Clinical trial results:
A 24-month, Phase 3b, randomized, double-masked, multicenter study assessing the efficacy and safety of two treatment regimens of 0.5 mg ranibizumab intravitreal injections guided by functional and/or anatomical criteria, in patients with neovascular age-related macular degeneration (OCTAVE)

Summary

EudraCT number	2011-004959-39
Trial protocol	CZ LT ES IE DE SK AT IT GB GR SE FI PT HU NL FR
Global end of trial date	09 July 2015

Results information

Result version number	v1 (current)
This version publication date	24 July 2016
First version publication date	24 July 2016

Trial information

Trial identification

Sponsor protocol code	CRFB002A2405

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01780935
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111,
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111,

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	09 July 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 July 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The original primary objective was to evaluate the effectiveness of 2 treatment regimens by assessing the average best corrected visual acuity (BCVA) change from Month 4 to Month 12 compared to Month 3 based on both BCVA stability in each treatment group and comparison of the 2 treatment groups. For the analysis of these objectives a reference margin of 2 letters was planned to be applied.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 June 2013
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	Argentina: 18
Country: Number of subjects enrolled	Austria: 26
Country: Number of subjects enrolled	Canada: 23
Country: Number of subjects enrolled	Colombia: 12
Country: Number of subjects enrolled	Czech Republic: 58
Country: Number of subjects enrolled	Finland: 7
Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Germany: 59
Country: Number of subjects enrolled	United Kingdom: 67
Country: Number of subjects enrolled	Greece: 20
Country: Number of subjects enrolled	Guatemala: 10
Country: Number of subjects enrolled	Hungary: 107
Country: Number of subjects enrolled	Ireland: 12
Country: Number of subjects enrolled	Italy: 47
Country: Number of subjects enrolled	Lithuania: 21
Country: Number of subjects enrolled	Mexico: 1
Country: Number of subjects enrolled	Netherlands: 19
Country: Number of subjects enrolled	Panama: 2

Country: Number of subjects enrolled	Portugal: 32
Country: Number of subjects enrolled	Slovakia: 44
Country: Number of subjects enrolled	Spain: 21
Country: Number of subjects enrolled	Sweden: 10
Country: Number of subjects enrolled	Switzerland: 32
Country: Number of subjects enrolled	Turkey: 18
Worldwide total number of subjects	671
EEA total number of subjects	555

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)	78
From 65 to 84 years	527
85 years and over	66

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study was originally designed to be a 24-month Phase 3b, randomized, double-masked, multicenter study, with 26 visits planned. Assuming an approximate 20% screen failure rate, approximately 840 patients needed to be screened to have 670 eligible in the study. A total of 671 patients were randomized.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	RBZ 0.5 mg: VA only (Group I)

Arm description:

RBZ 0.5 mg: Visual Acuity (VA) only (Group I) 0.5 mg intravitreal injections of ranibizumab with retreatment based on best-corrected visual acuity (BCVA) loss due to neovascular (wet) age-related macular degeneration (nAMD)

Arm type	Experimental
Investigational medicinal product name	ranibizumab
Investigational medicinal product code	RFB002
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

RBZ 0.5 mg intravitreal injections monthly

Arm title	RBZ 0.5 mg: VA and/or OCT (Group II)

Arm description:

RBZ 0.5 mg: VA and/or OCT (Group II) 0.5 mg intravitreal injections of ranibizumab with retreatment based on best-corrected visual acuity (BCVA)loss due to neovascular (wet) age-related macular degeneration (nAMD) and/or signs of wet AMD disease activity on optical coherence tomography (OCT).

Arm type	Experimental
Investigational medicinal product name	ranibizumab
Investigational medicinal product code	RFB002
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

RBZ 0.5 mg intravitreal injections monthly

Number of subjects in period 1	RBZ 0.5 mg: VA only (Group I)	RBZ 0.5 mg: VA and/or OCT (Group II)
Started	335	336
Completed	0	0
Not completed	335	336
Adverse event, serious fatal	1	6
Physician decision	1	1
Patient withdrew consent	8	9
Adverse event, non-fatal	2	4
Protocol deviation	-	1
Lost to follow-up	2	6
early termination/administrative problems	321	309

Baseline characteristics

Reporting groups	
Reporting group title	RBZ 0.5 mg: VA only (Group I)
Reporting group description:	
RBZ 0.5 mg: Visual Acuity (VA) only (Group I) 0.5 mg intravitreal injections of ranibizumab with retreatment based on best-corrected visual acuity (BCVA) loss due to neovascular (wet) age-related macular degeneration (nAMD)	
Reporting group title	RBZ 0.5 mg: VA and/or OCT (Group II)
Reporting group description:	
RBZ 0.5 mg: VA and/or OCT (Group II) 0.5 mg intravitreal injections of ranibizumab with retreatment based on best-corrected visual acuity (BCVA)loss due to neovascular (wet) age-related macular degeneration (nAMD) and/or signs of wet AMD disease activity on optical coherence tomography (OCT).	

Reporting group values	RBZ 0.5 mg: VA only (Group I)	RBZ 0.5 mg: VA and/or OCT (Group II)	Total
Number of subjects	335	336	671
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	47	31	78
From 65-84 years	263	264	527
85 years and over	25	41	66
Age Continuous Units: years			
arithmetic mean	73.9	75.3	
standard deviation	± 7.86	± 7.91	-
Gender, Male/Female Units: participants			
Male	122	142	264
Female	213	194	407

End points

End points reporting groups

Reporting group title	RBZ 0.5 mg: VA only (Group I)

Reporting group description:

RBZ 0.5 mg: Visual Acuity (VA) only (Group I) 0.5 mg intravitreal injections of ranibizumab with retreatment based on best-corrected visual acuity (BCVA) loss due to neovascular (wet) age-related macular degeneration (nAMD)

Reporting group title	RBZ 0.5 mg: VA and/or OCT (Group II)

Reporting group description:

RBZ 0.5 mg: VA and/or OCT (Group II) 0.5 mg intravitreal injections of ranibizumab with retreatment based on best-corrected visual acuity (BCVA)loss due to neovascular (wet) age-related macular degeneration (nAMD) and/or signs of wet AMD disease activity on optical coherence tomography (OCT).

Primary: Average best-corrected visual acuity (BCVA) (letters) change from Month 3 to Month 4 to Month 12

End point title	Average best-corrected visual acuity (BCVA) (letters) change from Month 3 to Month 4 to Month 12[1]

End point description:

Visual acuity (VA) was assessed during every study visit using best correction determined from protocol refraction. VA measurements (number of letters correctly identified) were performed with the patient in a sitting position using Early Treatment Diabetic Retinopathy Study (ETDRS)-like VA testing charts at a testing distance of 4 meters. This outcome measure describes the difference between the Visual Acuity averaged across all visits from Month 3 to Month 12 Level of VA (Letters) of the Study Eye. The treatment regimen up to Month 3 is the same in both treatment groups.

End point type	Primary

End point timeframe:

Month 3, Month 4, Month 12

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 was conducted due to early termination

End point values	RBZ 0.5 mg: VA only (Group I)	RBZ 0.5 mg: VA and/or OCT (Group II)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	335	336		
Units: Letters correctly read				
arithmetic mean (standard deviation)	0.1 (± 6.79)	1 (± 7.25)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Visual Acuity (Letters) of the Study Eye over time

End point title	Change from Baseline in Visual Acuity (Letters) of the Study Eye over time

End point description:

Visual acuity (VA) was assessed using best correction determined from protocol refraction. VA measurements (number of letters correctly identified) were performed with the patient in a sitting position using Early Treatment Diabetic Retinopathy Study (ETDRS)-like VA testing charts at a testing distance of 4 meters. This outcome measure describes the difference between the Visual Acuity averaged from Baseline to Month 12 Level of VA (Letters) of the Study Eye.

End point type	Secondary

End point timeframe:

Baseline to Month 12

End point values	RBZ 0.5 mg: VA only (Group I)	RBZ 0.5 mg: VA and/or OCT (Group II)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	335	336		
Units: letters correctly read				
arithmetic mean (standard deviation)	6.7 (± 13.48)	8.3 (± 13.53)		

Statistical analyses

No statistical analyses for this end point

Secondary: Gain of equal or more than 1, 5, 10, or 15 letters in Visual Acuity of the Study Eye from Baseline, at Month 12 and 24

End point title	Gain of equal or more than 1, 5, 10, or 15 letters in Visual Acuity of the Study Eye from Baseline, at Month 12 and 24

End point description:

During the course of the study, the use of optical coherence tomography (OCT)-guided therapy became a standard of care accepted by health authorities and the ophthalmology community in the treatment of neovascular (wet) age-related macular degeneration (nAMD), Novartis decided on 08-Oct-2014 the early termination of the study for futility. Therefore the 12-month cutoff date was not reached and the related analyses were not performed.

End point type	Secondary

End point timeframe:

Baseline to Month 12 and 24

End point values	RBZ 0.5 mg: VA only (Group I)	RBZ 0.5 mg: VA and/or OCT (Group II)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: number of letters				
number (not applicable)				

Notes:

[2] - Early termination - the 12-month cutoff date not reached and the related analysis was not performed

[3] - Early termination - the 12-month cutoff date not reached and the related analysis was not

performed

Statistical analyses

No statistical analyses for this end point

Secondary: Loss of less than 5, 10, and 15 letters in Visual Acuity in the Study Eye from Baseline, at Month 12 and 24

End point title	Loss of less than 5, 10, and 15 letters in Visual Acuity in the Study Eye from Baseline, at Month 12 and 24

End point description:

During the course of the study, the use of optical coherence tomography (OCT)-guided therapy became a standard of care accepted by health authorities and the ophthalmology community in the treatment of neovascular (wet) age-related macular degeneration (nAMD), Novartis decided on 08-Oct-2014 the early termination of the study for futility. Therefore the 12-month cutoff date was not reached and the related analyses were not performed.

End point type	Secondary

End point timeframe:

Baseline to Month 12 and 24

End point values	RBZ 0.5 mg: VA only (Group I)	RBZ 0.5 mg: VA and/or OCT (Group II)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[4]	0[5]		
Units: numbers of letters				
number (not applicable)				

Notes:

[4] - Early termination - the 12-month cutoff date not reached and the related analysis was not performed

[5] - Early termination - the 12-month cutoff date not reached and the related analysis was not performed

Statistical analyses

No statistical analyses for this end point

Secondary: Visual Acuity of 73 letters or more in the Study Eye at Month 12 and 24

End point title	Visual Acuity of 73 letters or more in the Study Eye at Month 12 and 24

End point description:

During the course of the study, the use of optical coherence tomography (OCT)-guided therapy became a standard of care accepted by health authorities and the ophthalmology community in the treatment of neovascular (wet) age-related macular degeneration (nAMD), Novartis decided on 08-Oct-2014 the early termination of the study for futility. Therefore the 12-month cutoff date was not reached and the related analyses were not performed.

End point type	Secondary

End point timeframe:

Month 12 and 24

End point values	RBZ 0.5 mg: VA only (Group I)	RBZ 0.5 mg: VA and/or OCT (Group II)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[6]	0[7]		
Units: number of letters				
number (not applicable)				

Notes:

[6] - Early termination - the 12-month cutoff date not reached and the related analysis was not performed
[7] - Early termination - the 12-month cutoff date not reached and the related analysis was not performed

Statistical analyses

No statistical analyses for this end point

Secondary: Average Visual Acuity change from Month 3 to Month 4 through Month 24 in the Study Eye

End point title	Average Visual Acuity change from Month 3 to Month 4 through Month 24 in the Study Eye

End point description:

During the course of the study, the use of optical coherence tomography (OCT)-guided therapy became a standard of care accepted by health authorities and the ophthalmology community in the treatment of neovascular (wet) age-related macular degeneration (nAMD), Novartis decided on 08-Oct-2014 the early termination of the study for futility. Therefore the 12-month cutoff date was not reached and the related analyses were not performed.

End point type	Secondary

End point timeframe:

Month 3 to Month 24

End point values	RBZ 0.5 mg: VA only (Group I)	RBZ 0.5 mg: VA and/or OCT (Group II)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[8]	0[9]		
Units: number of letters				
number (not applicable)				

Notes:

[8] - Early termination - the 12-month cutoff date not reached and the related analysis was not performed
[9] - Early termination - the 12-month cutoff date not reached and the related analysis was not performed

Statistical analyses

No statistical analyses for this end point

Secondary: Average Visual Acuity change from baseline to Month 1 through Month 12 and 24 in the Study Eye

End point title	Average Visual Acuity change from baseline to Month 1 through Month 12 and 24 in the Study Eye

End point description:

During the course of the study, the use of optical coherence tomography (OCT)-guided therapy became a standard of care accepted by health authorities and the ophthalmology community in the treatment of neovascular (wet) age-related macular degeneration (nAMD), Novartis decided on 08-Oct-2014 the early termination of the study for futility. Therefore the 12-month cutoff date was not reached and the related analyses were not performed.

End point type	Secondary

End point timeframe:

Baseline to Month 12 and 24

End point values	RBZ 0.5 mg: VA only (Group I)	RBZ 0.5 mg: VA and/or OCT (Group II)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[10]	0[11]		
Units: number of letters				
number (not applicable)				

Notes:

[10] - Early termination - the 12-month cutoff date not reached and the related analysis was not performed

[11] - Early termination - the 12-month cutoff date not reached and the related analysis was not performed

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Central Sub-Field Thickness (CSFT) and Central Sub-Field Volume (CSFV) of the Study Eye over time

End point title	Change from Baseline in Central Sub-Field Thickness (CSFT) and Central Sub-Field Volume (CSFV) of the Study Eye over time

End point description:

During the course of the study, the use of optical coherence tomography (OCT)-guided therapy became a standard of care accepted by health authorities and the ophthalmology community in the treatment of neovascular (wet) age-related macular degeneration (nAMD), Novartis decided on 08-Oct-2014 the early termination of the study for futility. Therefore the 12-month cutoff date was not reached and the related analyses were not performed.

End point type	Secondary

End point timeframe:

Baseline to Month 12 and 24

End point values	RBZ 0.5 mg: VA only (Group I)	RBZ 0.5 mg: VA and/or OCT (Group II)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[12]	0[13]		
Units: number of letters				
number (not applicable)				

Notes:

[12] - Early termination - the 12-month cutoff date not reached and the related analysis was not performed
[13] - Early termination - the 12-month cutoff date not reached and the related analysis was not performed

Statistical analyses

No statistical analyses for this end point

Secondary: Dry retina in the Study Eye on OCT at Month 12 and 24

End point title	Dry retina in the Study Eye on OCT at Month 12 and 24

End point description:

During the course of the study, the use of optical coherence tomography (OCT)-guided therapy became a standard of care accepted by health authorities and the ophthalmology community in the treatment of neovascular (wet) age-related macular degeneration (nAMD), Novartis decided on 08-Oct-2014 the early termination of the study for futility. Therefore the 12-month cutoff date was not reached and the related analyses were not performed.

End point type	Secondary

End point timeframe:

Month 12 and 24

End point values	RBZ 0.5 mg: VA only (Group I)	RBZ 0.5 mg: VA and/or OCT (Group II)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[14]	0[15]		
Units: number of occurences				
number (not applicable)				

Notes:

[14] - Early termination - the 12-month cutoff date not reached and the related analysis was not performed
[15] - Early termination - the 12-month cutoff date not reached and the related analysis was not performed

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in lesion size and morphology based on fluorescein angiography at Month 12 and 24

End point title	Change from Baseline in lesion size and morphology based on fluorescein angiography at Month 12 and 24

End point description:

During the course of the study, the use of optical coherence tomography (OCT)-guided therapy became a standard of care accepted by health authorities and the ophthalmology community in the treatment of neovascular (wet) age-related macular degeneration (nAMD), Novartis decided on 08-Oct-2014 the early termination of the study for futility. Therefore the 12-month cutoff date was not reached and the related analyses were not performed.

End point type	Secondary

End point timeframe:

Baseline to Month 12 and 24

End point values	RBZ 0.5 mg: VA only (Group I)	RBZ 0.5 mg: VA and/or OCT (Group II)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[16]	0[17]		
Units: lesion size				
number (not applicable)				

Notes:

[16] - Early termination - the 12-month cutoff date not reached and the related analysis was not performed

[17] - Early termination - the 12-month cutoff date not reached and the related analysis was not performed

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment patterns over time in both treatment arms

End point title	Treatment patterns over time in both treatment arms

End point description:

During the course of the study, the use of optical coherence tomography (OCT)-guided therapy became a standard of care accepted by health authorities and the ophthalmology community in the treatment of neovascular (wet) age-related macular degeneration (nAMD), Novartis decided on 08-Oct-2014 the early termination of the study for futility. Therefore the 12-month cutoff date was not reached and the related analyses were not performed.

End point type	Secondary

End point timeframe:

Baseline to Month 12 and 24

End point values	RBZ 0.5 mg: VA only (Group I)	RBZ 0.5 mg: VA and/or OCT (Group II)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[18]	0[19]		
Units: treatment patterns				
number (not applicable)				

Notes:

[18] - Early termination - the 12-month cutoff date not reached and the related analysis was not performed

[19] - Early termination - the 12-month cutoff date not reached and the related analysis was not performed

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the National Eye Institute Visual Functioning Questionnaire (NEI-VFQ-25) scores over time

End point title	Change from Baseline in the National Eye Institute Visual Functioning Questionnaire (NEI-VFQ-25) scores over time

End point description:

During the course of the study, the use of optical coherence tomography (OCT)-guided therapy became a standard of care accepted by health authorities and the ophthalmology community in the treatment of neovascular (wet) age-related macular degeneration (nAMD), Novartis decided on 08-Oct-2014 the early termination of the study for futility. Therefore the 12-month cutoff date was not reached and the related analyses were not performed.

End point type	Secondary

End point timeframe:

Baseline to Month 12 and 24

End point values	RBZ 0.5 mg: VA only (Group I)	RBZ 0.5 mg: VA and/or OCT (Group II)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[20]	0[21]		
Units: scores on a scale				
number (not applicable)				

Notes:

[20] - Early termination - the 12-month cutoff date not reached and the related analysis was not performed
[21] - Early termination - the 12-month cutoff date not reached and the related analysis was not performed

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency and severity of ocular and non-ocular adverse events over time

End point title	Frequency and severity of ocular and non-ocular adverse events over time

End point description:

During the course of the study, the use of optical coherence tomography (OCT)-guided therapy became a standard of care accepted by health authorities and the ophthalmology community in the treatment of neovascular (wet) age-related macular degeneration (nAMD), Novartis decided on 08-Oct-2014 the early termination of the study for futility. Therefore the 12-month cutoff date was not reached and the related analyses were not performed.

End point type	Secondary

End point timeframe:

Screening to Month 12 and 24

End point values	RBZ 0.5 mg: VA only (Group I)	RBZ 0.5 mg: VA and/or OCT (Group II)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[22]	0[23]		
Units: frequency of adverse events				
number (not applicable)				

Notes:

[22] - Early termination - the 12-month cutoff date not reached and the related analysis was not performed
[23] - Early termination - the 12-month cutoff date not reached and the related analysis was not performed

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All adverse events reported in this record are from date of First Patient First Treatment until Last Patient Last Visit

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	RBZ 0.5 mg: VA only (Group I)
Reporting group description:	
RBZ 0.5 mg: VA only (Group I)	
Reporting group title	RBZ 0.5 mg: VA and/or OCT (Group II)
Reporting group description:	
RBZ 0.5 mg: VA and/or OCT (Group II)	

Serious adverse events	RBZ 0.5 mg: VA only (Group I)	RBZ 0.5 mg: VA and/or OCT (Group II)	
Total subjects affected by serious adverse events			
subjects affected / exposed	30 / 334 (8.98%)	45 / 336 (13.39%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer			
subjects affected / exposed	1 / 334 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			

subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic myeloid leukaemia			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal stromal tumour			
subjects affected / exposed	1 / 334 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma			
subjects affected / exposed	1 / 334 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm			
subjects affected / exposed	1 / 334 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant neoplasm of ampulla of Vater			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesothelioma malignant			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to pleura			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to skin			

subjects affected / exposed	1 / 334 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oropharyngeal squamous cell carcinoma			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	0 / 334 (0.00%)	2 / 336 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Non-cardiac chest pain			
subjects affected / exposed	1 / 334 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Breast calcifications			
subjects affected / exposed	1 / 334 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst			
subjects affected / exposed	0 / 334 (0.00%)	2 / 336 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Bronchitis chronic			
subjects affected / exposed	1 / 334 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 334 (0.30%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Visual acuity tests abnormal (Study eye)			
subjects affected / exposed	1 / 334 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			

Ankle fracture			
subjects affected / exposed	1 / 334 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Concussion			
subjects affected / exposed	1 / 334 (0.30%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	1 / 334 (0.30%)	4 / 336 (1.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	1 / 334 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	1 / 334 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laceration			

subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus injury			
subjects affected / exposed	1 / 334 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	1 / 334 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 334 (0.00%)	3 / 336 (0.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block complete			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiogenic shock			

subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiopulmonary failure			
subjects affected / exposed	1 / 334 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiovascular insufficiency			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve incompetence			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Carotid artery occlusion			
subjects affected / exposed	1 / 334 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery stenosis			
subjects affected / exposed	1 / 334 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			
subjects affected / exposed	1 / 334 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dementia Alzheimer's type			

subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis post varicella (Study eye)			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	2 / 334 (0.60%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertebrobasilar insufficiency			
subjects affected / exposed	1 / 334 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Lymphadenopathy			

subjects affected / exposed	1 / 334 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo positional			
subjects affected / exposed	1 / 334 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Choroidal haemorrhage (Study eye)			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Optic ischaemic neuropathy (Fellow untreated eye)			
subjects affected / exposed	1 / 334 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal artery embolism (Study eye)			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Visual acuity reduced (Study eye)			
subjects affected / exposed	1 / 334 (0.30%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colitis ischaemic			
subjects affected / exposed	1 / 334 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Constipation			
subjects affected / exposed	1 / 334 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer haemorrhage			
subjects affected / exposed	1 / 334 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiatus hernia			
subjects affected / exposed	1 / 334 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic hepatitis			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Calculus ureteric			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	1 / 334 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Urinary retention			
subjects affected / exposed	1 / 334 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	2 / 334 (0.60%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal column stenosis			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal pain			
subjects affected / exposed	1 / 334 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spondylolisthesis			
subjects affected / exposed	1 / 334 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tenosynovitis			
subjects affected / exposed	1 / 334 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 334 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Appendicitis perforated			
subjects affected / exposed	1 / 334 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious pleural effusion			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 334 (0.30%)	2 / 336 (0.60%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic sepsis			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media chronic			
subjects affected / exposed	1 / 334 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 334 (0.00%)	3 / 336 (0.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheobronchitis			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			

subjects affected / exposed	1 / 334 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	0 / 334 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus			
subjects affected / exposed	1 / 334 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	RBZ 0.5 mg: VA only (Group I)	RBZ 0.5 mg: VA and/or OCT (Group II)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	66 / 334 (19.76%)	49 / 336 (14.58%)	
Investigations			
Intraocular pressure increased (Study eye)			
subjects affected / exposed	12 / 334 (3.59%)	21 / 336 (6.25%)	
occurrences (all)	16	35	
Vascular disorders			
Hypertension			
subjects affected / exposed	18 / 334 (5.39%)	15 / 336 (4.46%)	
occurrences (all)	21	16	
Eye disorders			
Conjunctival haemorrhage (Study eye)			
subjects affected / exposed	19 / 334 (5.69%)	10 / 336 (2.98%)	
occurrences (all)	20	10	

Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	24 / 334 (7.19%) 25	11 / 336 (3.27%) 11	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 September 2013	Amendment 1, issued after the inclusion of 12% of the patients, aimed to provide a more extensive risk-benefit assessment and to clarify some aspects of the protocol following Health Authority review. Minor revisions were done to the inclusion and exclusion criteria and clarifications were provided around assessing and treating the patient and the statistical analysis. Also, the amendment introduced the use of the pre-filled syringe (PFS) of ranibizumab. The safety and efficacy of ranibizumab administered with the PFS was not considered different from ranibizumab supplied in a vial.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

The use of OCT guided therapy in the treatment of nAMD became a standard of care during the study course. Early termination was therefore decided. The 12 month cutoff date was not reached and planned analyses were not performed.

Notes: