Clinical trial results:
Safety and Efficacy of Abicipar Pegol (AGN-150998) in Patients With Neovascular Age-related Macular Degeneration (CEDAR Study)

Summary

EudraCT number	2014-004579-22
Trial protocol	CZ DE AT LV ES
Global end of trial date	19 June 2019

Results information

Result version number	v1 (current)
This version publication date	01 July 2020
First version publication date	01 July 2020

Trial information

Trial identification

Sponsor protocol code	150998-005

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02462928
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Allergan
Sponsor organisation address	1st Floor, Marlow International, The Parkway, Marlow, Buckinghamshire, United Kingdom, SL7 1YL
Public contact	Clinical Trials Registry Team, Allergan plc, 001 8772778566, IR-CTRegistration@Allergan.com
Scientific contact	Therapeutic Area Head, Allergan, 001 862-261-7000, IR-CTRegistration@Allergan.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	19 June 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 June 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this trial is to evaluate safety and efficacy of abicipar pegol in participants with neovascular age-related macular degeneration.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 June 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 20
Country: Number of subjects enrolled	Switzerland: 24
Country: Number of subjects enrolled	Czech Republic: 55
Country: Number of subjects enrolled	Germany: 63
Country: Number of subjects enrolled	Spain: 85
Country: Number of subjects enrolled	France: 24
Country: Number of subjects enrolled	Latvia: 17
Country: Number of subjects enrolled	Argentina: 38
Country: Number of subjects enrolled	Chile: 6
Country: Number of subjects enrolled	Colombia: 13
Country: Number of subjects enrolled	Hong Kong: 12
Country: Number of subjects enrolled	Israel: 67
Country: Number of subjects enrolled	Korea, Republic of: 80
Country: Number of subjects enrolled	New Zealand: 9
Country: Number of subjects enrolled	Philippines: 16
Country: Number of subjects enrolled	Singapore: 17
Country: Number of subjects enrolled	United States: 393
Worldwide total number of subjects	939
EEA total number of subjects	264

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)	72
From 65 to 84 years	706
85 years and over	161

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 939 participants were enrolled in the study and 934 of them were treated.

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	Investigator, Assessor, Carer, Monitor, Subject, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	Abicipar Pegol 2 mg (2Q8)

Arm description:

Abicipar pegol 2 mg was administered to the study eye by intravitreal injection on Day 1, Week 4, Week 8 and every 8 weeks (2Q8) thereafter through Week 96. Scheduled visits occurred every 4 weeks. To maintain masking, sham was administered to the study eye at scheduled visits where abicipar was not administered.

Arm type	Experimental
Investigational medicinal product name	Sham Procedure
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in needle-free injector
Routes of administration	Intravitreal use

Dosage and administration details:

Sham injection.

Investigational medicinal product name	Abicipar Pegol
Investigational medicinal product code	
Other name	AGN-150998
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

Abicipar pegol intravitreal injection.

Arm title	Abicipar Pegol 2 mg (2Q12)

Arm description:

Abicipar pegol 2 mg was administered to the study eye by intravitreal injection on Day 1, Week 4, Week 12, and every 12 weeks (2Q12) thereafter through week 96. Scheduled visits occurred every 4 weeks. To maintain masking, sham was administered to the study eye at scheduled visits where abicipar was not administered.

Arm type	Experimental
Investigational medicinal product name	Abicipar Pegol
Investigational medicinal product code	
Other name	AGN-150998
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

Abicipar pegol intravitreal injection.

Investigational medicinal product name	Sham Procedure
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in needle-free injector
Routes of administration	Intravitreal use

Dosage and administration details:

Sham injection.

Arm title	Ranibizumab 0.5 mg (rQ4)

Arm description:

Ranibizumab (Lucentis®) 0.5 mg was administered to the study eye by intravitreal injection every 4 weeks (rQ4) from Day 1 through Week 96.

Arm type	Active comparator
Investigational medicinal product name	Ranibizumab
Investigational medicinal product code	
Other name	Lucentis®
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

Ranibizumab intravitreal injection.

Number of subjects in period 1	Abicipar Pegol 2 mg (2Q8)	Abicipar Pegol 2 mg (2Q12)	Ranibizumab 0.5 mg (rQ4)
Started	314	313	312
Completed	224	221	255
Not completed	90	92	57
Screen Failure:Missed Exclusion Criteria	1	1	2
Adverse event, non-fatal	47	51	25
Withdrawal by Patient	31	21	21
Lost to follow-up	4	4	1
Reason not Specified	4	6	5
Lack of efficacy	3	8	3
Protocol deviation	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Abicipar Pegol 2 mg (2Q8)
Reporting group description:	
Abicipar pegol 2 mg was administered to the study eye by intravitreal injection on Day 1, Week 4, Week 8 and every 8 weeks (2Q8) thereafter through Week 96. Scheduled visits occurred every 4 weeks. To maintain masking, sham was administered to the study eye at scheduled visits where abicipar was not administered.	
Reporting group title	Abicipar Pegol 2 mg (2Q12)
Reporting group description:	
Abicipar pegol 2 mg was administered to the study eye by intravitreal injection on Day 1, Week 4, Week 12, and every 12 weeks (2Q12) thereafter through week 96. Scheduled visits occurred every 4 weeks. To maintain masking, sham was administered to the study eye at scheduled visits where abicipar was not administered.	
Reporting group title	Ranibizumab 0.5 mg (rQ4)
Reporting group description:	
Ranibizumab (Lucentis®) 0.5 mg was administered to the study eye by intravitreal injection every 4 weeks (rQ4) from Day 1 through Week 96.	

Reporting group values	Abicipar Pegol 2 mg (2Q8)	Abicipar Pegol 2 mg (2Q12)	Ranibizumab 0.5 mg (rQ4)
Number of subjects	314	313	312
Age categorical Units: Subjects			
Adults (18-64 years)	29	20	23
From 65-84 years	238	243	225
85 years and over	47	50	64
Age Continuous Units: years			
arithmetic mean	75.5	76.9	77.1
standard deviation	± 8.4	± 8.0	± 8.4
Sex: Female, Male Units: participants			
Female	162	183	169
Male	152	130	143
Race/Ethnicity, Customized Units: Subjects			
White	249	248	243
Black	2	1	1
Asian	49	44	45
Hispanic	12	12	11
Not Reported	2	8	12
Best-corrected Visual Acuity (BCVA)			
BCVA was measured using eye chart and is reported as number of letters read correctly using the ETDRS Scale (ranging from 0 to 100 letters) in study eye. Lower number of letters read correctly on eye chart, worse the vision (or visual acuity). Study eye is defined as eye that meets entry criteria. If both eyes met entry criteria, eye with worse BCVA at baseline (Day 1) was selected as study eye. If both eyes had same BCVA values at baseline (Day 1), then participant had to select their non-dominant eye for treatment, or else right eye was selected as study eye. [n=313, 313, 312]			
Units: letters			
arithmetic mean	56.4	56.5	56.5
standard deviation	± 13.4	± 12.9	± 12.5

Central Retinal Thickness (CRT)			
CRT was assessed using spectral domain optical coherence tomography (SD-OCT), a non-invasive diagnostic system providing high-resolution imaging sections of the retina. SD-OCT was performed in the study eye after pupil dilation. The study eye is defined as the eye that meets the entry criteria. If both eyes met the entry criteria, the eye with the worse BCVA at baseline (Day 1) was selected as the study eye. If both eyes had same BCVA values at Day 1, then the participant selected their non-dominant eye for treatment, or else the right eye was selected as the study eye. [n=313, 313, 312]			
Units: microns			
arithmetic mean	384.7	378.4	378.2
standard deviation	± 142.7	± 119.1	± 120.5
National Eye Institute Visual Functioning Questionnaire-25 (NEI-VFQ-25)			
NEI-VFQ-25 consists of 25 vision-targeted questions that represent 11 vision-related quality of life subscales and one general health item. Responses of individual participants were recorded as scores that ranged between 0 (worst) to 100 (best vision related function) with higher scale indicating better vision related function. The overall composite score is then calculated by averaging over all 11 vision-targeted subscale scores, excluding the general health score. Overall composite score was calculated based on mean of non-missing subscales. [n=313, 313, 311]			
Units: score on a scale			
arithmetic mean	78.7	77.3	77.1
standard deviation	± 14.8	± 15.1	± 15.6

Reporting group values	Total		
Number of subjects	939		
Age categorical			
Units: Subjects			
Adults (18-64 years)	72		
From 65-84 years	706		
85 years and over	161		
Age Continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male			
Units: participants			
Female	514		
Male	425		
Race/Ethnicity, Customized			
Units: Subjects			
White	740		
Black	4		
Asian	138		
Hispanic	35		
Not Reported	22		
Best-corrected Visual Acuity (BCVA)			
BCVA was measured using eye chart and is reported as number of letters read correctly using the ETDRS Scale (ranging from 0 to 100 letters) in study eye. Lower number of letters read correctly on eye chart, worse the vision (or visual acuity). Study eye is defined as eye that meets entry criteria. If both eyes met entry criteria, eye with worse BCVA at baseline (Day 1) was selected as study eye. If both eyes had same BCVA values at baseline (Day 1), then participant had to select their non-dominant eye for treatment, or else right eye was selected as study eye. [n=313, 313, 312]			
Units: letters			
arithmetic mean			
standard deviation	-		
Central Retinal Thickness (CRT)			
CRT was assessed using spectral domain optical coherence tomography (SD-OCT), a non-invasive			

diagnostic system providing high-resolution imaging sections of the retina. SD-OCT was performed in the study eye after pupil dilation. The study eye is defined as the eye that meets the entry criteria. If both eyes met the entry criteria, the eye with the worse BCVA at baseline (Day 1) was selected as the study eye. If both eyes had same BCVA values at Day 1, then the participant selected their non-dominant eye for treatment, or else the right eye was selected as the study eye. [n=313, 313, 312]			
Units: microns arithmetic mean standard deviation	- 		
National Eye Institute Visual Functioning Questionnaire-25 (NEI-VFQ-25)			
NEI-VFQ-25 consists of 25 vision-targeted questions that represent 11 vision-related quality of life subscales and one general health item. Responses of individual participants were recorded as scores that ranged between 0 (worst) to 100 (best vision related function) with higher scale indicating better vision related function. The overall composite score is then calculated by averaging over all 11 vision-targeted subscale scores, excluding the general health score. Overall composite score was calculated based on mean of non-missing subscales. [n=313, 313, 311]			
Units: score on a scale arithmetic mean standard deviation	- 		

Subject analysis sets

Subject analysis set title	Abicipar Pegol 2 mg (2Q8)
Subject analysis set type	Per protocol

Subject analysis set description:

Abicipar pegol 2 mg was administered to the study eye by intravitreal injection on Day 1, Week 4, Week 8 and every 8 weeks (2Q8) thereafter through Week 96. Scheduled visits occurred every 4 weeks. To maintain masking, sham was administered to the study eye at scheduled visits where abicipar was not administered. Per-protocol (PP) population included all randomized and treated participants without any protocol deviations that impacted the primary efficacy variable and with treatment compliance to represent the intended regimen adequately.

Subject analysis set title	Abicipar Pegol 2 mg (2Q12)
Subject analysis set type	Per protocol

Subject analysis set description:

Abicipar pegol 2 mg was administered to the study eye by intravitreal injection on Day 1, Week 4, Week 12, and every 12 weeks (2Q12) thereafter through week 96. Scheduled visits occurred every 4 weeks. To maintain masking, sham was administered to the study eye at scheduled visits where abicipar was not administered. PP population included all randomized and treated participants without any protocol deviations that impacted the primary efficacy variable and with treatment compliance to represent the intended regimen adequately.

Subject analysis set title	Ranibizumab 0.5 mg (rQ4)
Subject analysis set type	Per protocol

Subject analysis set description:

Ranibizumab (Lucentis®) 0.5 mg was administered to the study eye by intravitreal injection every 4 weeks (rQ4) from Day 1 through Week 96. PP population included all randomized and treated participants without any protocol deviations that impacted the primary efficacy variable and with treatment compliance to represent the intended regimen adequately.

