Clinical trial results:
Single and Repeat Dose Study of the Safety and Efficacy of AGN-150998 in Patients with Exudative Age-related Macular Degeneration

Summary

EudraCT number	2011-002526-43
Trial protocol	DE AT IT
Global end of trial date	09 April 2014

Results information

Result version number	v1 (current)
This version publication date	08 April 2016
First version publication date	08 April 2016

Trial information

Trial identification

Sponsor protocol code	150998-001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01397409
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Allergan, Inc
Sponsor organisation address	2525 Dupont Drive, Irvine, United States, 92612
Public contact	Medical Director, Allergan, +1 714-246-4500, clinicaltrials@allergan.com
Scientific contact	Medical Director, Allergan, +1 714-246-4500, clinicaltrials@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	17 December 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 March 2014
Global end of trial reached?	Yes
Global end of trial date	09 April 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study was conducted in 3 stages. Stage 1 was an open-label, dose-escalation assessment of the safety of AGN-150998 administered as a single intravitreal injection to patients with advanced exudative Age-related Macular Degeneration (AMD). Stage 2 and Stage 3 were randomized, double-masked, comparisons of the safety and treatment effects on retinal edema and best-corrected visual acuity (BCVA) of AGN-150998 and ranibizumab in treatment-naive patients with exudative AMD. Study medication was administered as needed in Stage 2 and with a fixed-dosing schedule in Stage 3. The study objectives were (1) to identify the highest tolerated dose of AGN-150998, (2) to assess the safety and duration of treatment effects on retinal edema and BCVA, and (3) to characterize the systemic pharmacokinetic profile of AGN-150998.

Protection of trial subjects:

All participants were required to read an sign an informed consent form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 September 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 167
Country: Number of subjects enrolled	France: 19
Country: Number of subjects enrolled	Israel: 25
Country: Number of subjects enrolled	Italy: 9
Country: Number of subjects enrolled	Germany: 6
Country: Number of subjects enrolled	Australia: 23
Country: Number of subjects enrolled	Switzerland: 12
Country: Number of subjects enrolled	Austria: 10
Worldwide total number of subjects	271
EEA total number of subjects	44

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)	16
From 65 to 84 years	201
85 years and over	54

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled in 43 study centers in 8 countries: Austria, Australia, France, Germany, Israel, Italy, Switzerland and the United States from 29 September 2011 to 09 April 2014.

Pre-assignment

Screening details:

Patients with Age-related Macular Degeneration enrolled in the Stage 1 open label dose escalation study starting at a 1.0 mg dose. In Stage 2, patients were randomized in a 1:1:1 ratio to ranibizumab, 3.0 mg abicipar or 4.2 mg abicipar. In Stage 3, patients were randomized in a 3:3:2 ratio of 1.0 mg abicipar, 2.0 mg abicipar or 0.5 mg ranibizumab.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Stage 1: AGN-150998 4.2 mg

Arm description:

Stage 1: AGN-150998 4.2 mg given as a single intravitreal injection.

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

Dosage and administration details:

Single intravitreal injection

Arm title	Stage 1: AGN-150998 3.0 mg

Arm description:

Stage 1: AGN-150998 3.0 mg given as a single intravitreal injection.

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

Dosage and administration details:

Single intravitreal injection

Arm title	Stage 1: AGN-150998 2.0 mg

Arm description:

Stage 1: AGN-150998 2.0 mg given as a single intravitreal injection

Arm type	Experimental

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

Dosage and administration details:

Single intravitreal injection

Arm title	Stage 1: AGN-150998 1.0 mg

Arm description:

Stage 1: AGN-150998 1.0 mg given as a single intravitreal injection.

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

Dosage and administration details:

Single intravitreal injection

Arm title	Stage 2: AGN-150998 4.2 mg

Arm description:

Stage 2: AGN-150998 4.2 mg (highest tolerated dose from Stage 1) given as a single intravitreal injection at baseline. A second intravitreal injection will be given by week 16.

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

Dosage and administration details:

Single intravitreal injection

Arm title	Stage 2: AGN-150998 3.0 mg

Arm description:

Stage 2: AGN-150998 3.0 mg (one dose below highest tolerated dose from Stage 1) given as a single intravitreal injection at baseline. A second intravitreal injection will be given by week 16.

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

Dosage and administration details:

Single intravitreal injection

Arm title	Stage 2: Ranibizumab 0.5 mg

Arm description:

Stage 2: ranibizumab 0.5 mg given as a single intravitreal injection at baseline. A second intravitreal injection will be given by week 16.

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:

Single intavitreal injection

Arm title	Stage 3: AGN-150998 2.0 mg

Arm description:

Stage 3: AGN-150998 2.0 mg given as intravitreal injections at Baseline, Weeks 4 and 8, followed by sham injections at Weeks 12 and 16.

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

Dosage and administration details:

Single intravitreal injection

Arm title	Stage 3: AGN-150998 1.0 mg

Arm description:

Stage 3: AGN-150998 1.0 mg given as intravitreal injections at Baseline, Weeks 4 and 8, followed by sham injections at Weeks 12 and 16.

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

Dosage and administration details:

Single intravitreal injection

Arm title	Stage 3: Ranibizumab 0.5 mg

Arm description:

Stage 3: ranibizumab 0.5 mg given as intravitreal injections every 4 weeks for 16 weeks

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:

Single intavitreal injection

Number of subjects in period 1	Stage 1: AGN-150998 4.2 mg	Stage 1: AGN-150998 3.0 mg	Stage 1: AGN-150998 2.0 mg
Started	9	6	6
Completed	9	6	6
Not completed	0	0	0
Adverse event, non-fatal	-	-	-
Personal Reasons	-	-	-
Other Miscellaneous Reasons	-	-	-

Number of subjects in period 1	Stage 1: AGN-150998 1.0 mg	Stage 2: AGN-150998 4.2 mg	Stage 2: AGN-150998 3.0 mg
Started	3	67	58
Completed	3	59	54
Not completed	0	8	4
Adverse event, non-fatal	-	6	3
Personal Reasons	-	1	-
Other Miscellaneous Reasons	-	1	1

Number of subjects in period 1	Stage 2: Ranibizumab 0.5 mg	Stage 3: AGN-150998 2.0 mg	Stage 3: AGN-150998 1.0 mg
Started	58	23	25
Completed	58	21	25
Not completed	0	2	0
Adverse event, non-fatal	-	1	-
Personal Reasons	-	-	-
Other Miscellaneous Reasons	-	1	-

Number of subjects in period 1	Stage 3: Ranibizumab 0.5 mg
Started	16
Completed	16
Not completed	0
Adverse event, non-fatal	-
Personal Reasons	-
Other Miscellaneous Reasons	-

Baseline characteristics

Reporting groups	
Reporting group title	Stage 1: AGN-150998 4.2 mg
Reporting group description:	
Stage 1: AGN-150998 4.2 mg given as a single intravitreal injection.	
Reporting group title	Stage 1: AGN-150998 3.0 mg
Reporting group description:	
Stage 1: AGN-150998 3.0 mg given as a single intravitreal injection.	
Reporting group title	Stage 1: AGN-150998 2.0 mg
Reporting group description:	
Stage 1: AGN-150998 2.0 mg given as a single intravitreal injection	
Reporting group title	Stage 1: AGN-150998 1.0 mg
Reporting group description:	
Stage 1: AGN-150998 1.0 mg given as a single intravitreal injection.	
Reporting group title	Stage 2: AGN-150998 4.2 mg
Reporting group description:	
Stage 2: AGN-150998 4.2 mg (highest tolerated dose from Stage 1) given as a single intravitreal injection at baseline. A second intravitreal injection will be given by week 16.	
Reporting group title	Stage 2: AGN-150998 3.0 mg
Reporting group description:	
Stage 2: AGN-150998 3.0 mg (one dose below highest tolerated dose from Stage 1) given as a single intravitreal injection at baseline. A second intravitreal injection will be given by week 16.	
Reporting group title	Stage 2: Ranibizumab 0.5 mg
Reporting group description:	
Stage 2: ranibizumab 0.5 mg given as a single intravitreal injection at baseline. A second intravitreal injection will be given by week 16.	
Reporting group title	Stage 3: AGN-150998 2.0 mg
Reporting group description:	
Stage 3: AGN-150998 2.0 mg given as intravitreal injections at Baseline, Weeks 4 and 8, followed by sham injections at Weeks 12 and 16.	
Reporting group title	Stage 3: AGN-150998 1.0 mg
Reporting group description:	
Stage 3: AGN-150998 1.0 mg given as intravitreal injections at Baseline, Weeks 4 and 8, followed by sham injections at Weeks 12 and 16.	
Reporting group title	Stage 3: Ranibizumab 0.5 mg
Reporting group description:	
Stage 3: ranibizumab 0.5 mg given as intravitreal injections every 4 weeks for 16 weeks	

Reporting group values	Stage 1: AGN-150998 4.2 mg	Stage 1: AGN-150998 3.0 mg	Stage 1: AGN-150998 2.0 mg
Number of subjects	9	6	6
Age categorical Units: Subjects			
Adults 18-64 years	0	1	0
Adults 65-84 years	9	5	6
Adults ≥85 years	0	0	0
Age Continuous | Units: years			
arithmetic mean	82.3	75.3	79.3
full range (min-max)	68 to 89	62 to 86	72 to 91

Gender, Male/Female Units: Participants			
Female	5	2	4
Male	4	4	2

Reporting group values	Stage 1: AGN-150998 1.0 mg	Stage 2: AGN-150998 4.2 mg	Stage 2: AGN-150998 3.0 mg
Number of subjects	3	67	58
Age categorical Units: Subjects			
Adults 18-64 years	1	3	3
Adults 65-84 years	2	64	55
Adults ≥85 years	0	0	0
Age Continuous | Units: years			
arithmetic mean	67.7	80.4	78.6
full range (min-max)	64 to 71	58 to 95	63 to 94
Gender, Male/Female Units: Participants			
Female	2	34	35
Male	1	33	23

Reporting group values	Stage 2: Ranibizumab 0.5 mg	Stage 3: AGN-150998 2.0 mg	Stage 3: AGN-150998 1.0 mg
Number of subjects	58	23	25
Age categorical Units: Subjects			
Adults 18-64 years	5	0	6
Adults 65-84 years	53	23	19
Adults ≥85 years	0	0	0
Age Continuous | Units: years			
arithmetic mean	78.5	77.9	75.5
full range (min-max)	59 to 92	67 to 89	54 to 91
Gender, Male/Female Units: Participants			
Female	38	13	18
Male	20	10	7

Reporting group values	Stage 3: Ranibizumab 0.5 mg	Total	
Number of subjects	16	271	
Age categorical Units: Subjects			
Adults 18-64 years	2	21	
Adults 65-84 years	14	250	
Adults ≥85 years	0	0	
Age Continuous | Units: years			
arithmetic mean	76.5		
full range (min-max)	53 to 86	-	

Gender, Male/Female Units: Participants			
Female	8	159	
Male	8	112	

Subject analysis sets

Subject analysis set title	All Stage 1 Participants
Subject analysis set type	Safety analysis

Subject analysis set description:
Stage 1 Al lParticipants

Reporting group values	All Stage 1 Participants		
Number of subjects	24		
Age categorical Units: Subjects			
Adults 18-64 years	0		
Adults 65-84 years	0		
Adults ≥85 years	0		
Age Continuous | Units: years			
arithmetic mean	0		
full range (min-max)	0 to 0		
Gender, Male/Female Units: Participants			
Female	0		
Male	0		

End points

End points reporting groups

Reporting group title	Stage 1: AGN-150998 4.2 mg
Reporting group description:	
Stage 1: AGN-150998 4.2 mg given as a single intravitreal injection.	
Reporting group title	Stage 1: AGN-150998 3.0 mg
Reporting group description:	
Stage 1: AGN-150998 3.0 mg given as a single intravitreal injection.	
Reporting group title	Stage 1: AGN-150998 2.0 mg
Reporting group description:	
Stage 1: AGN-150998 2.0 mg given as a single intravitreal injection	
Reporting group title	Stage 1: AGN-150998 1.0 mg
Reporting group description:	
Stage 1: AGN-150998 1.0 mg given as a single intravitreal injection.	
Reporting group title	Stage 2: AGN-150998 4.2 mg
Reporting group description:	
Stage 2: AGN-150998 4.2 mg (highest tolerated dose from Stage 1) given as a single intravitreal injection at baseline. A second intravitreal injection will be given by week 16.	
Reporting group title	Stage 2: AGN-150998 3.0 mg
Reporting group description:	
Stage 2: AGN-150998 3.0 mg (one dose below highest tolerated dose from Stage 1) given as a single intravitreal injection at baseline. A second intravitreal injection will be given by week 16.	
Reporting group title	Stage 2: Ranibizumab 0.5 mg
Reporting group description:	
Stage 2: ranibizumab 0.5 mg given as a single intravitreal injection at baseline. A second intravitreal injection will be given by week 16.	
Reporting group title	Stage 3: AGN-150998 2.0 mg
Reporting group description:	
Stage 3: AGN-150998 2.0 mg given as intravitreal injections at Baseline, Weeks 4 and 8, followed by sham injections at Weeks 12 and 16.	
Reporting group title	Stage 3: AGN-150998 1.0 mg
Reporting group description:	
Stage 3: AGN-150998 1.0 mg given as intravitreal injections at Baseline, Weeks 4 and 8, followed by sham injections at Weeks 12 and 16.	
Reporting group title	Stage 3: Ranibizumab 0.5 mg
Reporting group description:	
Stage 3: ranibizumab 0.5 mg given as intravitreal injections every 4 weeks for 16 weeks	
Subject analysis set title	All Stage 1 Participants
Subject analysis set type	Safety analysis
Subject analysis set description:	
Stage 1 Al lParticipants	

Primary: Highest Tolerated Dose (HTD) of AGN-150998

End point title	Highest Tolerated Dose (HTD) of AGN-150998[1]
End point description:	
Stage 1 evaluated the safety of a single intravitreal injection of AGN-150998 with doses ranging from 1.0 to 4.2 mg.	
End point type	Primary
End point timeframe:	
24 Weeks	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No Statistical Analysis is reported for this outcome measure.

End point values	All Stage 1 Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	24			
Units: mg				
number (not applicable)	4.2			

Statistical analyses

No statistical analyses for this end point

Primary: Stage 1: Change from Baseline in Central Retinal Thickness (CRT) in the Study Eye

End point title	Stage 1: Change from Baseline in Central Retinal Thickness (CRT) in the Study Eye[2][3]

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.

End point type	Primary

End point timeframe:

Baseline, Week 4

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No Statistical Analysis is reported for this outcome measure.

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all arms in the baseline period are applicable to this outcome measure.

End point values	Stage 1: AGN-150998 4.2 mg	Stage 1: AGN-150998 3.0 mg	Stage 1: AGN-150998 2.0 mg	Stage 1: AGN-150998 1.0 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	6	6	3
Units: microns				
arithmetic mean (standard deviation)				
Baseline	527.6 (± 126.79)	540.3 (± 284.34)	500.3 (± 155.65)	564.3 (± 115.68)
Change from Baseline at Week 4 (n=9,6,6,2)	-185.4 (± 161.23)	-239.5 (± 234.03)	-212.3 (± 182.94)	-113.5 (± 135.06)

Statistical analyses

No statistical analyses for this end point

Primary: Stage 2: Time between Baseline Treatment and Recurrence of Active Disease

End point title	Stage 2: Time between Baseline Treatment and Recurrence of Active Disease[4][5]

End point description:

Recurrence of Active Disease was based on Best Corrected Visual Acuity (BCVA), Central Retinal Thickness (CRT) values as evaluated by the Central Reading Center (CRC) and the investigator assessments of haemorrhage.

End point type	Primary

End point timeframe:

Baseline, Week 16

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No Statistical Analysis is reported for this outcome measure.

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all arms in the baseline period are applicable to this outcome measure.

End point values	Stage 2: AGN-150998 4.2 mg	Stage 2: AGN-150998 3.0 mg	Stage 2: Ranibizumab 0.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	65	57	57	
Units: days				
median (inter-quartile range (Q1-Q3))	59 (43 to 109)	57 (43 to 86)	57 (43 to 85)	

Statistical analyses

No statistical analyses for this end point

Primary: Stage 3: Change from Baseline in Best Corrected Visual Acuity (BCVA) in the Study Eye

End point title	Stage 3: Change from Baseline in Best Corrected Visual Acuity (BCVA) in the Study Eye[6][7]

End point description:

BCVA is measured using an eye chart and is reported as the number of letters read correctly (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.

End point type	Primary

End point timeframe:

Baseline, Week 16

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No Statistical Analysis is reported for this outcome measure.

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all arms in the baseline period are applicable to this outcome measure.

End point values	Stage 3: AGN-150998 2.0 mg	Stage 3: AGN-150998 1.0 mg	Stage 3: Ranibizumab 0.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	23	25	16	
Units: letters				
arithmetic mean (standard deviation)				
Baseline	58.5 (± 14.29)	58.4 (± 13.49)	60.4 (± 16.41)	
Change from Baseline at Week 16	8.2 (± 7.89)	6.3 (± 7.81)	5.3 (± 11.08)	

Statistical analyses

No statistical analyses for this end point

Secondary: Stage 2: Time between Second Treatment and Recurrence of Active Disease

End point title	Stage 2: Time between Second Treatment and Recurrence of Active Disease[8]

End point description:

Recurrence of active disease is defined as the time in days to escape to standard of care. Time is calculated as (date of Escaping to Standard of Care/Censoring minus the date of the Second Injection) +1. Inter-Quartile Range High value result of 99999.99=Not estimable.

End point type	Secondary

End point timeframe:

32 Weeks

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all arms in the baseline period are applicable to this outcome measure.

End point values	Stage 2: AGN-150998 4.2 mg	Stage 2: AGN-150998 3.0 mg	Stage 2: Ranibizumab 0.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	62	55	58	
Units: days				
median (inter-quartile range (Q1-Q3))	85 (57 to 118)	112 (60 to 99999.99)	111 (57 to 99999.99)	

Statistical analyses

No statistical analyses for this end point

Secondary: Stage 2: Change from Baseline in Central Retinal Thickness (CRT) in the Study Eye

End point title	Stage 2: Change from Baseline in Central Retinal Thickness (CRT) in the Study Eye[9]

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.

End point type	Secondary

End point timeframe:

Baseline, Week 4

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all arms in the baseline period are applicable to this outcome measure.

End point values	Stage 2: AGN-150998 4.2 mg	Stage 2: AGN-150998 3.0 mg	Stage 2: Ranibizumab 0.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	65	57	57	
Units: microns				
arithmetic mean (standard deviation)				
Baseline	524.6 (± 170.71)	507.3 (± 139.88)	497.1 (± 122.04)	
Change from Baseline at Week 4 (n=61,56,57)	-179.5 (± 123.76)	-155.3 (± 109.13)	-157.3 (± 121.95)	

Statistical analyses

No statistical analyses for this end point

Secondary: Stage 2: Change from Baseline in Best Corrected Visual Acuity (BCVA) in the Study Eye

End point title	Stage 2: Change from Baseline in Best Corrected Visual Acuity (BCVA) in the Study Eye[10]

End point description:

BCVA is measured using an eye chart and is reported as the number of letters read correctly (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.

End point type	Secondary

End point timeframe:

Baseline, Week 4

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all arms in the baseline period are applicable to this outcome measure.

End point values	Stage 2: AGN-150998 4.2 mg	Stage 2: AGN-150998 3.0 mg	Stage 2: Ranibizumab 0.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	65	57	57	
Units: letters				
arithmetic mean (standard deviation)				
Baseline	54.5 (± 13.9)	52.7 (± 12.62)	55.4 (± 13)	
Change from Baseline at Week 4 (n=62,56,57)	4.7 (± 9.71)	8.4 (± 11.51)	5.9 (± 64)	

Statistical analyses

No statistical analyses for this end point

Secondary: Stage 3: Change from Baseline in Central Retinal Thickness (CRT) in the Study Eye

End point title	Stage 3: Change from Baseline in Central Retinal Thickness (CRT) in the Study Eye[11]

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.

End point type	Secondary

End point timeframe:

Baseline, Week 4

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all arms in the baseline period are applicable to this outcome measure.

End point values	Stage 3: AGN-150998 2.0 mg	Stage 3: AGN-150998 1.0 mg	Stage 3: Ranibizumab 0.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	23	25	16	
Units: microns				
arithmetic mean (standard deviation)				
Baseline	466 (± 125.96)	526.1 (± 165.09)	463.3 (± 94.56)	
Change from Baseline at Week 4	-119.8 (± 68.5)	-168.3 (± 137.07)	-98.4 (± 65.22)	

Statistical analyses

No statistical analyses for this end point

Secondary: Stage 3: Change from Baseline in BCVA in the Study Eye

End point title	Stage 3: Change from Baseline in BCVA in the Study Eye[12]

End point description:

BCVA is measured using an eye chart and is reported as the number of letters read correctly (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.

End point type	Secondary

End point timeframe:

Baseline, Week 4

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Not all arms in the baseline period are applicable to this outcome measure.

End point values	Stage 3: AGN-150998 2.0 mg	Stage 3: AGN-150998 1.0 mg	Stage 3: Ranibizumab 0.5 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	23	25	16	
Units: letters				
arithmetic mean (standard deviation)				
Baseline	58.5 (± 14.29)	58.4 (± 13.49)	60.4 (± 16.41)	
Change from Baseline at Week 4	5 (± 7.4)	4.6 (± 5.98)	3.9 (± 6.01)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Stage 1: Up to 24 Weeks, Stage 2: Up to 32 Weeks and Stage 3: Up to 20 Weeks

Adverse event reporting additional description:

Adverse Events (AEs) are analyzed and reported independently for Stage 1, Stage 2 and Stage 3, For non-serious Adverse Events, a result of 0 means there were no AEs greater than or equal to the threshold of 5% in the reporting group/arm.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Stage 1: AGN-150998 4.2 mg

Reporting group description:

Stage 1: AGN-150998 4.2 mg given as a single intravitreal injection.

Reporting group title	Stage 1: AGN-150998 3.0 mg

Reporting group description:

Stage 1: AGN-150998 3.0 mg given as a single intravitreal injection.

Reporting group title	Stage 1: AGN-150998 2.0 mg

Reporting group description:

Stage 1: AGN-150998 2.0 mg given as a single intravitreal injection

Reporting group title	Stage 1: AGN-150998 1.0 mg

Reporting group description:

Stage 1: AGN-150998 1.0 mg given as a single intravitreal injection.

Reporting group title	Stage 2: AGN-150998 4.2 mg

Reporting group description:

Stage 2: AGN-150998 4.2 mg (highest tolerated dose from Stage 1) given as a single intravitreal injection at baseline. A second intravitreal injection will be given by week 16.

Reporting group title	Stage 2: Ranibizumab 0.5 mg

Reporting group description:

Stage 2: ranibizumab 0.5 mg given as a single intravitreal injection at baseline. A second intravitreal injection will be given by week 16.

Reporting group title	Stage 2: AGN-150998 3.0 mg

Reporting group description:

Stage 2: AGN-150998 3.0 mg (one dose below highest tolerated dose from Stage 1) given as a single intravitreal injection at baseline. A second intravitreal injection will be given by week 16.

Reporting group title	Stage 3: AGN-150998 1.0 mg

Reporting group description:

Stage 3: AGN-150998 1.0 mg given as intravitreal injections at Baseline, Weeks 4 and 8, followed by sham injections at Weeks 12 and 16.

Reporting group title	Stage 3: AGN-150998 2.0 mg

Reporting group description:

Stage 3: AGN-150998 2.0 mg given as intravitreal injections at Baseline, Weeks 4 and 8, followed by sham injections at Weeks 12 and 16.

Reporting group title	Stage 3: Ranibizumab 0.5 mg

Reporting group description:

Stage 3: ranibizumab 0.5 mg given as intravitreal injections every 4 weeks for 16 weeks

Serious adverse events	Stage 1: AGN-150998 4.2 mg	Stage 1: AGN-150998 3.0 mg	Stage 1: AGN-150998 2.0 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Rectal cancer			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal cell carcinoma			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal adenocarcinoma			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Temporal arteritis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Aortic valve stenosis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			

subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Uveitus			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anterior chamber inflammation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vitritis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Choroiditis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glaucoma			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Optic ischaemic neuropathy			

subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal artery occlusion			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Pancreatitis acute			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer haemorrhage			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			

subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endophthalmitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atypical pneumonia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Stage 1: AGN-150998 1.0 mg	Stage 2: AGN-150998 4.2 mg	Stage 2: Ranibizumab 0.5 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	11 / 67 (16.42%)	5 / 58 (8.62%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Rectal cancer			
subjects affected / exposed	0 / 3 (0.00%)	0 / 67 (0.00%)	1 / 58 (1.72%)
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 cell carcinoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 67 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 3 (0.00%)	0 / 67 (0.00%)	1 / 58 (1.72%)
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 adenocarcinoma			
subjects affected / exposed	0 / 3 (0.00%)	1 / 67 (1.49%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Vascular disorders			
Temporal arteritis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 67 (1.49%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Aortic valve stenosis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 67 (1.49%)	0 / 58 (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
Angina pectoris			
subjects affected / exposed	0 / 3 (0.00%)	0 / 67 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 67 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 3 (0.00%)	0 / 67 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Uveitus			
subjects affected / exposed	0 / 3 (0.00%)	3 / 67 (4.48%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anterior chamber inflammation			
subjects affected / exposed	0 / 3 (0.00%)	2 / 67 (2.99%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vitritis			

subjects affected / exposed	0 / 3 (0.00%)	1 / 67 (1.49%)	0 / 58 (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
Choroiditis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 67 (1.49%)	0 / 58 (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
Glaucoma			
subjects affected / exposed	0 / 3 (0.00%)	1 / 67 (1.49%)	0 / 58 (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
Optic ischaemic neuropathy			
subjects affected / exposed	0 / 3 (0.00%)	1 / 67 (1.49%)	0 / 58 (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
Retinal artery occlusion			
subjects affected / exposed	0 / 3 (0.00%)	1 / 67 (1.49%)	0 / 58 (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 disorders			
Pancreatitis acute			
subjects affected / exposed	0 / 3 (0.00%)	1 / 67 (1.49%)	0 / 58 (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
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 67 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 67 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			

Cholecystitis acute			
subjects affected / exposed	0 / 3 (0.00%)	1 / 67 (1.49%)	0 / 58 (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			
Renal failure acute			
subjects affected / exposed	0 / 3 (0.00%)	0 / 67 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 67 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endophthalmitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 67 (1.49%)	0 / 58 (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
Atypical pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 67 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Stage 2: AGN-150998 3.0 mg	Stage 3: AGN-150998 1.0 mg	Stage 3: AGN-150998 2.0 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 58 (10.34%)	0 / 25 (0.00%)	0 / 23 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Rectal cancer			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal cell carcinoma			

subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal adenocarcinoma			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Temporal arteritis			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Aortic valve stenosis			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	1 / 58 (1.72%)	0 / 25 (0.00%)	0 / 23 (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
Myocardial infarction			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 58 (1.72%)	0 / 25 (0.00%)	0 / 23 (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

Eye disorders			
Uveitus			
subjects affected / exposed	2 / 58 (3.45%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anterior chamber inflammation			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vitritis			
subjects affected / exposed	1 / 58 (1.72%)	0 / 25 (0.00%)	0 / 23 (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
Choroiditis			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glaucoma			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Optic ischaemic neuropathy			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal artery occlusion			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Pancreatitis acute			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Duodenal ulcer haemorrhage			
subjects affected / exposed	1 / 58 (1.72%)	0 / 25 (0.00%)	0 / 23 (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
Gastric ulcer haemorrhage			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endophthalmitis			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atypical pneumonia			
subjects affected / exposed	1 / 58 (1.72%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Stage 3: Ranibizumab 0.5 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 16 (0.00%)		

number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Rectal cancer			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal cell carcinoma			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rectal adenocarcinoma			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Temporal arteritis			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Aortic valve stenosis			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Angina pectoris			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			

subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Uveitus			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anterior chamber inflammation			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vitritis			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Choroiditis			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Glaucoma			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Optic ischaemic neuropathy			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Retinal artery occlusion			

subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Pancreatitis acute			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastric ulcer haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endophthalmitis			

subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atypical pneumonia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Stage 1: AGN-150998 4.2 mg	Stage 1: AGN-150998 3.0 mg	Stage 1: AGN-150998 2.0 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 9 (33.33%)	5 / 6 (83.33%)	4 / 6 (66.67%)
Injury, poisoning and procedural complications			
Laceration			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Contusion			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 9 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Ventricular extrasystoles			
subjects affected / exposed	0 / 9 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			

Headache			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Anterior chamber inflammation			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Retinal pigment epithelial tear			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Conjunctival haemorrhage			
subjects affected / exposed	0 / 9 (0.00%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Eye irritation			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 9 (0.00%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Anterior chamber cell			
subjects affected / exposed	0 / 9 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Anterior chamber flare			
subjects affected / exposed	0 / 9 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Eye pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 9 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hyalosis asteroid			
subjects affected / exposed	0 / 9 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Macular oedema			

subjects affected / exposed	0 / 9 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Foreign body sensation in eyes alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Retinal haemorrhage			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vitreous detachment			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Visual acuity reduced			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vitritis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vitreous floaters alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dry eye alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Age-related macular degeneration			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Macular scar			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Choroidal neovascularisation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Eye pruritus			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ocular discomfort			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Visual impairment			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Respiratory tract congestion			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 9 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Cough			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Urticaria			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 9 (11.11%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Nasopharyngitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 9 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Influenza			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Stage 1: AGN-150998 1.0 mg	Stage 2: AGN-150998 4.2 mg	Stage 2: Ranibizumab 0.5 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)	35 / 67 (52.24%)	19 / 58 (32.76%)
Injury, poisoning and procedural complications			
Laceration			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 67 (0.00%)	0 / 58 (0.00%)
occurrences (all)	0	0	0
Contusion			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 67 (0.00%)	0 / 58 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			

Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 67 (0.00%)	0 / 58 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 3 (0.00%)	0 / 67 (0.00%)	0 / 58 (0.00%)
occurrences (all)	0	0	0
Ventricular extrasystoles			
subjects affected / exposed	0 / 3 (0.00%)	0 / 67 (0.00%)	0 / 58 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 3 (0.00%)	1 / 67 (1.49%)	3 / 58 (5.17%)
occurrences (all)	0	2	5
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 67 (0.00%)	0 / 58 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Anterior chamber inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 67 (0.00%)	0 / 58 (0.00%)
occurrences (all)	0	0	0
Retinal pigment epithelial tear			
subjects affected / exposed	0 / 3 (0.00%)	0 / 67 (0.00%)	0 / 58 (0.00%)
occurrences (all)	0	0	0
Conjunctival haemorrhage			
subjects affected / exposed	1 / 3 (33.33%)	9 / 67 (13.43%)	5 / 58 (8.62%)
occurrences (all)	1	9	5
Eye irritation			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 3 (0.00%)	5 / 67 (7.46%)	2 / 58 (3.45%)
occurrences (all)	0	6	2
Anterior chamber cell			
subjects affected / exposed	0 / 3 (0.00%)	0 / 67 (0.00%)	0 / 58 (0.00%)
occurrences (all)	0	0	0
Anterior chamber flare			

subjects affected / exposed	0 / 3 (0.00%)	0 / 67 (0.00%)	0 / 58 (0.00%)
occurrences (all)	0	0	0
Eye pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 3 (0.00%)	6 / 67 (8.96%)	4 / 58 (6.90%)
occurrences (all)	0	7	6
Hyalosis asteroid			
subjects affected / exposed	0 / 3 (0.00%)	0 / 67 (0.00%)	0 / 58 (0.00%)
occurrences (all)	0	0	0
Macular oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 67 (0.00%)	0 / 58 (0.00%)
occurrences (all)	0	0	0
Foreign body sensation in eyes			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 3 (0.00%)	4 / 67 (5.97%)	1 / 58 (1.72%)
occurrences (all)	0	4	1
Retinal haemorrhage			
subjects affected / exposed	1 / 3 (33.33%)	6 / 67 (8.96%)	4 / 58 (6.90%)
occurrences (all)	1	7	5
Vitreous detachment			
subjects affected / exposed	0 / 3 (0.00%)	5 / 67 (7.46%)	2 / 58 (3.45%)
occurrences (all)	0	5	3
Visual acuity reduced			
subjects affected / exposed	0 / 3 (0.00%)	5 / 67 (7.46%)	3 / 58 (5.17%)
occurrences (all)	0	6	5
Vitritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 67 (0.00%)	0 / 58 (0.00%)
occurrences (all)	0	0	0
Vitreous floaters			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 3 (0.00%)	1 / 67 (1.49%)	0 / 58 (0.00%)
occurrences (all)	0	1	0
Dry eye			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 3 (0.00%)	0 / 67 (0.00%)	1 / 58 (1.72%)
occurrences (all)	0	0	1
Age-related macular degeneration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 67 (0.00%)	0 / 58 (0.00%)
occurrences (all)	0	0	0
Macular scar			
subjects affected / exposed	0 / 3 (0.00%)	0 / 67 (0.00%)	0 / 58 (0.00%)
occurrences (all)	0	0	0
Choroidal neovascularisation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 67 (0.00%)	0 / 58 (0.00%)
occurrences (all)	0	0	0
Eye pruritus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 67 (0.00%)	0 / 58 (0.00%)
occurrences (all)	0	0	0
Ocular discomfort			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 67 (0.00%)	0 / 58 (0.00%)
occurrences (all)	0	0	0
Visual impairment			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 67 (0.00%)	0 / 58 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Respiratory tract congestion			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 67 (0.00%)	0 / 58 (0.00%)
occurrences (all)	0	0	0
Cough			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 67 (0.00%)	0 / 58 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 67 (0.00%)	0 / 58 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			

Urticaria			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 67 (0.00%)	0 / 58 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 3 (0.00%)	4 / 67 (5.97%)	2 / 58 (3.45%)
occurrences (all)	0	4	2
Pain in extremity			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 3 (0.00%)	1 / 67 (1.49%)	1 / 58 (1.72%)
occurrences (all)	0	1	1
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 67 (0.00%)	0 / 58 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	4 / 67 (5.97%)	1 / 58 (1.72%)
occurrences (all)	0	5	1
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 67 (0.00%)	0 / 58 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 3 (0.00%)	0 / 67 (0.00%)	3 / 58 (5.17%)
occurrences (all)	0	0	3
Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 67 (0.00%)	0 / 58 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 67 (0.00%)	0 / 58 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Stage 2: AGN-150998 3.0 mg	Stage 3: AGN-150998 1.0 mg	Stage 3: AGN-150998 2.0 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 58 (34.48%)	10 / 25 (40.00%)	6 / 23 (26.09%)

Injury, poisoning and procedural complications			
Laceration			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Contusion			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Ventricular extrasystoles			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 58 (5.17%)	0 / 25 (0.00%)	1 / 23 (4.35%)
occurrences (all)	3	0	1
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Anterior chamber inflammation			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Retinal pigment epithelial tear			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Conjunctival haemorrhage			

subjects affected / exposed	3 / 58 (5.17%)	2 / 25 (8.00%)	1 / 23 (4.35%)
occurrences (all)	5	4	1
Eye irritation			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 58 (3.45%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences (all)	2	0	0
Anterior chamber cell			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Anterior chamber flare			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Eye pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 58 (5.17%)	1 / 25 (4.00%)	2 / 23 (8.70%)
occurrences (all)	3	1	3
Hyalosis asteroid			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Macular oedema			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Foreign body sensation in eyes			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 58 (0.00%)	1 / 25 (4.00%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Retinal haemorrhage			
subjects affected / exposed	3 / 58 (5.17%)	3 / 25 (12.00%)	0 / 23 (0.00%)
occurrences (all)	3	3	0
Vitreous detachment			
subjects affected / exposed	6 / 58 (10.34%)	2 / 25 (8.00%)	2 / 23 (8.70%)
occurrences (all)	7	2	3
Visual acuity reduced			
subjects affected / exposed	3 / 58 (5.17%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences (all)	8	0	0

Vitritis			
subjects affected / exposed	3 / 58 (5.17%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences (all)	3	0	0
Vitreous floaters			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 58 (5.17%)	3 / 25 (12.00%)	1 / 23 (4.35%)
occurrences (all)	3	3	1
Dry eye			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 58 (5.17%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences (all)	5	0	0
Age-related macular degeneration			
subjects affected / exposed	0 / 58 (0.00%)	1 / 25 (4.00%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Macular scar			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Choroidal neovascularisation			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Eye pruritus			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Ocular discomfort			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Visual impairment			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Respiratory tract congestion			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Cough			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Urticaria			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 58 (3.45%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences (all)	2	0	0
Pain in extremity			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 58 (5.17%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences (all)	3	0	0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	2 / 58 (3.45%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences (all)	5	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Influenza			

subjects affected / exposed	1 / 58 (1.72%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Bronchitis			
subjects affected / exposed	0 / 58 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Stage 3: Ranibizumab 0.5 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 16 (56.25%)		
Injury, poisoning and procedural complications			
Laceration			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Contusion			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Ventricular extrasystoles			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Eye disorders			
Anterior chamber inflammation			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Retinal pigment epithelial tear			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Conjunctival haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Eye irritation			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Anterior chamber cell			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Anterior chamber flare			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Eye pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Hyalosis asteroid			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Macular oedema			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		

Foreign body sensation in eyes				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Retinal haemorrhage				
subjects affected / exposed	2 / 16 (12.50%)			
occurrences (all)	2			
Vitreous detachment				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Visual acuity reduced				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Vitritis				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Vitreous floaters				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Dry eye				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Age-related macular degeneration				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Macular scar				
subjects affected / exposed	2 / 16 (12.50%)			
occurrences (all)	2			
Choroidal neovascularisation				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Eye pruritus				

subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	2		
Ocular discomfort			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	2		
Visual impairment			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Respiratory tract congestion			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Cough			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Urticaria			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Back pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Pain in extremity			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Influenza			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Upper respiratory tract infection			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Bronchitis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 July 2011	Amendment 1: An error in an inclusion criterion was corrected.
05 December 2011	Amendment 2: The protocol was amended to add a second injection of the study medication to assess the safety of repeat injection of the study medication and to add a cohort of Japanese patients to compare the safety, Pharmacokinetics (PK), and treatment effect of the study drug across ethnic groups.
24 August 2012	Amendment 3: The protocol was amended to add a potential interim analysis. Per protocol Population was used for Analysis. Week 16 Key Secondary time-point.
01 May 2013	Amendment 4: The protocol was amended to add a Stage 3 to explore the safety and effects of treatment with AGN-150998 administered at 4-week intervals on Best Corrected Visual Acuity (BCVA) and Central Retinal Thickness (CRT) versus ranibizumab.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported