Clinical trial results:
A 12-Month, Multicentre, Randomised, Parallel Group Study to Compare the Efficacy and Safety of OZURDEX® Versus Lucentis® in Patients with Branch Retinal Vein Occlusion

Summary

EudraCT number	2010-023900-29
Trial protocol	GB DE ES IT
Global end of trial date	04 November 2014

Results information

Result version number	v1 (current)
This version publication date	21 April 2016
First version publication date	21 April 2016

Trial information

Trial identification

Sponsor protocol code	MAF-AGN-OPH-RET-004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01427751
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Allergan Pharmaceuticals Ireland
Sponsor organisation address	Allergan Limited Marlow International The Parkway, Marlow, United Kingdom,
Public contact	Allergan Limited EU Regulatory Dept, Allergan Limited, +44 1628 494444,
Scientific contact	Allergan Limited EU Regulatory Dept, Allergan Limited, +44 1628 494444, ml-eu_reg_affairs@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	28 September 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 November 2014
Global end of trial reached?	Yes
Global end of trial date	04 November 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study evaluated the safety and efficacy of dexamethasone intravitreal implant (Ozurdex®) compared to ranibizumab (Lucentis®) in patients with branch retinal vein occlusion (BRVO).

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 October 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	France: 31
Country: Number of subjects enrolled	Germany: 22
Country: Number of subjects enrolled	Israel: 96
Country: Number of subjects enrolled	Italy: 27
Country: Number of subjects enrolled	Spain: 69
Country: Number of subjects enrolled	United Kingdom: 62
Worldwide total number of subjects	307
EEA total number of subjects	211

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)	123

From 65 to 84 years	167
85 years and over	17

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study at 42 sites in France, Germany, Israel, Italy, Spain, and the United Kingdom from 11 Oct 2011 to 04 Nov 2014.

Pre-assignment

Screening details:

Participants with a diagnosis of Branch Retinal Vein Occlusion were enrolled in one of two treatment groups: OZURDEX® or Lucentis®.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Assessor[1]

Arms

Are arms mutually exclusive?	Yes
Arm title	Ozurdex®

Arm description:

Injection of Ozurdex® (dexamethasone intravitreal implant) into the study eye on Day 1 and Month 5. Participants may receive up to one additional treatment, thereafter.

Arm type	Active comparator
Investigational medicinal product name	Ozurdex®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Intravitreal implant in applicator
Routes of administration	Intravitreal use

Dosage and administration details:

OZURDEX® intravitreal implant 700 µg

Arm title	Lucentis®

Arm description:

Injection of Lucentis® (ranibizumab) into the study eye on Day 1 and monthly for five months. Participants will receive additional treatment thereafter based on re-treatment criteria.

Arm type	Active comparator
Investigational medicinal product name	Lucentis®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravitreal use

Dosage and administration details:

Lucentis® intravitreal injection 10 mg/mL

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: Only the Outcome Assessor was blinded for this trial.

Number of subjects in period 1	Ozurdex®	Lucentis®
Started	154	153
Completed	112	139
Not completed	42	14
Adverse event, serious fatal	2	-
Adverse event, non-fatal	18	2
Other miscellaneous reasons	6	4
Withdrawal of consent	2	2
No further treatment benefit expected	5	1
Lost to follow-up	3	1
Protocol deviation	6	4

Baseline characteristics

Reporting groups	
Reporting group title	Ozurdex®
Reporting group description:	
Injection of Ozurdex® (dexamethasone intravitreal implant) into the study eye on Day 1 and Month 5. Participants may receive up to one additional treatment, thereafter.	
Reporting group title	Lucentis®
Reporting group description:	
Injection of Lucentis® (ranibizumab) into the study eye on Day 1 and monthly for five months. Participants will receive additional treatment thereafter based on re-treatment criteria.	

Reporting group values	Ozurdex®	Lucentis®	Total
Number of subjects	154	153	307
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)	52	71	123
Elderly (From 65-84 years)	92	75	167
Elderly 85 years and over	10	7	17
Age Continuous | Units: years			
arithmetic mean	68.4	65.5	
standard deviation	± 10.58	± 12.04	-
Gender, Male/Female Units: participants			
Female	62	66	128
Male	92	87	179

End points

End points reporting groups

Reporting group title	Ozurdex®
Reporting group description:	
Injection of Ozurdex® (dexamethasone intravitreal implant) into the study eye on Day 1 and Month 5. Participants may receive up to one additional treatment, thereafter.	
Reporting group title	Lucentis®
Reporting group description:	
Injection of Lucentis® (ranibizumab) into the study eye on Day 1 and monthly for five months. Participants will receive additional treatment thereafter based on re-treatment criteria.	

Primary: Change from Baseline in Best Corrected Visual Acuity (BCVA)

End point title	Change from Baseline in Best Corrected Visual Acuity (BCVA)[1]
End point description:	
BCVA was measured in the study eye using an eye chart and was recorded as the number of letters read correctly for a total possible score of 0 to 100. The lower the number of letters read correctly on the eye chart, the worse the vision (or visual acuity). The higher the number of letters read correctly, the better the vision (or visual acuity) A positive change from Baseline (more letters read correctly) indicates improvement.	
End point type	Primary
End point timeframe:	
Baseline, 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 is reported for this outcome measure.

End point values	Ozurdex®	Lucentis®		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	153		
Units: letters				
arithmetic mean (standard deviation)				
Baseline (n=153,153)	56.6 (± 10.89)	59.2 (± 10.92)		
Change from Baseline at Month 12 (n=153,151)	7.9 (± 14.42)	16.9 (± 12.08)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Central Retinal Subfield Thickness Using Optical Coherence Tomography (OCT)

End point title	Change From Baseline in Central Retinal Subfield Thickness Using Optical Coherence Tomography (OCT)
End point description:	
Optical Coherence Tomography (OCT), a laser based non-invasive diagnostic system providing high-resolution imaging sections of the retina, was performed in the study eye after pupil dilation at Baseline and Month 12. A negative change from Baseline indicates improvement.	

End point type	Secondary

End point timeframe:

Baseline, Month 12

End point values	Ozurdex®	Lucentis®		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	153		
Units: microns				
arithmetic mean (standard deviation)				
Baseline (n=149, 149)	553.2 (± 170.15)	561 (± 188.93)		
Change from Baseline at Month 12 (n=140,144)	-219.2 (± 180.51)	-253.5 (± 197.08)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Patients with 15-or-More Letter Improvement in BCVA

End point title	Percentage of Patients with 15-or-More Letter Improvement in BCVA

End point description:

BCVA was measured in the study eye using an eye chart and was recorded as the number of letters read correctly for a total possible score of 0 to 100. The lower the number of letters read correctly on the eye chart, the worse the vision (or visual acuity). The higher the number of letters read correctly, the better the vision (or visual acuity). An improvement in the number of letters read means that the vision has improved.

End point type	Secondary

End point timeframe:

Baseline, Month 12

End point values	Ozurdex®	Lucentis®		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	153		
Units: percentage of participants				
number (not applicable)	33.8	59.5		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Patients with a 15-or-More Letter Decrease in BCVA

End point title	Percentage of Patients with a 15-or-More Letter Decrease in BCVA

End point description:

BCVA was measured in the study eye using an eye chart and was recorded as the number of letters read correctly for a total possible score of 0 to 100. The lower the number of letters read correctly on the eye chart, the worse the vision (or visual acuity).

End point type	Secondary

End point timeframe:

Baseline, Month 12

End point values	Ozurdex®	Lucentis®		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	153		
Units: percentage of participants				
number (not applicable)	9.1	0.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to BCVA Improvement of 15-or-More Letters

End point title	Time to BCVA Improvement of 15-or-More Letters

End point description:

BCVA was measured in the study eye using an eye chart and was recorded as the number of letters read correctly for a total possible score of 0 to 100. The time in days to BCVA improvement of 15-or-More letters.

End point type	Secondary

End point timeframe:

12 Months

End point values	Ozurdex®	Lucentis®		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	153		
Units: days				
arithmetic mean (standard deviation)	73.7 (± 79.68)	82 (± 93.78)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in National Eye Institute Visual Functioning Questionnaire-25 (VFQ-25)

End point title	Change From Baseline in National Eye Institute Visual Functioning Questionnaire-25 (VFQ-25)

End point description:

The VFQ-25 includes 25 vision-targeted questions plus one general health question which assess visual impairment on functioning and specific aspects of health-related quality of life for a total possible composite score of 0 (worst) to 100 (best functionality). A positive change from Baseline indicates improvement.

End point type	Secondary

End point timeframe:

Baseline, Month 12

End point values	Ozurdex®	Lucentis®		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	153		
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline (n=143,139)	78.1 (± 16.58)	80.7 (± 14.34)		
Change from Baseline at Month 12 (n=143, 139)	3.5 (± 12.21)	6.6 (± 13.45)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants not Completing the Month 12 Visit due to Treatment Failure

End point title	Percentage of Participants not Completing the Month 12 Visit due to Treatment Failure

End point description:

Treatment failure was defined as withdrawal of the participant from treatment or from the study by the investigator before the final visit because of a lack of efficacy.

End point type	Secondary

End point timeframe:

12 Months

End point values	Ozurdex®	Lucentis®		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	153		
Units: percentage of participants				
number (not applicable)	4.5	0.7		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 60 Weeks

Adverse event reporting additional description:

Safety population, all randomized participants who received at least 1 dose of study drug, was used to determine the number of participants at risk for Serious Adverse Events and Adverse Events.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.1

Reporting groups

Reporting group title	Lucentis®

Reporting group description:

Injection of Lucentis® (ranibizumab) into the study eye on Day 1 and monthly for five months. Participants will receive additional treatment thereafter based on re-treatment criteria.

Reporting group title	Ozurdex®

Reporting group description:

Injection of Ozurdex® (dexamethasone intravitreal implant) into the study eye on Day 1 and Month 5. Participants may receive up to one additional treatment, thereafter.

Serious adverse events	Lucentis®	Ozurdex®	
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 150 (10.67%)	12 / 153 (7.84%)	
number of deaths (all causes)	0	2	
number of deaths resulting from adverse events	0	0	
Vascular disorders			
Thrombophlebitis superficial			
subjects affected / exposed	0 / 150 (0.00%)	1 / 153 (0.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 150 (0.00%)	1 / 153 (0.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheter site related reaction			

subjects affected / exposed	1 / 150 (0.67%)	0 / 153 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 150 (0.00%)	1 / 153 (0.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Respiratory distress			
subjects affected / exposed	0 / 150 (0.00%)	1 / 153 (0.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Agitated depression			
subjects affected / exposed	0 / 150 (0.00%)	1 / 153 (0.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional state			
subjects affected / exposed	0 / 150 (0.00%)	1 / 153 (0.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anxiety			
subjects affected / exposed	1 / 150 (0.67%)	0 / 153 (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			
Hip fracture			
subjects affected / exposed	1 / 150 (0.67%)	1 / 153 (0.65%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Craniocerebral injury			

subjects affected / exposed	1 / 150 (0.67%)	0 / 153 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural complication			
subjects affected / exposed	1 / 150 (0.67%)	0 / 153 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haemorrhage			
subjects affected / exposed	1 / 150 (0.67%)	0 / 153 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 150 (0.00%)	1 / 153 (0.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Atrial fibrillation			
subjects affected / exposed	0 / 150 (0.00%)	1 / 153 (0.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradyarrhythmia			
subjects affected / exposed	0 / 150 (0.00%)	1 / 153 (0.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	1 / 150 (0.67%)	0 / 153 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 150 (0.67%)	0 / 153 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			

subjects affected / exposed	1 / 150 (0.67%)	0 / 153 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Palpitations			
subjects affected / exposed	1 / 150 (0.67%)	0 / 153 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 150 (0.00%)	1 / 153 (0.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 150 (0.00%)	1 / 153 (0.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 150 (0.67%)	0 / 153 (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	1 / 150 (0.67%)	0 / 153 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Ocular hypertension			
subjects affected / exposed	0 / 150 (0.00%)	1 / 153 (0.65%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastrointestinal haemorrhage			

subjects affected / exposed	0 / 150 (0.00%)	1 / 153 (0.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Diverticulum intestinal			
subjects affected / exposed	1 / 150 (0.67%)	0 / 153 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	1 / 150 (0.67%)	0 / 153 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			
subjects affected / exposed	1 / 150 (0.67%)	0 / 153 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal failure chronic			
subjects affected / exposed	0 / 150 (0.00%)	1 / 153 (0.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	1 / 150 (0.67%)	0 / 153 (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			
Arthralgia			
subjects affected / exposed	0 / 150 (0.00%)	1 / 153 (0.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal pain			
subjects affected / exposed	1 / 150 (0.67%)	0 / 153 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Osteoarthritis			
subjects affected / exposed	1 / 150 (0.67%)	0 / 153 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal column stenosis			
subjects affected / exposed	1 / 150 (0.67%)	0 / 153 (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			
Pneumonia			
subjects affected / exposed	0 / 150 (0.00%)	1 / 153 (0.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Endophthalmitis			
subjects affected / exposed	1 / 150 (0.67%)	0 / 153 (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			
Dehydration			
subjects affected / exposed	1 / 150 (0.67%)	0 / 153 (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	Lucentis®	Ozurdex®	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	104 / 150 (69.33%)	127 / 153 (83.01%)	
Investigations			
Intraocular pressure increased			
subjects affected / exposed	16 / 150 (10.67%)	50 / 153 (32.68%)	
occurrences (all)	28	83	
Vascular disorders			
Hypertension			

subjects affected / exposed	10 / 150 (6.67%)	5 / 153 (3.27%)	
occurrences (all)	10	6	
Nervous system disorders			
Headache			
subjects affected / exposed	9 / 150 (6.00%)	4 / 153 (2.61%)	
occurrences (all)	11	4	
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	17 / 150 (11.33%)	28 / 153 (18.30%)	
occurrences (all)	20	32	
Macular oedema			
subjects affected / exposed	4 / 150 (2.67%)	20 / 153 (13.07%)	
occurrences (all)	5	25	
Visual acuity reduced			
subjects affected / exposed	3 / 150 (2.00%)	18 / 153 (11.76%)	
occurrences (all)	4	22	
Cataract			
subjects affected / exposed	2 / 150 (1.33%)	13 / 153 (8.50%)	
occurrences (all)	2	17	
Lenticular opacities			
subjects affected / exposed	0 / 150 (0.00%)	10 / 153 (6.54%)	
occurrences (all)	0	10	
Ocular hypertension			
subjects affected / exposed	1 / 150 (0.67%)	9 / 153 (5.88%)	
occurrences (all)	2	15	
Blepharitis			
subjects affected / exposed	3 / 150 (2.00%)	9 / 153 (5.88%)	
occurrences (all)	3	9	
Dry eye			
subjects affected / exposed	7 / 150 (4.67%)	9 / 153 (5.88%)	
occurrences (all)	7	9	
Vitreous floaters			
subjects affected / exposed	9 / 150 (6.00%)	9 / 153 (5.88%)	
occurrences (all)	11	9	
Eye pain			

subjects affected / exposed	9 / 150 (6.00%)	6 / 153 (3.92%)	
occurrences (all)	13	8	
Conjunctivitis			
subjects affected / exposed	9 / 150 (6.00%)	6 / 153 (3.92%)	
occurrences (all)	12	7	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	5 / 150 (3.33%)	8 / 153 (5.23%)	
occurrences (all)	5	9	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 July 2011	Amendment 1 provided for the following revisions: • Addition of secondary efficacy endpoint for treatment failures (proportion of subjects in each treatment arm not completing the Month 12 visit) • Addition of specific wording for the recommended dose and administration of Lucentis • Addition of wording to provide guidance to the investigator in the event that a subject is not responding to treatment • Addition of instructions for contraception to be continued for 3 months after the last Lucentis injection • Additional revisions included corrected typographical errors, removed confusing text on assignment of randomization numbers, and inserted specific temperature storage requirements for Lucentis and OZURDEX.
13 September 2011	Amendment 2 provided for the following revisions: • Clarification that treatment allocation was to be made at each investigational site, but randomization and stratification were centralized • Revision of fluorescein angiography (FA) text to correct an erroneous statement in the original protocol regarding certification of technicians conducting the single FA required at the screening visit. Certification of FA technicians was not required for this assessment.
08 November 2012	Amendment 3 provided for the following revisions: • Removal of inclusion criterion 3 that specified a separate data protection consent form (Authorization/Data Protection Form) for European sites • Revision of exclusion criterion 12 in line with new safety information regarding the status of the posterior capsule of the study eye • Removal of requirement that optical coherence tomography (OCT) technician be masked to study treatment assignment • Clarification of wording for serious adverse event (SAE)-reporting procedures after the final dose of study drug • Additional revisions included administrative changes, removal of any additional references to the Authorization/Data Protection Form, clearly defining that 1 month was considered equivalent to 28 days, and separation of assessments for the study eye and fellow eye in the Schedule of Visits and Procedures.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported