Clinical trial results:
A Multicenter, Open-label, Randomized Study Comparing the Efficacy and Safety of 700 g Dexamethasone Posterior Segment Drug Delivery System (DEX PS DDS) to Ranibizumab in Patients With Diabetic Macular Edema

Summary

EudraCT number	2011-005631-20
Trial protocol	DE BE PT SE ES GB NL AT DK IT
Global end of trial date	13 February 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	206207-024

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01492400
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Allergan Limited
Sponsor organisation address	Allergan Limited Marlow International The Parkway, Marlow, United Kingdom, SL7 1YL
Public contact	Allergan Limited EU Regulatory Dept, Allergan Limited, 44 1628 494444, ml-eu_reg_affairs@allergan.com
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	21 May 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 February 2014
Global end of trial reached?	Yes
Global end of trial date	13 February 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate whether treatment with 700 µg DEX PS DDS every 5 months provides a similar treatment effect on average change of best-corrected visual acuity (BCVA) as ranibizumab administered as per its European Summary of Product Characteristics (SmPC) in patients with DME

Protection of trial subjects:

All study participants were required to read and sign an Informed Consent Form .

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 March 2012
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: 143
Country: Number of subjects enrolled	United Kingdom: 29
Country: Number of subjects enrolled	Denmark: 5
Country: Number of subjects enrolled	Spain: 14
Country: Number of subjects enrolled	France: 33
Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	Israel: 85
Country: Number of subjects enrolled	Italy: 26
Country: Number of subjects enrolled	Netherlands Antilles: 2
Country: Number of subjects enrolled	Portugal: 17
Country: Number of subjects enrolled	South Africa: 2
Worldwide total number of subjects	363
EEA total number of subjects	131

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)	187
From 65 to 84 years	173
85 years and over	3

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Patients were screened up to 2 weeks prior to randomization on Day 1.

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	dexamethasone Intravitreal Implant

Arm description:

Injection of 700 ug dexamethasone intravitreal implant into the study eye on Day 1, Month 5, and Month 10.

Arm type	Experimental
Investigational medicinal product name	dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Implant
Routes of administration	Implantation

Dosage and administration details:

Injection of 700 ug dexamethasone intravitreal implant into the study eye on Day 1, Month 5, and Month 10.

Arm title	ranibizumab

Arm description:

Injection of ranibizumab 0.5 mg into the study eye on Day 1. Patients may receive additional injections on a monthly basis, as needed, for disease progression.

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

Dosage and administration details:

Injection of ranibizumab 0.5 mg into the study eye on Day 1. Patients may receive additional injections on a monthly basis, as needed, for disease progression.

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	dexamethasone Intravitreal Implant	ranibizumab
Started	181	182
Completed	165	166
Not completed	16	16
Adverse event, non-fatal	10	5
Miscellaneous Reasons	2	3
Pregnancy	-	1
Personal Reasons	-	5
Lost to follow-up	3	1
Lack of efficacy	1	1

Baseline characteristics

Reporting groups	
Reporting group title	dexamethasone Intravitreal Implant
Reporting group description:	
Injection of 700 ug dexamethasone intravitreal implant into the study eye on Day 1, Month 5, and Month 10.	
Reporting group title	ranibizumab
Reporting group description:	
Injection of ranibizumab 0.5 mg into the study eye on Day 1. Patients may receive additional injections on a monthly basis, as needed, for disease progression.	

Reporting group values	dexamethasone Intravitreal Implant	ranibizumab	Total
Number of subjects	181	182	363
Age categorical Units: Subjects			
Adults (18-64 years)	98	89	187
From 65-84 years	81	92	173
85 years and over	2	1	3
Age continuous Units: years			
arithmetic mean	63.4	63.7	
standard deviation	± 9.39	± 10.05	-
Gender, Male/Female Units: Participants			
Female	69	66	135
Male	112	116	228

End points

End points reporting groups

Reporting group title	dexamethasone Intravitreal Implant
Reporting group description:	
Injection of 700 ug dexamethasone intravitreal implant into the study eye on Day 1, Month 5, and Month 10.	
Reporting group title	ranibizumab
Reporting group description:	
Injection of ranibizumab 0.5 mg into the study eye on Day 1. Patients may receive additional injections on a monthly basis, as needed, for disease progression.	

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

End point title	Average Change from Baseline in Best Corrected Visual Acuity (BCVA) in the Study Eye[1]
End point description:	
BCVA is measured using an eye chart and is reported as the number of letters read correctly (ranging from 0 to 100 letters) in the study eye. The lower the number of letters read correctly on the eye chart, the worse the vision (or visual acuity). The average BCVA is calculated across study visits for each patient. A positive number change from baseline indicates an improvement and a negative number change from baseline indicates a worsening.	
End point type	Primary
End point timeframe:	
Baseline, 12 Months	

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	dexamethasone Intravitreal Implant	ranibizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	181	182		
Units: Letters				
arithmetic mean (standard deviation)				
Baseline	60.2 (± 9.74)	60.4 (± 9.34)		
Change from Baseline at 12 Months	4.34 (± 7.342)	7.6 (± 6.735)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Foveal Thickness Measured by Optical Coherence Tomography (OCT) in the Study Eye

End point title	Change from Baseline in Foveal Thickness Measured by Optical Coherence Tomography (OCT) in the Study Eye

End point description:

OCT is a laser based non-invasive diagnostic system providing high-resolution imaging sections of the fovea (part of the retina) in the study eye after pupil dilation. A negative change from baseline indicates an improvement (less foveal thickness) and a positive change from baseline indicates a worsening (more foveal thickness).

End point type	Secondary

End point timeframe:

Baseline, Month 12

End point values	dexamethasone Intravitreal Implant	ranibizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	181	182		
Units: Microns				
arithmetic mean (standard deviation)				
Baseline	465.1 (± 136.09)	471.2 (± 139.51)		
Change from Baseline at Month 12 (N=163, 166)	-173.9 (± 129.64)	-163.5 (± 161.34)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Total Area of Macular Leakage in the Study Eye Measured on Fluorescein Angiography (FA)

End point title	Change from Baseline in Total Area of Macular Leakage in the Study Eye Measured on Fluorescein Angiography (FA)

End point description:

FA is a technique for examining the circulation of the retina (and detecting any leakage) using a dye-tracing method. Photographs are taken with a specialized low-power microscope with an attached camera designed to photograph the interior of the eye, including the retina and optic disc. A negative change from baseline indicates a decrease in leakage (improvement) and a positive change from baseline indicates an increase in leakage (worsening).

End point type	Secondary

End point timeframe:

Baseline, Month 12

End point values	dexamethasone Intravitreal Implant	ranibizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	172	177		
Units: Square Millimeters (mm^2)				
arithmetic mean (standard deviation)				
Baseline	19.2 (± 13.01)	18.9 (± 12.55)		

Change from Baseline at Month 12 (N=125, 142)	-16.1 (± 11.64)	-12 (± 10.54)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment emergent adverse events (TEAE) are reported and include all adverse events (AEs) and serious adverse events (SAEs) that began or worsened after study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	dexamethasone Intravitreal Implant

Reporting group description:

Injection of 700 ug dexamethasone intravitreal implant into the study eye on Day 1, Month 5, and Month 10.

Reporting group title	ranibizumab

Reporting group description:

Injection of ranibizumab 0.5 mg into the study eye on Day 1. Patients may receive additional injections on a monthly basis, as needed, for disease progression.

Serious adverse events	dexamethasone Intravitreal Implant	ranibizumab	
Total subjects affected by serious adverse events			
subjects affected / exposed	40 / 181 (22.10%)	41 / 182 (22.53%)	
number of deaths (all causes)	3	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	3 / 181 (1.66%)	0 / 182 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder Transitional Cell Carcinoma			
subjects affected / exposed	1 / 181 (0.55%)	0 / 182 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung Squamous Cell Carcinoma Metastatic			
subjects affected / exposed	1 / 181 (0.55%)	0 / 182 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Mantle Cell Lymphoma			

subjects affected / exposed	1 / 181 (0.55%)	0 / 182 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasm Malignant			
subjects affected / exposed	1 / 181 (0.55%)	0 / 182 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate Cancer			
subjects affected / exposed	1 / 181 (0.55%)	0 / 182 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous Cell Carcinoma of the Tongue			
subjects affected / exposed	1 / 181 (0.55%)	0 / 182 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon Cancer			
subjects affected / exposed	0 / 181 (0.00%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic Carcinoma			
subjects affected / exposed	0 / 181 (0.00%)	1 / 182 (0.55%)	
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 / 181 (0.00%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Orthostatic Hypotension			
subjects affected / exposed	1 / 181 (0.55%)	0 / 182 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive Crisis			

subjects affected / exposed	0 / 181 (0.00%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral Ischaemia			
subjects affected / exposed	0 / 181 (0.00%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral Vascular Disorder			
subjects affected / exposed	0 / 181 (0.00%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Cardiac Pacemaker Insertion			
subjects affected / exposed	1 / 181 (0.55%)	0 / 182 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liposuction			
subjects affected / exposed	1 / 181 (0.55%)	0 / 182 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest Pain			
subjects affected / exposed	2 / 181 (1.10%)	0 / 182 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthenia			
subjects affected / exposed	1 / 181 (0.55%)	0 / 182 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Local Swelling			
subjects affected / exposed	1 / 181 (0.55%)	0 / 182 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pyrexia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 181 (0.00%)	2 / 182 (1.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised Oedema			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 181 (0.00%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 181 (0.00%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Endometrial Hyperplasia			
subjects affected / exposed	0 / 181 (0.00%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute Respiratory Failure			
subjects affected / exposed	2 / 181 (1.10%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	1 / 181 (0.55%)	0 / 182 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	1 / 181 (0.55%)	0 / 182 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Respiratory Depression			
subjects affected / exposed	1 / 181 (0.55%)	0 / 182 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary Oedema			
subjects affected / exposed	0 / 181 (0.00%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Intraocular Pressure Increased			
subjects affected / exposed	2 / 181 (1.10%)	0 / 182 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight Decreased			
subjects affected / exposed	0 / 181 (0.00%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Hip Fracture			
subjects affected / exposed	2 / 181 (1.10%)	0 / 182 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post Procedural Haemorrhage			
subjects affected / exposed	1 / 181 (0.55%)	0 / 182 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal Fracture			
subjects affected / exposed	1 / 181 (0.55%)	0 / 182 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon Rupture			
subjects affected / exposed	1 / 181 (0.55%)	0 / 182 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Femoral Neck Fracture			
subjects affected / exposed	0 / 181 (0.00%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand Fracture			
subjects affected / exposed	0 / 181 (0.00%)	1 / 182 (0.55%)	
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	0 / 181 (0.00%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post Procedural Haematoma			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 181 (0.00%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac Failure Congestive			
subjects affected / exposed	4 / 181 (2.21%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary Artery Disease			
subjects affected / exposed	2 / 181 (1.10%)	2 / 182 (1.10%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina Pectoris			
subjects affected / exposed	1 / 181 (0.55%)	2 / 182 (1.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial Fibrillation			
subjects affected / exposed	1 / 181 (0.55%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac Failure			
subjects affected / exposed	1 / 181 (0.55%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Acute Myocardial Infarction			
subjects affected / exposed	1 / 181 (0.55%)	0 / 182 (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 / 181 (0.55%)	0 / 182 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial Effusion			
subjects affected / exposed	1 / 181 (0.55%)	0 / 182 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			
subjects affected / exposed	1 / 181 (0.55%)	0 / 182 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial Ischaemia			
subjects affected / exposed	0 / 181 (0.00%)	2 / 182 (1.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic Valve Stenosis			
subjects affected / exposed	0 / 181 (0.00%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Palpitations			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 181 (0.00%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Ventricular Tachyarrhythmia			
subjects affected / exposed	0 / 181 (0.00%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Syncope			
subjects affected / exposed	2 / 181 (1.10%)	0 / 182 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Grand Mal Convulsion			
subjects affected / exposed	1 / 181 (0.55%)	0 / 182 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningorrhagia			
subjects affected / exposed	1 / 181 (0.55%)	0 / 182 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular Accident			
subjects affected / exposed	0 / 181 (0.00%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Convulsion			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 181 (0.00%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic Stroke			
subjects affected / exposed	0 / 181 (0.00%)	1 / 182 (0.55%)	
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 / 181 (0.00%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 181 (0.55%)	2 / 182 (1.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukocytosis			
subjects affected / exposed	1 / 181 (0.55%)	0 / 182 (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			
Sudden Hearing Loss			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 181 (0.00%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Open Angle Glaucoma			
subjects affected / exposed	1 / 181 (0.55%)	0 / 182 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Choroiditis			
subjects affected / exposed	0 / 181 (0.00%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lacrimation Increased			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 181 (0.00%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vitreous Haemorrhage			
subjects affected / exposed	0 / 181 (0.00%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			

Colitis			
subjects affected / exposed	1 / 181 (0.55%)	0 / 182 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal Ulcer Haemorrhage			
subjects affected / exposed	1 / 181 (0.55%)	0 / 182 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal Hernia			
subjects affected / exposed	1 / 181 (0.55%)	0 / 182 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal Pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 181 (0.00%)	2 / 182 (1.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 181 (0.00%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper Gastrointestinal Haemorrhage			
subjects affected / exposed	0 / 181 (0.00%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 181 (0.00%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Jaundice			

subjects affected / exposed	0 / 181 (0.00%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Diabetic Foot			
subjects affected / exposed	1 / 181 (0.55%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal Failure Acute			
subjects affected / exposed	4 / 181 (2.21%)	3 / 182 (1.65%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal Failure Chronic			
subjects affected / exposed	1 / 181 (0.55%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	1 / 181 (0.55%)	0 / 182 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephropathy			
subjects affected / exposed	0 / 181 (0.00%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Renal Failure			
subjects affected / exposed	0 / 181 (0.00%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Rotator Cuff Syndrome			
subjects affected / exposed	1 / 181 (0.55%)	0 / 182 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Osteonecrosis			
subjects affected / exposed	0 / 181 (0.00%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Sepsis			
subjects affected / exposed	2 / 181 (1.10%)	2 / 182 (1.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 181 (0.55%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endophthalmitis			
subjects affected / exposed	1 / 181 (0.55%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 181 (0.55%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound Infection			
subjects affected / exposed	1 / 181 (0.55%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess Limb			
subjects affected / exposed	1 / 181 (0.55%)	0 / 182 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal Abscess			
subjects affected / exposed	1 / 181 (0.55%)	0 / 182 (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	1 / 181 (0.55%)	0 / 182 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney Infection			
subjects affected / exposed	1 / 181 (0.55%)	0 / 182 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	1 / 181 (0.55%)	0 / 182 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sialoadenitis			
subjects affected / exposed	1 / 181 (0.55%)	0 / 182 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal Wall Abscess			
subjects affected / exposed	0 / 181 (0.00%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical Pneumonia			
subjects affected / exposed	0 / 181 (0.00%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected Bites			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 181 (0.00%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic Shock			
subjects affected / exposed	0 / 181 (0.00%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metabolism and nutrition disorders			

Hypoglycaemia			
subjects affected / exposed	2 / 181 (1.10%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	1 / 181 (0.55%)	0 / 182 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes Mellitus Inadequate Control			
subjects affected / exposed	0 / 181 (0.00%)	2 / 182 (1.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 181 (0.00%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 181 (0.00%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic Acidosis			
subjects affected / exposed	0 / 181 (0.00%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Type 2 Diabetes Mellitus			
subjects affected / exposed	0 / 181 (0.00%)	1 / 182 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

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

Non-serious adverse events	dexamethasone Intravitreal Implant	ranibizumab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	160 / 181 (88.40%)	104 / 182 (57.14%)	
Investigations			
Intraocular Pressure Increased			
subjects affected / exposed	65 / 181 (35.91%)	12 / 182 (6.59%)	
occurrences (all)	117	22	
Vascular disorders			
Hypertension			
subjects affected / exposed	8 / 181 (4.42%)	10 / 182 (5.49%)	
occurrences (all)	11	10	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	6 / 181 (3.31%)	10 / 182 (5.49%)	
occurrences (all)	5	14	
Eye disorders			
Conjunctival Haemorrhage			
subjects affected / exposed	36 / 181 (19.89%)	24 / 182 (13.19%)	
occurrences (all)	51	52	
Vitreous Haemorrhage			
subjects affected / exposed	22 / 181 (12.15%)	7 / 182 (3.85%)	
occurrences (all)	27	7	
Cataract			
subjects affected / exposed	28 / 181 (15.47%)	8 / 182 (4.40%)	
occurrences (all)	33	13	
Visual Acuity Reduced			
alternative assessment type: Non-systematic			
subjects affected / exposed	14 / 181 (7.73%)	5 / 182 (2.75%)	
occurrences (all)	16	6	
Cataract Subcapsular			
subjects affected / exposed	14 / 181 (7.73%)	1 / 182 (0.55%)	
occurrences (all)	20	2	
Vitreous Floaters			
alternative assessment type: Non-systematic			
subjects affected / exposed	13 / 181 (7.18%)	2 / 182 (1.10%)	
occurrences (all)	20	6	
Ocular Hypertension			

subjects affected / exposed	11 / 181 (6.08%)	2 / 182 (1.10%)	
occurrences (all)	19	3	
Eye Pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	10 / 181 (5.52%)	6 / 182 (3.30%)	
occurrences (all)	15	7	
Diabetic Retinal Oedema			
subjects affected / exposed	10 / 181 (5.52%)	5 / 182 (2.75%)	
occurrences (all)	11	6	
Vitreous Detachment			
subjects affected / exposed	10 / 181 (5.52%)	5 / 182 (2.75%)	
occurrences (all)	11	8	
Punctate Keratitis			
subjects affected / exposed	9 / 181 (4.97%)	3 / 182 (1.65%)	
occurrences (all)	9	3	
Macular Oedema			
subjects affected / exposed	3 / 181 (1.66%)	10 / 182 (5.49%)	
occurrences (all)	3	15	
Infections and infestations			
Influenza			
subjects affected / exposed	9 / 181 (4.97%)	4 / 182 (2.20%)	
occurrences (all)	9	4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported