condition, or any deterioration in a laboratory value or other clinical test. The safety-evaluable population included all subjects who enrolled in the extension study and received at least one lampalizumab injection in the extension study.

End point type	Primary
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End point timeframe:

Up to approximately one year

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics only

End point values	Lampalizumab Q4W - Treatment-Naive	Lampalizumab Q4W - Previously Treated	Lampalizumab Q6W - Treatment-Naive	Lampalizumab Q6W - Previously Treated
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	145	274	146	277
Units: percentage of subjects				
number (not applicable)				
Any severity	55.2	54.0	41.8	51.3
Mild	18.6	20.1	17.8	20.9
Moderate	28.3	20.4	18.5	20.2
Severe	8.3	13.5	5.5	10.1

End point values	All Subjects			
Subject group type	Subject analysis set			
Number of subjects analysed	842			
Units: percentage of subjects				
number (not applicable)				
Any severity	51.2			
Mild	19.7			
Moderate	21.4			
Severe	10.1			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Anti-Lampalizumab Antibodies

End point title	Percentage of Subjects with Anti-Lampalizumab Antibodies ^[3]
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End point description:

The immunogenicity analysis included subjects with at least one predose and one postdose anti-lampalizumab antibodies assessment. Predose was defined as prior to the first dose in the extension study for the prior sham subjects, and prior to the first dose in the parent study for the prior lampalizumab subjects. The safety-evaluable population included all subjects who enrolled in the extension study and received at least one lampalizumab injection in the extension study. Data is reported for evaluable subjects.

End point type	Primary
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End point timeframe:

Week 48

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics only

End point values	Lampalizumab Q4W - Treatment-Naive	Lampalizumab Q4W - Previously Treated	Lampalizumab Q6W - Treatment-Naive	Lampalizumab Q6W - Previously Treated
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	6	2	6
Units: percentage of subjects				
number (not applicable)	0.0	0.0	0.0	0.0

End point values	All Subjects			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: percentage of subjects				
number (not applicable)	0.0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to approximately one year

Adverse event reporting additional description:

The safety-evaluable population included all subjects who enrolled in the extension study and received at least one lampalizumab injection in the extension study.

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	Lampalizumab Q4W - Treatment-Naive
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Reporting group description:

Subjects who received sham comparator every 4 weeks in one of the parent studies and completed the Week 96 visit received lampalizumab, 10 milligrams (mg), by intravitreal (ITV) injection, administered every 4 weeks.

Reporting group title	Lampalizumab Q4W – Previously Treated
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Reporting group description:

Subjects who received lampalizumab every 4 weeks in one of the parent studies and completed the Week 96 visit received lampalizumab, 10 mg, by ITV injection, administered every 4 weeks.

Reporting group title	Lampalizumab Q6W - Treatment-Naive
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Reporting group description:

Subjects who received sham comparator every 6 weeks in one of the parent studies and completed the Week 96 visit received lampalizumab, 10 mg, by ITV injection, administered every 6 weeks.

Reporting group title	Lampalizumab Q6W – Previously Treated
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Reporting group description:

Subjects who received lampalizumab every 6 weeks in one of the parent studies and completed the Week 96 visit received lampalizumab, 10 mg, by ITV injection, administered every 6 weeks.

Reporting group title	All Subjects
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Reporting group description:

All subjects in the study received lampalizumab 10 mg, ITV, Q4W or Q6W.

Serious adverse events	Lampalizumab Q4W - Treatment-Naive	Lampalizumab Q4W - Previously Treated	Lampalizumab Q6W - Treatment-Naive
Total subjects affected by serious adverse events			
subjects affected / exposed	31 / 145 (21.38%)	58 / 274 (21.17%)	14 / 146 (9.59%)
number of deaths (all causes)	3	3	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer			
subjects affected / exposed	0 / 145 (0.00%)	1 / 274 (0.36%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer metastatic			

subjects affected / exposed	0 / 145 (0.00%)	1 / 274 (0.36%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Adenocarcinoma gastric			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal cell carcinoma			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder neoplasm			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	0 / 145 (0.00%)	1 / 274 (0.36%)	0 / 146 (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
Myelodysplastic syndrome			
subjects affected / exposed	1 / 145 (0.69%)	0 / 274 (0.00%)	0 / 146 (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
Neoplasm malignant			
subjects affected / exposed	0 / 145 (0.00%)	1 / 274 (0.36%)	0 / 146 (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
Pancreatic carcinoma			
subjects affected / exposed	0 / 145 (0.00%)	1 / 274 (0.36%)	0 / 146 (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
Pancreatic carcinoma metastatic			

subjects affected / exposed	1 / 145 (0.69%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Skin cancer			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small cell lung cancer metastatic			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of the vulva			
subjects affected / exposed	0 / 145 (0.00%)	1 / 274 (0.36%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Vascular disorders			
Aortic calcification			
subjects affected / exposed	1 / 145 (0.69%)	0 / 274 (0.00%)	0 / 146 (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
Deep vein thrombosis			
subjects affected / exposed	0 / 145 (0.00%)	1 / 274 (0.36%)	0 / 146 (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
Hypertension			
subjects affected / exposed	0 / 145 (0.00%)	1 / 274 (0.36%)	0 / 146 (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
Hypotension			
subjects affected / exposed	0 / 145 (0.00%)	1 / 274 (0.36%)	0 / 146 (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
Peripheral artery occlusion			

subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Temporal arteritis			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vasculitis			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 145 (0.69%)	2 / 274 (0.73%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	1 / 145 (0.69%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden cardiac death			
subjects affected / exposed	0 / 145 (0.00%)	1 / 274 (0.36%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Systemic inflammatory response syndrome			
subjects affected / exposed	1 / 145 (0.69%)	0 / 274 (0.00%)	0 / 146 (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
Reproductive system and breast			

disorders			
Cystocele			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postmenopausal haemorrhage			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectocele			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 145 (0.69%)	0 / 274 (0.00%)	0 / 146 (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
Pneumonia aspiration			
subjects affected / exposed	1 / 145 (0.69%)	0 / 274 (0.00%)	0 / 146 (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
Pulmonary embolism			
subjects affected / exposed	0 / 145 (0.00%)	1 / 274 (0.36%)	0 / 146 (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
Pulmonary fibrosis			
subjects affected / exposed	0 / 145 (0.00%)	1 / 274 (0.36%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			

subjects affected / exposed	0 / 145 (0.00%)	1 / 274 (0.36%)	0 / 146 (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
Dyspnoea			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercapnia			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleurisy			
subjects affected / exposed	0 / 145 (0.00%)	1 / 274 (0.36%)	0 / 146 (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
Respiratory distress			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	1 / 146 (0.68%)
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 failure			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sleep apnoea syndrome			

subjects affected / exposed	1 / 145 (0.69%)	0 / 274 (0.00%)	0 / 146 (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
Psychiatric disorders			
Hallucination			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status changes			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Intraocular pressure increased			
subjects affected / exposed	3 / 145 (2.07%)	4 / 274 (1.46%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	1 / 6	1 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood lactic acid increased			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
International normalised ratio increased			
subjects affected / exposed	1 / 145 (0.69%)	0 / 274 (0.00%)	0 / 146 (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
Injury, poisoning and procedural complications			
Corneal abrasion			
subjects affected / exposed	0 / 145 (0.00%)	1 / 274 (0.36%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			

subjects affected / exposed	0 / 145 (0.00%)	4 / 274 (1.46%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic fracture			
subjects affected / exposed	0 / 145 (0.00%)	3 / 274 (1.09%)	0 / 146 (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
Femoral neck fracture			
subjects affected / exposed	0 / 145 (0.00%)	1 / 274 (0.36%)	0 / 146 (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
Foot fracture			
subjects affected / exposed	0 / 145 (0.00%)	1 / 274 (0.36%)	0 / 146 (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
Radius fracture			
subjects affected / exposed	0 / 145 (0.00%)	1 / 274 (0.36%)	0 / 146 (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
Tendon rupture			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle fracture			
subjects affected / exposed	0 / 145 (0.00%)	1 / 274 (0.36%)	0 / 146 (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
Femur fracture			

subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fracture displacement			
subjects affected / exposed	1 / 145 (0.69%)	0 / 274 (0.00%)	0 / 146 (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
Hand fracture			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laceration			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar vertebral fracture			
subjects affected / exposed	0 / 145 (0.00%)	1 / 274 (0.36%)	0 / 146 (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 fracture			
subjects affected / exposed	0 / 145 (0.00%)	1 / 274 (0.36%)	0 / 146 (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
Upper limb fracture			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skull fracture			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			

subjects affected / exposed	2 / 145 (1.38%)	3 / 274 (1.09%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	1 / 145 (0.69%)	1 / 274 (0.36%)	0 / 146 (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
Myocardial infarction			
subjects affected / exposed	1 / 145 (0.69%)	1 / 274 (0.36%)	0 / 146 (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
Acute myocardial infarction			
subjects affected / exposed	1 / 145 (0.69%)	0 / 274 (0.00%)	0 / 146 (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
Angina pectoris			
subjects affected / exposed	1 / 145 (0.69%)	0 / 274 (0.00%)	0 / 146 (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
Atrial flutter			
subjects affected / exposed	0 / 145 (0.00%)	1 / 274 (0.36%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diastolic dysfunction			

subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 145 (0.00%)	2 / 274 (0.73%)	0 / 146 (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
Transient ischaemic attack			
subjects affected / exposed	0 / 145 (0.00%)	2 / 274 (0.73%)	0 / 146 (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
Cerebral small vessel ischaemic disease			
subjects affected / exposed	1 / 145 (0.69%)	0 / 274 (0.00%)	0 / 146 (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 with lewy bodies			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wernicke's encephalopathy			

subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Visual acuity reduced			
subjects affected / exposed	1 / 145 (0.69%)	4 / 274 (1.46%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 1	0 / 4	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neovascular age-related macular degeneration			
subjects affected / exposed	1 / 145 (0.69%)	1 / 274 (0.36%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ocular hypertension			
subjects affected / exposed	0 / 145 (0.00%)	2 / 274 (0.73%)	0 / 146 (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
Visual impairment			
subjects affected / exposed	1 / 145 (0.69%)	1 / 274 (0.36%)	0 / 146 (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
Dellen			
subjects affected / exposed	0 / 145 (0.00%)	1 / 274 (0.36%)	0 / 146 (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
Dry age-related macular degeneration			
subjects affected / exposed	1 / 145 (0.69%)	0 / 274 (0.00%)	0 / 146 (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

Iritis			
subjects affected / exposed	0 / 145 (0.00%)	1 / 274 (0.36%)	0 / 146 (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
Vitreous haemorrhage			
subjects affected / exposed	1 / 145 (0.69%)	0 / 274 (0.00%)	0 / 146 (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
Cataract			
subjects affected / exposed	1 / 145 (0.69%)	0 / 274 (0.00%)	0 / 146 (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
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 145 (0.00%)	1 / 274 (0.36%)	0 / 146 (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
Ileus			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal incarcerated hernia			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	1 / 145 (0.69%)	0 / 274 (0.00%)	0 / 146 (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
Diverticulum intestinal			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			

subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malabsorption			
subjects affected / exposed	1 / 145 (0.69%)	0 / 274 (0.00%)	0 / 146 (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 gastrointestinal haemorrhage			
subjects affected / exposed	1 / 145 (0.69%)	0 / 274 (0.00%)	0 / 146 (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
Vomiting			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 145 (0.00%)	1 / 274 (0.36%)	0 / 146 (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	0 / 145 (0.00%)	1 / 274 (0.36%)	0 / 146 (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 and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal artery stenosis			
subjects affected / exposed	0 / 145 (0.00%)	1 / 274 (0.36%)	0 / 146 (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 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 145 (0.00%)	1 / 274 (0.36%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis			
subjects affected / exposed	0 / 145 (0.00%)	2 / 274 (0.73%)	0 / 146 (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	0 / 145 (0.00%)	0 / 274 (0.00%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coccydynia			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	1 / 145 (0.69%)	0 / 274 (0.00%)	0 / 146 (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
Joint instability			
subjects affected / exposed	1 / 145 (0.69%)	0 / 274 (0.00%)	0 / 146 (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
Pain in extremity			
subjects affected / exposed	1 / 145 (0.69%)	0 / 274 (0.00%)	0 / 146 (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
Rotator cuff syndrome			

subjects affected / exposed	0 / 145 (0.00%)	1 / 274 (0.36%)	0 / 146 (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
Infections and infestations			
Endophthalmitis			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	3 / 145 (2.07%)	2 / 274 (0.73%)	2 / 146 (1.37%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	2 / 145 (1.38%)	1 / 274 (0.36%)	0 / 146 (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
Cellulitis			
subjects affected / exposed	0 / 145 (0.00%)	2 / 274 (0.73%)	0 / 146 (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
Sepsis			
subjects affected / exposed	1 / 145 (0.69%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Central nervous system infection			

subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	1 / 145 (0.69%)	0 / 274 (0.00%)	0 / 146 (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
Device related infection			
subjects affected / exposed	0 / 145 (0.00%)	1 / 274 (0.36%)	0 / 146 (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	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis bacterial			
subjects affected / exposed	1 / 145 (0.69%)	0 / 274 (0.00%)	0 / 146 (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
Escherichia bacteraemia			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	0 / 145 (0.00%)	1 / 274 (0.36%)	0 / 146 (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 tract infection			
subjects affected / exposed	1 / 145 (0.69%)	0 / 274 (0.00%)	0 / 146 (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
Metabolism and nutrition disorders			
Dehydration			

subjects affected / exposed	1 / 145 (0.69%)	0 / 274 (0.00%)	1 / 146 (0.68%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	1 / 145 (0.69%)	1 / 274 (0.36%)	0 / 146 (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
Gout			
subjects affected / exposed	0 / 145 (0.00%)	1 / 274 (0.36%)	0 / 146 (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
Hypoalbuminaemia			
subjects affected / exposed	1 / 145 (0.69%)	0 / 274 (0.00%)	0 / 146 (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
Hypoglycaemia			
subjects affected / exposed	0 / 145 (0.00%)	0 / 274 (0.00%)	0 / 146 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	1 / 145 (0.69%)	0 / 274 (0.00%)	0 / 146 (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
Hypovolaemia			
subjects affected / exposed	1 / 145 (0.69%)	0 / 274 (0.00%)	0 / 146 (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

Serious adverse events	Lampalizumab Q6W – Previously Treated	All Subjects	
Total subjects affected by serious adverse events			
subjects affected / exposed	50 / 277 (18.05%)	153 / 842 (18.17%)	
number of deaths (all causes)	9	15	
number of deaths resulting from adverse events	0	0	

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer			
subjects affected / exposed	0 / 277 (0.00%)	2 / 842 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer metastatic			
subjects affected / exposed	0 / 277 (0.00%)	2 / 842 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Adenocarcinoma gastric			
subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Basal cell carcinoma			
subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder neoplasm			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelodysplastic syndrome			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasm malignant			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pancreatic carcinoma			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma metastatic			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Skin cancer			
subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small cell lung cancer metastatic			
subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of the vulva			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Vascular disorders			
Aortic calcification			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hypotension			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery occlusion			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Temporal arteritis			
subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vasculitis			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 277 (0.36%)	5 / 842 (0.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	3 / 277 (1.08%)	4 / 842 (0.48%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 3	0 / 4	
Oedema peripheral			
subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden cardiac death			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Cystocele			
subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postmenopausal haemorrhage			
subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectocele			
subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	2 / 277 (0.72%)	3 / 842 (0.36%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	1 / 277 (0.36%)	2 / 842 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Pulmonary embolism			
subjects affected / exposed	1 / 277 (0.36%)	2 / 842 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary fibrosis			

subjects affected / exposed	0 / 277 (0.00%)	2 / 842 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercapnia			
subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleurisy			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			

subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Sleep apnoea syndrome			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Hallucination			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Intraocular pressure increased			
subjects affected / exposed	5 / 277 (1.81%)	13 / 842 (1.54%)	
occurrences causally related to treatment / all	2 / 10	4 / 22	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood lactic acid increased			
subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
International normalised ratio increased			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Corneal abrasion			

subjects affected / exposed	0 / 277 (0.00%)	2 / 842 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	5 / 277 (1.81%)	10 / 842 (1.19%)	
occurrences causally related to treatment / all	0 / 5	0 / 11	
deaths causally related to treatment / all	0 / 1	0 / 1	
Hip fracture			
subjects affected / exposed	2 / 277 (0.72%)	3 / 842 (0.36%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	0 / 277 (0.00%)	3 / 842 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	1 / 277 (0.36%)	2 / 842 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture			
subjects affected / exposed	1 / 277 (0.36%)	2 / 842 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	1 / 277 (0.36%)	2 / 842 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	2 / 277 (0.72%)	2 / 842 (0.24%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			

subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture displacement			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand fracture			
subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laceration			
subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skull fracture			

subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 277 (0.36%)	6 / 842 (0.71%)	
occurrences causally related to treatment / all	0 / 1	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	4 / 277 (1.44%)	4 / 842 (0.48%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			
subjects affected / exposed	0 / 277 (0.00%)	2 / 842 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 277 (0.00%)	2 / 842 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			

subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Diastolic dysfunction			
subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 277 (0.00%)	2 / 842 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 277 (0.00%)	2 / 842 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral small vessel ischaemic disease			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dementia with lewy bodies			
subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			

subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wernicke's encephalopathy			
subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Visual acuity reduced			
subjects affected / exposed	2 / 277 (0.72%)	8 / 842 (0.95%)	
occurrences causally related to treatment / all	0 / 2	1 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neovascular age-related macular degeneration			
subjects affected / exposed	2 / 277 (0.72%)	5 / 842 (0.59%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ocular hypertension			
subjects affected / exposed	0 / 277 (0.00%)	2 / 842 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Visual impairment			
subjects affected / exposed	0 / 277 (0.00%)	2 / 842 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dellen			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Dry age-related macular degeneration			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iritis			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vitreous haemorrhage			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cataract			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 277 (0.72%)	3 / 842 (0.36%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	2 / 277 (0.72%)	2 / 842 (0.24%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal incarcerated hernia			
subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Diverticulum intestinal			
subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malabsorption			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 277 (0.36%)	2 / 842 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Renal artery stenosis			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	1 / 277 (0.36%)	3 / 842 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis			
subjects affected / exposed	0 / 277 (0.00%)	2 / 842 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coccydynia			
subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint instability			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pain in extremity			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Endophthalmitis			
subjects affected / exposed	1 / 277 (0.36%)	2 / 842 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	5 / 277 (1.81%)	12 / 842 (1.43%)	
occurrences causally related to treatment / all	0 / 5	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	2 / 277 (0.72%)	5 / 842 (0.59%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 277 (0.36%)	3 / 842 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 277 (0.36%)	2 / 842 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Bacteraemia			
subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			

subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Central nervous system infection			
subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis bacterial			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia bacteraemia			
subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			

subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 277 (0.36%)	3 / 842 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 277 (0.00%)	2 / 842 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gout			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoalbuminaemia			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	1 / 277 (0.36%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemia			
subjects affected / exposed	0 / 277 (0.00%)	1 / 842 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Lampalizumab Q4W - Treatment-Naive	Lampalizumab Q4W - Previously Treated	Lampalizumab Q6W - Treatment-Naive
Total subjects affected by non-serious adverse events subjects affected / exposed	41 / 145 (28.28%)	63 / 274 (22.99%)	26 / 146 (17.81%)
Investigations Intraocular pressure increased subjects affected / exposed occurrences (all)	2 / 145 (1.38%) 2	23 / 274 (8.39%) 34	5 / 146 (3.42%) 7
Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all)	11 / 145 (7.59%) 12	12 / 274 (4.38%) 16	5 / 146 (3.42%) 6
Eye disorders Conjunctival haemorrhage subjects affected / exposed occurrences (all) Eye pain subjects affected / exposed occurrences (all)	17 / 145 (11.72%) 22 8 / 145 (5.52%) 8	17 / 274 (6.20%) 20 8 / 274 (2.92%) 14	12 / 146 (8.22%) 16 5 / 146 (3.42%) 6
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	11 / 145 (7.59%) 12	12 / 274 (4.38%) 13	3 / 146 (2.05%) 3

Non-serious adverse events	Lampalizumab Q6W - Previously Treated	All Subjects	
Total subjects affected by non-serious adverse events subjects affected / exposed	56 / 277 (20.22%)	186 / 842 (22.09%)	
Investigations Intraocular pressure increased subjects affected / exposed occurrences (all)	17 / 277 (6.14%) 22	47 / 842 (5.58%) 65	
Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all)	14 / 277 (5.05%) 14	42 / 842 (4.99%) 48	
Eye disorders			

Conjunctival haemorrhage subjects affected / exposed occurrences (all)	20 / 277 (7.22%) 25	66 / 842 (7.84%) 83	
Eye pain subjects affected / exposed occurrences (all)	11 / 277 (3.97%) 14	32 / 842 (3.80%) 42	
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	6 / 277 (2.17%) 7	32 / 842 (3.80%) 35	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 July 2017	Added an independent Data Monitoring Committee to monitor subjects long-term safety following a recommendation from Ethics Committee; information regarding lampalizumab formulation, packaging, storage, and handling as well as reconstitution and study administration instructions were moved from Section 4.3.1 of the protocol to Appendices 4 to 6 to the Pharmacy Manual to assist sites in locating necessary information promptly; clarified the procedures across various protocol sections to aid the transition of subjects from the parent studies to this extension study (e.g., clarified the dose-interruption, treatment-discontinuation, and study-withdrawal criteria language; reorganized the study treatment discontinuation criteria; clarified the reporting requirements for serious adverse events (SAEs) and adverse events of special interest (AESIs) during the transition period between the parent study and this extension study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

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

Notes:

Limitations and caveats

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

The study was terminated early by the Sponsor because the compound had demonstrated lack of efficacy. Thus, no participant in this study completed the full duration of treatment.

Notes: