Clinical trial results:
A PHASE 2, RANDOMIZED, DOUBLE-MASKED, CONTROLLED TRIAL TO ESTABLISH THE SAFETY AND EFFICACY OF INTRAVITREOUS INJECTIONS OF E10030 (ANTI-PDGF PEGYLATED APTAMER) GIVEN IN COMBINATION WITH LUCENTIS® IN SUBJECTS WITH NEOVASCULAR AGE-RELATED MACULAR DEGENERATION

Summary

EudraCT number	2010-018741-65
Trial protocol	LV FR BE DE ES HU IT AT
Global end of trial date	17 January 2012

Results information

Result version number	v1 (current)
This version publication date	31 December 2016
First version publication date	31 December 2016

Trial information

Trial identification

Sponsor protocol code	OPH1001A

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01089517
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Ophthotech Corporation
Sponsor organisation address	One Penn Plaza, New York, United States, NY 10119
Public contact	Jeffrey Nau, Ophthotech Corporation, 001 6465737045, jeff.nau@ophthotech.com
Scientific contact	Jeffrey Nau, Ophthotech Corporation, 001 6465737045, jeff.nau@ophthotech.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 January 2012
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 January 2012
Global end of trial reached?	Yes
Global end of trial date	17 January 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objectives of this study are to evaluate the safety and efficacy profile of E10030 intravitreous injection when administered in combination with Lucentis® 0.5 mg/eye versus monotherapy Lucentis® 0.5 mg/eye in subjects with subfoveal choroidal neovascularization secondary to age-related macular degeneration (AMD)

Protection of trial subjects:

To minimize pain, on the day of injection the subjects were prepared for injection by application of single use topical anesthetic to the eye.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 April 2010
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: 151
Country: Number of subjects enrolled	Israel: 34
Country: Number of subjects enrolled	European Union: 254
Country: Number of subjects enrolled	Colombia: 10
Worldwide total number of subjects	449
EEA total number of subjects	0

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)	25
From 65 to 84 years	323
85 years and over	101

Subject disposition

Recruitment

Recruitment details:

This study enrolled 449 patients at approximately 69 centers in North America, South America, Europe and Israel.

Pre-assignment

Screening details:

Subjects who had subfoveal choroidal neovascularization secondary to age-related macular degeneration (AMD), who were determined by the investigator as eligible and who provided informed consent were enrolled.

Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Lucentis

Arm description:

Sham/Lucentis

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

Dosage and administration details:

Subjects were randomized in a 1:1:1 ratio to the following dose groups:
E10030 0.3 mg/eye + Lucentis® 0. 5 mg/eye
E10030 1.5 mg/eye + Lucentis® 0. 5 mg/eye
E10030 sham + Lucentis® 0. 5 mg/eye
Subjects were treated with active E10030 or sham E10030 in combination with Lucentis® at Day 0, Week 4, Week 8, Week 12, Week 16 and Week 20.

Arm title	E10030 Low Dose Plus Lucentis

Arm description:

E10030 0.3 mg/Lucentis 0.5 mg

Arm type	Experimental
Investigational medicinal product name	Lucentis
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intravitreal use

Dosage and administration details:

Subjects were randomized in a 1:1:1 ratio to the following dose groups:
E10030 0.3 mg/eye + Lucentis® 0. 5 mg/eye
E10030 1.5 mg/eye + Lucentis® 0. 5 mg/eye
E10030 sham + Lucentis® 0. 5 mg/eye
Subjects were treated with active E10030 or sham E10030 in combination with Lucentis® at Day 0, Week 4, Week 8, Week 12, Week 16 and Week 20.

Investigational medicinal product name	E10030
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intravitreal use

Dosage and administration details:

Subjects were randomized in a 1:1:1 ratio to the following dose groups:
E10030 0.3 mg/eye + Lucentis® 0. 5 mg/eye
E10030 1.5 mg/eye + Lucentis® 0. 5 mg/eye
E10030 sham + Lucentis® 0. 5 mg/eye
Subjects were treated with active E10030 or sham E10030 in combination with Lucentis® at Day 0, Week 4, Week 8, Week 12, Week 16 and Week 20.

Arm title	E10030 HighDose Plus Lucentis

Arm description:

E10030 1.5 mg/Lucentis 0.5 mg

Arm type	Experimental
Investigational medicinal product name	Lucentis
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intravitreal use

Dosage and administration details:

Subjects were randomized in a 1:1:1 ratio to the following dose groups:
E10030 0.3 mg/eye + Lucentis® 0. 5 mg/eye
E10030 1.5 mg/eye + Lucentis® 0. 5 mg/eye
E10030 sham + Lucentis® 0. 5 mg/eye
Subjects were treated with active E10030 or sham E10030 in combination with Lucentis® at Day 0, Week 4, Week 8, Week 12, Week 16 and Week 20.

Investigational medicinal product name	E10030
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

Subjects were randomized in a 1:1:1 ratio to the following dose groups:
E10030 0.3 mg/eye + Lucentis® 0. 5 mg/eye
E10030 1.5 mg/eye + Lucentis® 0. 5 mg/eye
E10030 sham + Lucentis® 0. 5 mg/eye
Subjects were treated with active E10030 or sham E10030 in combination with Lucentis® at Day 0, Week 4, Week 8, Week 12, Week 16 and Week 20.

Number of subjects in period 1	Lucentis	E10030 Low Dose Plus Lucentis	E10030 HighDose Plus Lucentis
Started	148	149	152
Completed	148	149	152

Period 2

Period 2 title	Week 24
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Lucentis

Arm description:

Sham/Lucentis

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

Dosage and administration details:

Subjects were randomized in a 1:1:1 ratio to the following dose groups:
E10030 0.3 mg/eye + Lucentis® 0. 5 mg/eye
E10030 1.5 mg/eye + Lucentis® 0. 5 mg/eye
E10030 sham + Lucentis® 0. 5 mg/eye
Subjects were treated with active E10030 or sham E10030 in combination with Lucentis® at Day 0, Week 4, Week 8, Week 12, Week 16 and Week 20.

Arm title	E10030 Low Dose Plus Lucentis

Arm description:

E10030 0.3 mg/Lucentis 0.5 mg

Arm type	Experimental
Investigational medicinal product name	Lucentis
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intravitreal use

Dosage and administration details:

Subjects were randomized in a 1:1:1 ratio to the following dose groups:
E10030 0.3 mg/eye + Lucentis® 0. 5 mg/eye
E10030 1.5 mg/eye + Lucentis® 0. 5 mg/eye
E10030 sham + Lucentis® 0. 5 mg/eye
Subjects were treated with active E10030 or sham E10030 in combination with Lucentis® at Day 0, Week 4, Week 8, Week 12, Week 16 and Week 20.

Investigational medicinal product name	E10030
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

Subjects were randomized in a 1:1:1 ratio to the following dose groups:
E10030 0.3 mg/eye + Lucentis® 0. 5 mg/eye
E10030 1.5 mg/eye + Lucentis® 0. 5 mg/eye
E10030 sham + Lucentis® 0. 5 mg/eye
Subjects were treated with active E10030 or sham E10030 in combination with Lucentis® at Day 0, Week 4, Week 8, Week 12, Week 16 and Week 20.

Arm title	E10030 HighDose Plus Lucentis

Arm description:	
E10030 1.5 mg/Lucentis 0.5 mg	
Arm type	Experimental
Investigational medicinal product name	Lucentis
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intravitreal use

Dosage and administration details:

Subjects were randomized in a 1:1:1 ratio to the following dose groups:
E10030 0.3 mg/eye + Lucentis® 0. 5 mg/eye
E10030 1.5 mg/eye + Lucentis® 0. 5 mg/eye
E10030 sham + Lucentis® 0. 5 mg/eye
Subjects were treated with active E10030 or sham E10030 in combination with Lucentis® at Day 0, Week 4, Week 8, Week 12, Week 16 and Week 20.

Investigational medicinal product name	E10030
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

Subjects were randomized in a 1:1:1 ratio to the following dose groups:
E10030 0.3 mg/eye + Lucentis® 0. 5 mg/eye
E10030 1.5 mg/eye + Lucentis® 0. 5 mg/eye
E10030 sham + Lucentis® 0. 5 mg/eye
Subjects were treated with active E10030 or sham E10030 in combination with Lucentis® at Day 0, Week 4, Week 8, Week 12, Week 16 and Week 20.

Number of subjects in period 2	Lucentis	E10030 Low Dose Plus Lucentis	E10030 HighDose Plus Lucentis
Started	148	149	152
Completed	144	144	147
Not completed	4	5	5
Physician decision	-	-	1
At the subjects request	2	4	2
Adverse event, non-fatal	1	1	1
Sponsor descision	1	-	-
Lost to follow-up	-	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Lucentis
Reporting group description: Sham/Lucentis	
Reporting group title	E10030 Low Dose Plus Lucentis
Reporting group description: E10030 0.3 mg/Lucentis 0.5 mg	
Reporting group title	E10030 HighDose Plus Lucentis
Reporting group description: E10030 1.5 mg/Lucentis 0.5 mg	

Reporting group values	Lucentis	E10030 Low Dose Plus Lucentis	E10030 HighDose Plus Lucentis
Number of subjects	148	149	152
Age categorical Units: Subjects			
>= 65 years	140	139	141
Between 18 and 65 years	8	10	11
Age continuous Units: years			
arithmetic mean	78	77.6	77.8
standard deviation	± 7.98	± 8.19	± 8.36
Gender categorical Units: Subjects			
Female	93	90	92
Male	55	59	60

Reporting group values	Total		
Number of subjects	449		
Age categorical Units: Subjects			
>= 65 years	420		
Between 18 and 65 years	29		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	275		
Male	174		

End points

End points reporting groups	
Reporting group title	Lucentis
Reporting group description: Sham/Lucentis	
Reporting group title	E10030 Low Dose Plus Lucentis
Reporting group description: E10030 0.3 mg/Lucentis 0.5 mg	
Reporting group title	E10030 HighDose Plus Lucentis
Reporting group description: E10030 1.5 mg/Lucentis 0.5 mg	
Reporting group title	Lucentis
Reporting group description: Sham/Lucentis	
Reporting group title	E10030 Low Dose Plus Lucentis
Reporting group description: E10030 0.3 mg/Lucentis 0.5 mg	
Reporting group title	E10030 HighDose Plus Lucentis
Reporting group description: E10030 1.5 mg/Lucentis 0.5 mg	

Primary: Mean Change in Visual Acuity From Baseline at the Week 24 Visit	
End point title	Mean Change in Visual Acuity From Baseline at the Week 24 Visit
End point description: The primary efficacy endpoint is the mean change in visual acuity from baseline at the Week 24 visit.	
End point type	Primary
End point timeframe: 24 Weeks	

End point values	Lucentis	E10030 Low Dose Plus Lucentis	E10030 HighDose Plus Lucentis	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	147	147	151	
Units: ETDRS Letters				
arithmetic mean (standard deviation)	6.5 (± 1.09)	8.8 (± 1.09)	10.6 (± 1.07)	

Statistical analyses

Statistical analysis title	Primary analysis
Comparison groups	E10030 Low Dose Plus Lucentis v Lucentis v E10030 HighDose Plus Lucentis

Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.019
Method	ANCOVA

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Week 24	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	11.1
Reporting groups	
Reporting group title	Lucentis
Reporting group description: Sham/Lucentis	
Reporting group title	E10030 Low Dose Plus Lucentis
Reporting group description: E10030 0.3 mg/Lucentis 0.5 mg	
Reporting group title	E10030 HighDose Plus Lucentis
Reporting group description: E10030 1.5 mg/Lucentis 0.5 mg	

Serious adverse events	Lucentis	E10030 Low Dose Plus Lucentis	E10030 HighDose Plus Lucentis
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 148 (8.11%)	14 / 149 (9.40%)	10 / 152 (6.58%)
number of deaths (all causes)	1	1	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung squamous cell carcinoma			
subjects affected / exposed	0 / 148 (0.00%)	1 / 149 (0.67%)	0 / 152 (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
Metastatic neoplasm			
subjects affected / exposed	0 / 148 (0.00%)	1 / 149 (0.67%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Neoplasm skin			
subjects affected / exposed	0 / 148 (0.00%)	1 / 149 (0.67%)	0 / 152 (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

Rectal cancer			
subjects affected / exposed	0 / 148 (0.00%)	0 / 149 (0.00%)	1 / 152 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Benign salivary gland neoplasm			
subjects affected / exposed	1 / 148 (0.68%)	0 / 149 (0.00%)	0 / 152 (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
Brain cancer metastatic			
subjects affected / exposed	1 / 148 (0.68%)	0 / 149 (0.00%)	0 / 152 (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
Breast cancer			
subjects affected / exposed	1 / 148 (0.68%)	0 / 149 (0.00%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Arterial disorder			
subjects affected / exposed	0 / 148 (0.00%)	0 / 149 (0.00%)	1 / 152 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma			
subjects affected / exposed	0 / 148 (0.00%)	1 / 149 (0.67%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 148 (0.00%)	2 / 149 (1.34%)	2 / 152 (1.32%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			

subjects affected / exposed	0 / 148 (0.00%)	1 / 149 (0.67%)	0 / 152 (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
Haemoptysis			
subjects affected / exposed	0 / 148 (0.00%)	0 / 149 (0.00%)	1 / 152 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	1 / 148 (0.68%)	0 / 149 (0.00%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Subdural haematoma			
subjects affected / exposed	1 / 148 (0.68%)	0 / 149 (0.00%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Aortic valve stenosis			
subjects affected / exposed	0 / 148 (0.00%)	1 / 149 (0.67%)	0 / 152 (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
Atrial fibrillation			
subjects affected / exposed	1 / 148 (0.68%)	1 / 149 (0.67%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 148 (0.00%)	1 / 149 (0.67%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 148 (0.00%)	0 / 149 (0.00%)	1 / 152 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac failure congestive			
subjects affected / exposed	1 / 148 (0.68%)	0 / 149 (0.00%)	1 / 152 (0.66%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arrhythmia			
subjects affected / exposed	1 / 148 (0.68%)	0 / 149 (0.00%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cardiac disorder			
subjects affected / exposed	1 / 148 (0.68%)	0 / 149 (0.00%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	0 / 148 (0.00%)	1 / 149 (0.67%)	0 / 152 (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
Cerebrovascular accident			
subjects affected / exposed	2 / 148 (1.35%)	0 / 149 (0.00%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Loss of consciousness			
subjects affected / exposed	1 / 148 (0.68%)	0 / 149 (0.00%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular encephalopathy			
subjects affected / exposed	1 / 148 (0.68%)	0 / 149 (0.00%)	0 / 152 (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			
Corneal erosion			
subjects affected / exposed	0 / 148 (0.00%)	0 / 149 (0.00%)	1 / 152 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Uveitis			
subjects affected / exposed	0 / 148 (0.00%)	1 / 149 (0.67%)	0 / 152 (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
Visual acuity reduced			
subjects affected / exposed	1 / 148 (0.68%)	0 / 149 (0.00%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 148 (0.00%)	0 / 149 (0.00%)	1 / 152 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 148 (0.00%)	0 / 149 (0.00%)	1 / 152 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer			
subjects affected / exposed	0 / 148 (0.00%)	1 / 149 (0.67%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 148 (0.00%)	1 / 149 (0.67%)	0 / 152 (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
Inguinal hernia, obstructive			
subjects affected / exposed	0 / 148 (0.00%)	0 / 149 (0.00%)	1 / 152 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	0 / 148 (0.00%)	0 / 149 (0.00%)	1 / 152 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ulcerative			

subjects affected / exposed	1 / 148 (0.68%)	0 / 149 (0.00%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 148 (0.68%)	0 / 149 (0.00%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	0 / 148 (0.00%)	0 / 149 (0.00%)	1 / 152 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 148 (0.00%)	0 / 149 (0.00%)	2 / 152 (1.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spondylitis			
subjects affected / exposed	1 / 148 (0.68%)	0 / 149 (0.00%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Osteomyelitis			
subjects affected / exposed	0 / 148 (0.00%)	1 / 149 (0.67%)	0 / 152 (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
Sepsis			
subjects affected / exposed	0 / 148 (0.00%)	1 / 149 (0.67%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			

subjects affected / exposed	0 / 148 (0.00%)	1 / 149 (0.67%)	0 / 152 (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
Bronchitis			
subjects affected / exposed	1 / 148 (0.68%)	0 / 149 (0.00%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Lucentis	E10030 Low Dose Plus Lucentis	E10030 HighDose Plus Lucentis
Total subjects affected by non-serious adverse events			
subjects affected / exposed	94 / 148 (63.51%)	97 / 149 (65.10%)	99 / 152 (65.13%)
Investigations			
Intraocular pressure increased			
subjects affected / exposed	4 / 148 (2.70%)	8 / 149 (5.37%)	9 / 152 (5.92%)
occurrences (all)	5	13	16
Vascular disorders			
Hypertension			
subjects affected / exposed	8 / 148 (5.41%)	7 / 149 (4.70%)	5 / 152 (3.29%)
occurrences (all)	8	7	5
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	37 / 148 (25.00%)	34 / 149 (22.82%)	51 / 152 (33.55%)
occurrences (all)	80	91	133
Punctate keratitis			
subjects affected / exposed	10 / 148 (6.76%)	19 / 149 (12.75%)	15 / 152 (9.87%)
occurrences (all)	25	43	39
Eye pain			
subjects affected / exposed	8 / 148 (5.41%)	10 / 149 (6.71%)	13 / 152 (8.55%)
occurrences (all)	10	12	31
Conjunctival hyperaemia			
subjects affected / exposed	13 / 148 (8.78%)	9 / 149 (6.04%)	13 / 152 (8.55%)
occurrences (all)	35	21	30
Subretinal fibrosis			

subjects affected / exposed occurrences (all)	8 / 148 (5.41%) 8	6 / 149 (4.03%) 7	5 / 152 (3.29%) 5

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 March 2011	provide clarification of inclusion/exclusion criteria and fix typographical errors.
16 November 2011	primary endpoint modified to be in conformity with the primary endpoint utilized in other Phase 2 trials for wet AMD, as well as a change in the timing of this endpoint from Week 12 to Week 24.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported