# 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<br>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 \|<br>Units: years | | | |
| arithmetic mean | 68.4 | 65.5 | |
| standard deviation | ± 10.58 | ± 12.04 | - |
| Gender, Male/Female<br>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