Reporting group values	Abicipar Pegol 2 mg (2Q8)	Abicipar Pegol 2 mg (2Q12)	Ranibizumab 0.5 mg (rQ4)
Number of subjects	265	262	290
Age categorical Units: Subjects			
Adults (18-64 years) From 65-84 years 85 years and over			

Age Continuous Units: years arithmetic mean standard deviation	± 	± 	±
Sex: Female, Male Units: participants Female Male			
Race/Ethnicity, Customized Units: Subjects White Black Asian Hispanic Not Reported			
Best-corrected Visual Acuity (BCVA)			
BCVA was measured using eye chart and is reported as number of letters read correctly using the ETDRS Scale (ranging from 0 to 100 letters) in study eye. Lower number of letters read correctly on eye chart, worse the vision (or visual acuity). Study eye is defined as eye that meets entry criteria. If both eyes met entry criteria, eye with worse BCVA at baseline (Day 1) was selected as study eye. If both eyes had same BCVA values at baseline (Day 1), then participant had to select their non-dominant eye for treatment, or else right eye was selected as study eye. [n=313, 313, 312]			
Units: letters arithmetic mean standard deviation	56.7 ± 13.3	56.3 ± 13.1	56.5 ± 12.6
Central Retinal Thickness (CRT)			
CRT was assessed using spectral domain optical coherence tomography (SD-OCT), a non-invasive diagnostic system providing high-resolution imaging sections of the retina. SD-OCT was performed in the study eye after pupil dilation. The study eye is defined as the eye that meets the entry criteria. If both eyes met the entry criteria, the eye with the worse BCVA at baseline (Day 1) was selected as the study eye. If both eyes had same BCVA values at Day 1, then the participant selected their non-dominant eye for treatment, or else the right eye was selected as the study eye. [n=313, 313, 312]			
Units: microns arithmetic mean standard deviation	± 	± 	±
National Eye Institute Visual Functioning Questionnaire-25 (NEI-VFQ-25)			
NEI-VFQ-25 consists of 25 vision-targeted questions that represent 11 vision-related quality of life subscales and one general health item. Responses of individual participants were recorded as scores that ranged between 0 (worst) to 100 (best vision related function) with higher scale indicating better vision related function. The overall composite score is then calculated by averaging over all 11 vision-targeted subscale scores, excluding the general health score. Overall composite score was calculated based on mean of non-missing subscales. [n=313, 313, 311]			
Units: score on a scale arithmetic mean standard deviation	± 	± 	±

End points reporting groups

Reporting group title	Abicipar Pegol 2 mg (2Q8)

Reporting group description:

Abicipar pegol 2 mg was administered to the study eye by intravitreal injection on Day 1, Week 4, Week 8 and every 8 weeks (2Q8) thereafter through Week 96. Scheduled visits occurred every 4 weeks. To maintain masking, sham was administered to the study eye at scheduled visits where abicipar was not administered.

Reporting group title	Abicipar Pegol 2 mg (2Q12)

Reporting group description:

Abicipar pegol 2 mg was administered to the study eye by intravitreal injection on Day 1, Week 4, Week 12, and every 12 weeks (2Q12) thereafter through week 96. Scheduled visits occurred every 4 weeks. To maintain masking, sham was administered to the study eye at scheduled visits where abicipar was not administered.

Reporting group title	Ranibizumab 0.5 mg (rQ4)

Reporting group description:

Ranibizumab (Lucentis®) 0.5 mg was administered to the study eye by intravitreal injection every 4 weeks (rQ4) from Day 1 through Week 96.

Subject analysis set title	Abicipar Pegol 2 mg (2Q8)
Subject analysis set type	Per protocol

Subject analysis set description:

Abicipar pegol 2 mg was administered to the study eye by intravitreal injection on Day 1, Week 4, Week 8 and every 8 weeks (2Q8) thereafter through Week 96. Scheduled visits occurred every 4 weeks. To maintain masking, sham was administered to the study eye at scheduled visits where abicipar was not administered. Per-protocol (PP) population included all randomized and treated participants without any protocol deviations that impacted the primary efficacy variable and with treatment compliance to represent the intended regimen adequately.

Subject analysis set title	Abicipar Pegol 2 mg (2Q12)
Subject analysis set type	Per protocol

Subject analysis set description:

Abicipar pegol 2 mg was administered to the study eye by intravitreal injection on Day 1, Week 4, Week 12, and every 12 weeks (2Q12) thereafter through week 96. Scheduled visits occurred every 4 weeks. To maintain masking, sham was administered to the study eye at scheduled visits where abicipar was not administered. PP population included all randomized and treated participants without any protocol deviations that impacted the primary efficacy variable and with treatment compliance to represent the intended regimen adequately.

Subject analysis set title	Ranibizumab 0.5 mg (rQ4)
Subject analysis set type	Per protocol

Subject analysis set description:

Ranibizumab (Lucentis®) 0.5 mg was administered to the study eye by intravitreal injection every 4 weeks (rQ4) from Day 1 through Week 96. PP population included all randomized and treated participants without any protocol deviations that impacted the primary efficacy variable and with treatment compliance to represent the intended regimen adequately.

Primary: Percentage of Participants with Stable Vision

End point title	Percentage of Participants with Stable Vision

End point description:

Stable vision was loss of <15 letters in BCVA compared to baseline. BCVA is measured using eye chart, reported as number of letters read correctly using Early Treatment of Diabetic Retinopathy Study (ETDRS) Scale (ranging 0-100 letters) in study eye. Lower number of letters read correctly, worse vision (or visual acuity). Increase in number of letters read correctly means vision has improved. Percentage of participants with a BCVA loss of <15 letters reported. Study eye: eye that meets entry criteria. If both eyes met entry criteria, eye with worse BCVA at baseline (Day 1) was selected as study eye. If both eyes had same BCVA values at baseline, then participant had to select their non-dominant eye for treatment, or else right eye was selected as study eye. The PP population included all randomized and treated participants without any protocol deviations that impacted the primary efficacy variable and with treatment compliance to represent the intended regimen adequately.

End point type	Primary

End point timeframe:

Baseline to Week 52

End point values	Abicipar Pegol 2 mg (2Q8)	Abicipar Pegol 2 mg (2Q12)	Ranibizumab 0.5 mg (rQ4)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	265	262	290	
Units: percentage of participants				
number (not applicable)	91.7	91.2	95.5	

Statistical analyses

Statistical analysis title	Percentage of Participants with Stable Vision

Statistical analysis description:

For hypothesis testing, if the lower limit of 95.1% Confidence Interval (CI) for the difference between an abicipar group and ranibizumab was greater than or equal to -10%, non-inferiority of abicipar was established.

Comparison groups	Ranibizumab 0.5 mg (rQ4) v Abicipar Pegol 2 mg (2Q8)
Number of subjects included in analysis	555
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Percentage Difference
Point estimate	-3.8
Confidence interval	
level	95.1 %
sides	2-sided
lower limit	-8.2
upper limit	0.3

Notes:

[1] - The 95.1% CI for the weighted difference were calculated based on the Newcombe method using the Cochran-Mantel-Haenszel weights and baseline BCVA (≤55 vs >55 letters) as stratification factor.

Statistical analysis title	Percentage of Participants with Stable Vision

Statistical analysis description:

For hypothesis testing, if the lower limit of 95.1% Confidence Interval (CI) for the difference between an abicipar group and ranibizumab was greater than or equal to -10%, non-inferiority of abicipar was established.

Comparison groups	Abicipar Pegol 2 mg (2Q12) v Ranibizumab 0.5 mg (rQ4)
Number of subjects included in analysis	552
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	Percentage Difference
Point estimate	-4.2

Confidence interval	
level	95.1 %
sides	2-sided
lower limit	-8.7
upper limit	0

Notes:

[2] - The 95.1% CI for the weighted difference were calculated based on the Newcombe method using the Cochran-Mantel-Haenszel weights and baseline BCVA (≤55 vs >55 letters) as stratification factor.

Secondary: Mean Change from Baseline in BCVA in the Study Eye

End point title	Mean Change from Baseline in BCVA in the Study Eye

End point description:

BCVA was measured using eye chart and reported as number of letters read correctly using ETDRS Scale (ranging from 0 to 100 letters) in study eye. Lower the number of letters read correctly on eye chart, worse the vision (or visual acuity). An increase in number of letters read correctly means that vision has improved. Study eye is defined as eye that meets entry criteria. If both eyes met entry criteria, eye with worse BCVA at baseline (Day 1) was selected as study eye. If both eyes had same BCVA values at baseline (Day 1), then participant had to select their nondominant eye for treatment, or else right eye was selected as study eye. Mixed model for repeated measures (MMRM) analysis was used. PP population included all randomized and treated participants without any protocol deviations that impacted the primary efficacy variable and with treatment compliance to represent the intended regimen adequately. Number analyzed are participants with data available for analyses.

End point type	Secondary

End point timeframe:

Baseline to Week 52

End point values	Abicipar Pegol 2 mg (2Q8)	Abicipar Pegol 2 mg (2Q12)	Ranibizumab 0.5 mg (rQ4)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	241	239	272	
Units: letters				
arithmetic mean (standard deviation)	6.7 (± 12.9)	5.6 (± 13.3)	8.5 (± 13.6)	

Statistical analyses

Statistical analysis title	Mean Change from Baseline in BCVA at Week 52

Statistical analysis description:

For hypothesis testing, non-inferiority of abicipar is established if the lower limit of the CI is > - 5.0 letters.

Comparison groups	Abicipar Pegol 2 mg (2Q8) v Ranibizumab 0.5 mg (rQ4)
Number of subjects included in analysis	513
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	Least Squares (LS) Mean Difference
Point estimate	-2.4
Confidence interval	
level	95.1 %
sides	2-sided
lower limit	-4.7
upper limit	-0.1

Variability estimate	Standard error of the mean
Dispersion value	1.2

Notes:

[3] - MMRM included treatment, region, BL BCVA, BL CRT ≤400 or >400, choroidal neovascularization lesion type, visit, visit-by-BL BCVA interaction, and treatment-by-visit interaction term as covariates using an unstructured covariance matrix.

Statistical analysis title	Mean Change from Baseline in BCVA at Week 52

Statistical analysis description:

For hypothesis testing, non-inferiority of abicipar is established if the lower limit of the CI is > - 5.0 letters.

Comparison groups	Abicipar Pegol 2 mg (2Q12) v Ranibizumab 0.5 mg (rQ4)
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Parameter estimate	LS Mean Difference
Point estimate	-3.7
Confidence interval	
level	95.1 %
sides	2-sided
lower limit	-6
upper limit	-1.3
Variability estimate	Standard error of the mean
Dispersion value	1.2

Notes:

[4] - MMRM included treatment, region, BL BCVA, BL CRT ≤400 or >400, choroidal neovascularization lesion type, visit, visit-by-BL BCVA interaction, and treatment-by-visit interaction term as covariates using an unstructured covariance matrix.

Secondary: Mean Change from Baseline in Central Retinal Thickness (CRT) in the Study Eye

End point title	Mean Change from Baseline in Central Retinal Thickness (CRT) in the Study Eye

End point description:

CRT was assessed using spectral domain optical coherence tomography (SD-OCT), a non-invasive diagnostic system providing high-resolution imaging sections of the retina. SD-OCT was performed in the study eye after pupil dilation. A negative change from Baseline indicated improvement. The study eye is defined as the eye that meets the entry criteria. If both eyes met the entry criteria, the eye with the worse BCVA at baseline (Day 1) was selected as the study eye. If both eyes had same BCVA values at baseline (Day 1), then the participant had to select their non-dominant eye for treatment, or else the right eye was selected as the study eye. MMRM analysis was used. ITT population included all randomized participants. Number analyzed are participants with data available for analyses.

End point type	Secondary

End point timeframe:

Baseline to Week 52

End point values	Abicipar Pegol 2 mg (2Q8)	Abicipar Pegol 2 mg (2Q12)	Ranibizumab 0.5 mg (rQ4)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	242	235	269	
Units: microns				
arithmetic mean (standard deviation)	-141.5 (± 136.4)	-150.1 (± 127.4)	-141.3 (± 122.0)	

Statistical analyses

Statistical analysis title	Change from Baseline in CRT at Week 52
Statistical analysis description:	
Superiority of abicipar was demonstrated if the lower limit of CI for the treatment difference was greater than zero.	
Comparison groups	Abicipar Pegol 2 mg (2Q8) v Ranibizumab 0.5 mg (rQ4)
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	superiority[5]
Parameter estimate	LS Mean Difference
Point estimate	8.6
Confidence interval	
level	95.1 %
sides	2-sided
lower limit	-3.8
upper limit	20.9
Variability estimate	Standard error of the mean
Dispersion value	6.3

Notes:

[5] - MMRM was used for analyses with covariates (treatment, region, baseline BCVA, CRT, choroidal neovascularization lesion type, visit, visit by baseline BCVA and treatment by visit interaction) with unstructured covariance matrix.

Statistical analysis title	Change from Baseline in CRT at Week 52
Statistical analysis description:	
Superiority of abicipar was demonstrated if the lower limit of CI for the treatment difference was greater than zero.	
Comparison groups	Abicipar Pegol 2 mg (2Q12) v Ranibizumab 0.5 mg (rQ4)
Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	superiority[6]
Parameter estimate	LS Mean Difference
Point estimate	2.3
Confidence interval	
level	95.1 %
sides	2-sided
lower limit	-10.1
upper limit	14.7
Variability estimate	Standard error of the mean
Dispersion value	6.3

Notes:

[6] - MMRM was used for analyses with covariates (treatment, region, baseline BCVA, CRT, choroidal neovascularization lesion type, visit, visit by baseline BCVA and treatment by visit interaction) with unstructured covariance matrix.

Secondary: Percentage of Participants with a Gain of 15 or More ETDRS Letters in BCVA from Baseline in Study Eye

End point title	Percentage of Participants with a Gain of 15 or More ETDRS Letters in BCVA from Baseline in Study Eye

End point description:

BCVA was measured using an eye chart and reported as the number of letters read correctly using the ETDRS Scale (ranging 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). An increase in the number of letters read correctly means that vision has improved. The study eye is defined as the eye that meets the entry criteria. If both eyes met the entry criteria, the eye with the worse BCVA at baseline (Day 1) was selected as the study eye. If both eyes had same BCVA values at baseline (Day 1), then the participant had to select their non-dominant eye for treatment, or else the right eye was selected as the study eye. ITT population included all randomized participants. Number analyzed are participants with data available for analyses.

End point type	Secondary

End point timeframe:

Baseline to Week 52

End point values	Abicipar Pegol 2 mg (2Q8)	Abicipar Pegol 2 mg (2Q12)	Ranibizumab 0.5 mg (rQ4)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	314	313	312	
Units: percentage of participants				
number (not applicable)	22.6	19.2	27.2	

Statistical analyses

Statistical analysis title	Participants with BCVA Gain of >15 Letters
Comparison groups	Abicipar Pegol 2 mg (2Q8) v Ranibizumab 0.5 mg (rQ4)
Number of subjects included in analysis	626
Analysis specification	Pre-specified
Analysis type	superiority[7]
Parameter estimate	Percentage Difference
Point estimate	-4.7
Confidence interval	
level	95.1 %
sides	2-sided
lower limit	-11.5
upper limit	2.1

Notes:

[7] - The 95.1% CI for the weighted difference were calculated based on the Newcombe method using the Cochran-Mantel-Haenszel weights and baseline BCVA (≤55 vs >55 letters) as the stratification factor.

Statistical analysis title	Participants with BCVA Gain of >15 Letters
Comparison groups	Abicipar Pegol 2 mg (2Q12) v Ranibizumab 0.5 mg (rQ4)

Number of subjects included in analysis	625
Analysis specification	Pre-specified
Analysis type	superiority[8]
Parameter estimate	Percentage Difference
Point estimate	-8.2
Confidence interval	
level	95.1 %
sides	2-sided
lower limit	-14.7
upper limit	-1.5

Notes:

[8] - The 95.1% CI for the weighted difference were calculated based on the Newcombe method using the Cochran-Mantel-Haenszel weights and baseline BCVA (≤55 vs >55 letters) as the stratification factor.

Secondary: Mean Change from Baseline in the National Eye Institute Visual Functioning Questionnaire-25 (NEI-VFQ-25) Composite Score in Study Eye

End point title	Mean Change from Baseline in the National Eye Institute Visual Functioning Questionnaire-25 (NEI-VFQ-25) Composite Score in Study Eye

End point description:

NEI-VFQ-25 consists 25 vision-targeted questions that represent 11 vision-related quality of life subscales and one general health item. Responses of individual participants were recorded as scores that ranged between 0 (worst) to 100 (best vision related function) with higher scale indicating better vision. Overall composite score is then calculated by averaging over all 11 vision-targeted subscale scores, excluding general health score. Overall composite score was calculated based on mean of non-missing subscales. Study eye: eye that meets entry criteria. If both eyes met all of entry criteria, eye with worse BCVA at baseline (day 1) was selected. If BCVA values for both eyes were identical then participant had to select non-dominant eye, or else right eye was selected as study eye. A positive change from baseline indicates improvement. MMRM analysis was used. ITT population: all randomized participants. Number analyzed are participants with data available for analyses.

End point type	Secondary

End point timeframe:

Baseline to Week 52

End point values	Abicipar Pegol 2 mg (2Q8)	Abicipar Pegol 2 mg (2Q12)	Ranibizumab 0.5 mg (rQ4)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	250	253	273	
Units: score on a scale				
least squares mean (standard error)	2.7 (± 0.7)	3.7 (± 0.7)	4.6 (± 0.7)	

Statistical analyses

Statistical analysis title	Change from Baseline in NEI-VFQ-25 at Week 52

Statistical analysis description:

Superiority of abicipar was demonstrated if the lower limit of CI for the treatment difference was greater than zero.

Comparison groups	Abicipar Pegol 2 mg (2Q8) v Ranibizumab 0.5 mg (rQ4)

Number of subjects included in analysis	523
Analysis specification	Pre-specified
Analysis type	superiority[9]
Parameter estimate	LS Mean Difference
Point estimate	-1.8
Confidence interval	
level	95.1 %
sides	2-sided
lower limit	-3.7
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	0.9

Notes:

[9] - MMRM was used for analyses with covariates (treatment, region, baseline BCVA, visual function questionnaire (VFQ) score, visit, visit by baseline BCVA and treatment by visit interaction) with unstructured covariance matrix.

Statistical analysis title	Change from Baseline in NEI-VFQ-25 at Week 52

Statistical analysis description:

Superiority of abicipar was demonstrated if the lower limit of CI for the treatment difference was greater than zero.

Comparison groups	Abicipar Pegol 2 mg (2Q12) v Ranibizumab 0.5 mg (rQ4)
Number of subjects included in analysis	526
Analysis specification	Pre-specified
Analysis type	superiority[10]
Parameter estimate	LS Mean Difference
Point estimate	-0.8
Confidence interval	
level	95.1 %
sides	2-sided
lower limit	-2.7
upper limit	1
Variability estimate	Standard error of the mean
Dispersion value	0.9

Notes:

[10] - MMRM was used for analyses with covariates (treatment, region, baseline BCVA, visual function questionnaire (VFQ) score, visit, visit by baseline BCVA and treatment by visit interaction) with unstructured covariance matrix.

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From first dose to last dose of study drug (Up to Week 104)	
Adverse event reporting additional description:	
Safety population included all treated participants.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups	
Reporting group title	Abicipar Pegol 2 mg (2Q8)
Reporting group description:	
Abicipar pegol 2 mg administered to the study eye by intravitreal injection on Day 1, Week 4, Week 8 and every 8 weeks (2Q8) thereafter through Week 96. Scheduled visits occurred every 4 weeks. To maintain masking, sham was administered to the study eye at scheduled visits where abicipar was not administered.	
Reporting group title	Abicipar Pegol 2 mg (2Q12)
Reporting group description:	
Abicipar pegol 2 mg administered to the study eye by intravitreal injection on Day 1, Week 4, Week 12, and every 12 weeks (2Q12) thereafter through week 96. Scheduled visits occurred every 4 weeks. To maintain masking, sham was administered to the study eye at scheduled visits where abicipar was not administered.	
Reporting group title	Ranibizumab 0.5 mg (rQ4)
Reporting group description:	
Ranibizumab (Lucentis®) 0.5 mg administered to the study eye by intravitreal injection every 4 weeks (rQ4) from Day 1 through Week 96.	

Serious adverse events	Abicipar Pegol 2 mg (2Q8)	Abicipar Pegol 2 mg (2Q12)	Ranibizumab 0.5 mg (rQ4)
Total subjects affected by serious adverse events			
subjects affected / exposed	92 / 312 (29.49%)	102 / 312 (32.69%)	95 / 310 (30.65%)
number of deaths (all causes)	8	7	11
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	3 / 310 (0.97%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal cancer			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	2 / 310 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Metastases to bone			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	2 / 310 (0.65%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Lung carcinoma cell type unspecified stage IV			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	2 / 310 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Breast cancer			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer metastatic			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transitional cell carcinoma			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenocarcinoma of colon			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenocarcinoma pancreas			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone sarcoma			

subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
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 female			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clear cell renal cell carcinoma			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric cancer stage IV			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
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 carcinoma			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm malignant			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal adenocarcinoma			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
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 neoplasm			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			

subjects affected / exposed	0 / 312 (0.00%)	2 / 312 (0.64%)	0 / 310 (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 cancer			
subjects affected / exposed	1 / 312 (0.32%)	1 / 312 (0.32%)	0 / 310 (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
Bowen’s disease			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Cholangiocarcinoma			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Gastrointestinal stromal tumour			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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 stage IV			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Malignant melanoma			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Ovarian cancer metastatic			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Small cell lung cancer metastatic			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Squamous cell carcinoma of lung			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Acute myeloid leukaemia			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Benign neoplasm of skin			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Bladder neoplasm			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Bone cancer			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Colon cancer			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Head and neck cancer metastatic			

subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Lung adenocarcinoma			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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 cancer metastatic			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Metastases to adrenals			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Renal cell carcinoma			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Spinal cord neoplasm			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Testis cancer			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Tonsil cancer			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Vascular disorders			
Aortic aneurysm			

subjects affected / exposed	1 / 312 (0.32%)	2 / 312 (0.64%)	2 / 310 (0.65%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Aortic stenosis			
subjects affected / exposed	0 / 312 (0.00%)	2 / 312 (0.64%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	2 / 312 (0.64%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
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 vascular disorder			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
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 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Hypertensive crisis			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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 ischaemia			

subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	2 / 312 (0.64%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Pyrexia			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			
subjects affected / exposed	1 / 312 (0.32%)	1 / 312 (0.32%)	0 / 310 (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
Chest pain			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Fatigue			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Oedema peripheral			

subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 312 (0.32%)	1 / 312 (0.32%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostatitis			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	4 / 312 (1.28%)	1 / 312 (0.32%)	5 / 310 (1.61%)
occurrences causally related to treatment / all	0 / 5	0 / 1	0 / 6
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 1
Pleural effusion			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	3 / 310 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Dyspnoea			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	2 / 310 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pulmonary embolism			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	2 / 310 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			

subjects affected / exposed	2 / 312 (0.64%)	2 / 312 (0.64%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 2	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Bronchospasm			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
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 mass			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
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 disorder			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Bronchopneumopathy			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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 aspiration			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Pneumothorax			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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 congestion			

subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Acute respiratory failure			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Hypoxia			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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			
Depression			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intensive care unit delirium			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Completed suicide			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Mental status changes			

subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Investigations			
Heart rate increased			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intraocular pressure increased			
subjects affected / exposed	1 / 312 (0.32%)	1 / 312 (0.32%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood pressure increased			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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			
Fall			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	5 / 310 (1.61%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	1 / 312 (0.32%)	3 / 312 (0.96%)	3 / 310 (0.97%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fractured sacrum			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	2 / 310 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ulna fracture			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Upper limb fracture			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle fracture			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cataract operation complication			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower limb fracture			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
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 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pubis fracture			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
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 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			
subjects affected / exposed	0 / 312 (0.00%)	3 / 312 (0.96%)	0 / 310 (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
Meniscus injury			
subjects affected / exposed	0 / 312 (0.00%)	2 / 312 (0.64%)	0 / 310 (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
Radius fracture			
subjects affected / exposed	0 / 312 (0.00%)	2 / 312 (0.64%)	0 / 310 (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
Contusion			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Fibula fracture			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Hand fracture			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Inflammation of wound			

subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Joint injury			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Periprosthetic fracture			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Procedural pneumothorax			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Subdural haemorrhage			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Incisional hernia			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Ocular procedural complication			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Procedural nausea			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Procedural vomiting			

subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Spinal column injury			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Thermal burn			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Traumatic intracranial haemorrhage			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	3 / 312 (0.96%)	4 / 312 (1.28%)	4 / 310 (1.29%)
occurrences causally related to treatment / all	0 / 4	0 / 4	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Coronary artery disease			
subjects affected / exposed	1 / 312 (0.32%)	2 / 312 (0.64%)	3 / 310 (0.97%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	2 / 312 (0.64%)	3 / 312 (0.96%)	2 / 310 (0.65%)
occurrences causally related to treatment / all	0 / 2	0 / 7	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Acute myocardial infarction			
subjects affected / exposed	1 / 312 (0.32%)	3 / 312 (0.96%)	2 / 310 (0.65%)
occurrences causally related to treatment / all	0 / 1	2 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Angina pectoris			

subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	2 / 310 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	2 / 310 (0.65%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Arrhythmia			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	2 / 310 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block second degree			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic valve incompetence			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
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 disorder			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiomyopathy			

subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Hypertensive heart disease			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Supraventricular tachycardia			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
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 tachycardia			
subjects affected / exposed	0 / 312 (0.00%)	2 / 312 (0.64%)	0 / 310 (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
Left ventricular failure			
subjects affected / exposed	1 / 312 (0.32%)	1 / 312 (0.32%)	0 / 310 (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
Mitral valve incompetence			
subjects affected / exposed	1 / 312 (0.32%)	1 / 312 (0.32%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Aortic valve stenosis			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Mitral valve prolapse			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			

subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Cardiac tamponade			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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			
Cerebrovascular accident			
subjects affected / exposed	2 / 312 (0.64%)	2 / 312 (0.64%)	5 / 310 (1.61%)
occurrences causally related to treatment / all	1 / 2	1 / 2	2 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Carotid artery stenosis			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cognitive disorder			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic stroke			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic encephalopathy			

subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lacunar infarction			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic encephalopathy			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polyneuropathy			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
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 / 312 (0.32%)	2 / 312 (0.64%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar radiculopathy			
subjects affected / exposed	1 / 312 (0.32%)	1 / 312 (0.32%)	0 / 310 (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
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Quadrantanopia			

subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Syncope			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Hypoaesthesia			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Myelopathy			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Optic neuritis			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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 / 312 (0.32%)	2 / 312 (0.64%)	4 / 310 (1.29%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			

subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iron deficiency anaemia			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Eye disorders			
Retinal artery occlusion			
subjects affected / exposed	1 / 312 (0.32%)	3 / 312 (0.96%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	1 / 1	2 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal haemorrhage			
subjects affected / exposed	4 / 312 (1.28%)	1 / 312 (0.32%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	1 / 4	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neovascular age-related macular degeneration			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal pigment epithelial tear			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Macular degeneration			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vitreous haemorrhage			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uveitis			

subjects affected / exposed	10 / 312 (3.21%)	10 / 312 (3.21%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	12 / 12	13 / 13	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iridocyclitis			
subjects affected / exposed	1 / 312 (0.32%)	4 / 312 (1.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	1 / 1	4 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal vasculitis			
subjects affected / exposed	6 / 312 (1.92%)	3 / 312 (0.96%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	6 / 6	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Visual acuity reduced			
subjects affected / exposed	4 / 312 (1.28%)	3 / 312 (0.96%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	2 / 4	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vitritis			
subjects affected / exposed	5 / 312 (1.60%)	2 / 312 (0.64%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	6 / 6	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cataract			
subjects affected / exposed	3 / 312 (0.96%)	1 / 312 (0.32%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	2 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune uveitis			
subjects affected / exposed	2 / 312 (0.64%)	1 / 312 (0.32%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	2 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye pain			
subjects affected / exposed	1 / 312 (0.32%)	1 / 312 (0.32%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Macular fibrosis			

subjects affected / exposed	1 / 312 (0.32%)	1 / 312 (0.32%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ocular hypertension			
subjects affected / exposed	1 / 312 (0.32%)	1 / 312 (0.32%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Age-related macular degeneration			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Iritis			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Macular scar			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Optic disc haemorrhage			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Optic ischaemic neuropathy			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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 adhesions			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal detachment			

subjects affected / exposed	3 / 312 (0.96%)	0 / 312 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	2 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dacryostenosis acquired			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Diplopia			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Glaucoma			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lacrimation increased			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Necrotising retinitis			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Photopsia			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal oedema			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Retinal tear			

subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Retinal vein occlusion			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subretinal fibrosis			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Visual impairment			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 312 (0.32%)	1 / 312 (0.32%)	2 / 310 (0.65%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	2 / 310 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			

subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral hernia incarcerated			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Functional gastrointestinal disorder			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gingival bleeding			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematochezia			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal infarction			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
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 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			

subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
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	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Nausea			
subjects affected / exposed	0 / 312 (0.00%)	2 / 312 (0.64%)	0 / 310 (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
Abdominal pain			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Anal fistula			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Colitis ischaemic			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Diarrhoea			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Gastritis			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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 polyp haemorrhage			

subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Haemorrhoids			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Oesophageal stenosis			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Barrett’s oesophagus			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Haematemesis			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Incarcerated inguinal hernia			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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 spasm			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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			
Cholecystitis acute			
subjects affected / exposed	2 / 312 (0.64%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			

subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic mass			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary dilatation			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Skin and subcutaneous tissue disorders			
Panniculitis			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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 / 312 (0.00%)	1 / 312 (0.32%)	1 / 310 (0.32%)
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 kidney disease			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephritis			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
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 prolapse			

subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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 retention			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	2 / 312 (0.64%)	1 / 312 (0.32%)	3 / 310 (0.97%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	3 / 310 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthralgia			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dupuytren’s contracture			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
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 spinal stenosis			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			

subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhabdomyolysis			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
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 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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 deformity			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Sacroiliitis			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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			
Pneumonia			
subjects affected / exposed	9 / 312 (2.88%)	9 / 312 (2.88%)	14 / 310 (4.52%)
occurrences causally related to treatment / all	0 / 12	0 / 10	0 / 15
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 1
Endophthalmitis			
subjects affected / exposed	1 / 312 (0.32%)	4 / 312 (1.28%)	2 / 310 (0.65%)
occurrences causally related to treatment / all	1 / 1	5 / 5	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			

subjects affected / exposed	1 / 312 (0.32%)	2 / 312 (0.64%)	2 / 310 (0.65%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 312 (0.32%)	1 / 312 (0.32%)	2 / 310 (0.65%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	1 / 312 (0.32%)	5 / 312 (1.60%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 1	0 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	2 / 312 (0.64%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infective exacerbation of chronic obstructive airways disease			

subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
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 viral			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound infection			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth infection			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	1 / 312 (0.32%)	1 / 312 (0.32%)	0 / 310 (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
Appendicitis perforated			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Endocarditis			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Gastroenteritis			

subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Herpes zoster			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Influenza			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Localised infection			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Periorbital cellulitis			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonsillar abscess			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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 bacterial			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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 tuberculosis			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Tonsillitis			

subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Septic shock			
subjects affected / exposed	2 / 312 (0.64%)	0 / 312 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Abscess jaw			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Clostridium difficile infection			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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 sepsis			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Respiratory tract infection			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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
Retinitis			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheobronchitis			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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 enterococcal			

subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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 / 312 (0.32%)	3 / 312 (0.96%)	2 / 310 (0.65%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Adult failure to thrive			
subjects affected / exposed	0 / 312 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Hyperkalaemia			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Hyponatraemia			
subjects affected / exposed	0 / 312 (0.00%)	1 / 312 (0.32%)	0 / 310 (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
Diabetes mellitus inadequate control			
subjects affected / exposed	1 / 312 (0.32%)	0 / 312 (0.00%)	0 / 310 (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	Abicipar Pegol 2 mg (2Q8)	Abicipar Pegol 2 mg (2Q12)	Ranibizumab 0.5 mg (rQ4)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	202 / 312 (64.74%)	217 / 312 (69.55%)	196 / 310 (63.23%)
Investigations			
Intraocular pressure increased			
subjects affected / exposed	15 / 312 (4.81%)	25 / 312 (8.01%)	13 / 310 (4.19%)
occurrences (all)	22	39	18

Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	11 / 312 (3.53%)	12 / 312 (3.85%)	17 / 310 (5.48%)
occurrences (all)	12	13	17
Vascular disorders			
Hypertension			
subjects affected / exposed	25 / 312 (8.01%)	20 / 312 (6.41%)	28 / 310 (9.03%)
occurrences (all)	26	22	29
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	27 / 312 (8.65%)	32 / 312 (10.26%)	46 / 310 (14.84%)
occurrences (all)	38	46	72
Neovascular age-related macular degeneration			
subjects affected / exposed	26 / 312 (8.33%)	28 / 312 (8.97%)	39 / 310 (12.58%)
occurrences (all)	27	33	39
Eye pain			
subjects affected / exposed	26 / 312 (8.33%)	26 / 312 (8.33%)	22 / 310 (7.10%)
occurrences (all)	47	44	36
Cataract			
subjects affected / exposed	29 / 312 (9.29%)	19 / 312 (6.09%)	20 / 310 (6.45%)
occurrences (all)	42	25	24
Visual acuity reduced			
subjects affected / exposed	24 / 312 (7.69%)	33 / 312 (10.58%)	18 / 310 (5.81%)
occurrences (all)	36	56	23
Vitreous detachment			
subjects affected / exposed	19 / 312 (6.09%)	21 / 312 (6.73%)	17 / 310 (5.48%)
occurrences (all)	24	26	23
Retinal haemorrhage			
subjects affected / exposed	16 / 312 (5.13%)	23 / 312 (7.37%)	16 / 310 (5.16%)
occurrences (all)	22	27	22
Vitreous floaters			
subjects affected / exposed	22 / 312 (7.05%)	20 / 312 (6.41%)	16 / 310 (5.16%)
occurrences (all)	27	25	22
Eye irritation			
subjects affected / exposed	11 / 312 (3.53%)	16 / 312 (5.13%)	9 / 310 (2.90%)
occurrences (all)	17	20	11

Subretinal fluid			
subjects affected / exposed	8 / 312 (2.56%)	17 / 312 (5.45%)	7 / 310 (2.26%)
occurrences (all)	20	33	9
Iridocyclitis			
subjects affected / exposed	10 / 312 (3.21%)	18 / 312 (5.77%)	2 / 310 (0.65%)
occurrences (all)	15	26	3
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	14 / 312 (4.49%)	18 / 312 (5.77%)	10 / 310 (3.23%)
occurrences (all)	14	24	13
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	14 / 312 (4.49%)	21 / 312 (6.73%)	13 / 310 (4.19%)
occurrences (all)	18	28	16
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	37 / 312 (11.86%)	36 / 312 (11.54%)	36 / 310 (11.61%)
occurrences (all)	51	50	58
Urinary tract infection			
subjects affected / exposed	19 / 312 (6.09%)	21 / 312 (6.73%)	31 / 310 (10.00%)
occurrences (all)	28	22	39
Influenza			
subjects affected / exposed	15 / 312 (4.81%)	16 / 312 (5.13%)	24 / 310 (7.74%)
occurrences (all)	16	17	27
Bronchitis			
subjects affected / exposed	23 / 312 (7.37%)	19 / 312 (6.09%)	23 / 310 (7.42%)
occurrences (all)	28	21	28
Conjunctivitis			
subjects affected / exposed	21 / 312 (6.73%)	20 / 312 (6.41%)	11 / 310 (3.55%)
occurrences (all)	40	32	18

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 March 2015	The following changes were implemented with Amendment 1: Moved Ocular Exclusion Criteria (Either Eye) to immediately follow General Exclusion Criteria. Revised exclusion criterion #8, #9. Added ocular exclusion criterion #10. Reorganized list of Ocular Exclusion Criteria (Study Eye). Added ocular exclusion criterion (study eye) #11, #16. Clarified pre-treatment administration preparation protocol to include use of 5% povidone iodine irrigation/saline flush, periocular 10% povidone iodine, topical antibiotics instilled 15, 10, and 5 minutes prior to treatment administration, and topical anesthesia. Removed dispensing of participant administered antibiotic drops. Revised Randomization/Stratification as follows: Participants will be randomized by region to 3 treatment groups (2Q8, 2Q12, and rQ4). Within each region, allocation to Randomization to the treatment groups will be stratified by the following 3 factors using at a ratio of 1:1:1 and be based by region. Allocation to the treatment groups will be stratified by: Disease characteristics of the study eye assessed by the investigator at screening and subsequently confirmed by the central reading center prior to baseline (day 1): Added draw blood samples for immunogenicity analysis (week 4 only). Removed National Eye Institute Visual Functioning Questionnaire (25 questions) (NEI-VFQ-25) vision related subscale scores from secondary analyses.
28 April 2016	The following changes were implemented with Amendment 2: Updated study duration from 100 to 104 weeks. Revised inclusion criterion: Presence of active subfoveal and/or juxtafoveal choroidal neovascularization (CNV) (1 to 200 microns from the center) secondary to age-related macular degeneration (AMD) assessed by fluorescein angiogram. In addition, presence of retinal fluid on optical coherence tomography (OCT) and/or fluorescein leakage under the fovea as assessed by the investigator at screening and confirmed by the central reading center prior to baseline (day 1). Revised exclusion criterion: Active periocular, ocular, or /intraocular infection at baseline (day 1). Added week 104 as study exit or early termination visit, week 100 will be a study assessment visit without study treatment. Visit windows for weeks 4 through 24, weeks 28 through 48, weeks 52 through 96, and weeks 100 through 104/early exit has been changed from ±5 days to ±7 days; The timing for specular microscopy was set to a fixed visit at week 32. Added: In addition, a post-injection safety follow-up phone call (up to 3 days following the office visit) should be performed. Added that if non-inferiority for both abicipar arms is established, that superiority testing of abicipar over ranibizumab will be performed. Analysis updated to be based on analysis of covariance (ANCOVA) with baseline BCVA as a covariate. Updated week 100 visit procedures to reflect changes to Table 1. Updated as follows: Patients who discontinue early due to other reasons will be required to complete the study exit procedures indicated at the week 104/early exit visit and will be reevaluated at the subsequent follow-up visits: 1) approximately 16 weeks after the last study medication injection or 100 weeks from baseline whichever occurs earlier for immunogenicity, BCVA, CRT, and adverse events assessments, and 2) approximately 52 and 100 weeks after baseline for BCVA, CRT, and adverse event assessments.
23 February 2017	The following changes were implemented with Amendment 3: Removed references to participation in long-term safety study regarding an offer to evaluate participation in a long-term safety study. Also updated to reflect the current template language with regards to conducting the study in accordance with applicable laws and regulations.

10 April 2018	The following changes were implemented with Amendment 4: Changed the analysis population for the non-inferiority test of the primary and the key secondary efficacy variable of BCVA mean change from ITT; ITT analysis for non-inferiority will be performed as well but will be considered as sensitivity analysis. Added mixed-effect model for repeated measures (MMRM) for analysis of secondary efficacy (continuous) variables as the primary method; ANCOVA will be performed as well but will be considered as sensitivity analysis. Removed subgroup analyses section.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported