Clinical trial results:
A Prospective Randomised Controlled Trial of Intravitreal Ozurdex and Macular Laser Therapy versus Macular Laser Therapy only in Diabetic Macular Oedema (OZLASE study)

Summary

EudraCT number	2011-003339-74
Trial protocol	GB
Global end of trial date	22 October 2013

Results information

Result version number	v1 (current)
This version publication date	01 August 2019
First version publication date	01 August 2019
Summary attachment (see zip file)	Abstract (ABSTRACT - OZLASE.pdf)

Trial information

Trial identification

Sponsor protocol code	HYKP1016

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Moorfields Eye Hospital NHS Foundation Trust
Sponsor organisation address	162, City Road, London, United Kingdom, EC1V 2PD
Public contact	Tania West, Moorfields Eye Hospital, 0044 2075662937, tania.west2@nhs.net
Scientific contact	Tania West, Moorfields Eye Hospital, 0044 2075662937, tania.west2@nhs.net

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	22 October 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 October 2013
Global end of trial reached?	Yes
Global end of trial date	22 October 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To study the relative efficacy of repeated intravitreal Ozurdex + macular laser therapy versus macular laser therapy only in improving visual acuity and anatomical changes in eyes with diabetic macular oedema (DMO).

Protection of trial subjects:

This trial is designed as a randomised clinical trial so that a direct comparison can be made between subjects
receiving the combination therapy of ozurdex and macular laser therapy and macular laser therapy alone. While
diabetic eye disease may affect both eyes of a single subject in a similar way, this is not always the case.
In subjects where only one eye meets the inclusion criteria: the fellow eye (nonstudy
eye) will be monitored during the
course of the study by the trial investigators and will receive macular laser therapy in accordance with the NHS
standard of care. In subjects where both eyes meet the inclusion criteria: the eye with the worse visual acuity will be
included in the study and become the study eye. The fellow eye (nonstudy
eye) will be treated in accordance with
macular laser therapy as part of the NHS standard of care, and will continue to be monitored by the study investigators
throughout the study and receive further treatment if required in accordance with the standard guidelines for treating
diabetic eye disease.
Study data will be anonymised to ensure compliance with the data protection act and patients will be given as much
time as they need to decide whether they wish to participate in the study. All the research team are trained in GCP

Background therapy:

The intervention arm of this study will receive 2 mandated doses of Ozurdex at baseline and 16 weeks and then repeated intravitreal Ozurdex and macular laser therapy at weeks 32 and 48 if retreatment criteria are met. The comparison group in the control arm of this study will receive macular laser therapy to the study eye at weeks 0, and at weeks 16, 32 and 48 if retreatment criteria are met. Treatment will be performed in both study arms according to modified ETDRS guidelines which is the current standard of care in UK clinical practice.

Evidence for comparator:

Treatment will be performed in both study arms according to modified ETDRS guidelines which is the current standard of care in UK clinical practice.

Actual start date of recruitment	15 September 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 80
Worldwide total number of subjects	80
EEA total number of subjects	80

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)	43
From 65 to 84 years	35
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

A total of 219 patients were enrolled from October 2011 to August 2012 from Medical Retina Clinics at Moorfields Eye Hospital and its satellites. One eye per patient was enrolled in the trial. If both eyes of the patient met the eligibility criteria, the eye with the worse BCVA at baseline was designated as the study eye.

Pre-assignment

Screening details:

Full ophthalmic and medical history, refracted best corrected visual acuity, ophthalmic examination, LOCS II and IOP, blood pressure, HbA1C blood test, VFQ-25 and EQ-5D. Pregnancy test will be undertaken. Pupil dilation, 4-field stereo fundus photography, fluorescein angiography, and optical coherence tomography performed .

Pre-assignment period milestones

Number of subjects started	80
Number of subjects completed	80

Period 1

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

Blinding implementation details:

The visual acuity examiners and OCT technicians (i.e. assessors) masked to the subject study arm. A masked observer used to determine whether a 10 or more decrease in BCVA letter score is attributable to cataract.

Arms

Are arms mutually exclusive?	Yes
Arm title	combination arm of Ozurdex and laser photocoagulation

Arm description:

The patients randomised to the combination arm received two mandated doses of Ozurdex at baseline and at week 16. Further re-treatment occurred at 32 or 48 weeks with a combination of Ozurdex and macular laser if retreatment criteria were met.

Arm type	Experimental
Investigational medicinal product name	Ozurdex
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Other use

Dosage and administration details:

Patients randomized to the combination arm received 2 mandated doses of Ozurdex at screening and week 16. Further re-treatment occurred at 32 or 48 weeks with a combination of Ozurdex and modified ETDRS macular laser therapy if re-treatment criteria were met. Ozurdex administered via intravitreal injection in accordance with a trial prescription.

Arm title	Laser

Arm description:

Patients randomized to the laser arm received modified ETDRS macular laser therapy at screening and again at 16, 32 or 48 weeks if clinically significant macula oedema was present.

Arm type	Active comparator

Investigational medicinal product name	Laser
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Ophthalmic insert
Routes of administration	Intraocular use

Dosage and administration details:

The patients randomised to the MLT arm received laser therapy according to the modified Early Treatment Diabetic Retinopathy study (ETDRS) macular laser guidelines at screening and at 16, 32 or 48 weeks if the retreatment criteria were met.

Notes:

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

Justification: Optometrists and OCT technicians were the assessors who were masked to treatment allocation

Number of subjects in period 1	combination arm of Ozurdex and laser photocoagulation	Laser
Started	40	40
Completed	38	39
Not completed	2	1
Adverse event, non-fatal	1	1
Lost to follow-up	1	-

Baseline characteristics

Reporting groups	
Reporting group title	combination arm of Ozurdex and laser photocoagulation
Reporting group description:	
The patients randomised to the combination arm received two mandated doses of Ozurdex at baseline and at week 16. Further re-treatment occurred at 32 or 48 weeks with a combination of Ozurdex and macular laser if retreatment criteria were met.	
Reporting group title	Laser
Reporting group description:	
Patients randomized to the laser arm received modified ETDRS macular laser therapy at screening and again at 16, 32 or 48 weeks if clinically significant macula oedema was present.	

Reporting group values	combination arm of Ozurdex and laser photocoagulation	Laser	Total
Number of subjects	40	40	80
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Mean age in years (SD) Ozurdex +laser arm - 65.6 (10.6) Laser arm - 61.1 (12.8)			
Units: years			
arithmetic mean	65.6	61.1	
standard deviation	± 10.6	± 12.8	-
Gender categorical Units: Subjects			
Female	6	8	14
Male	34	32	66
Type of diabetes Units: Subjects			
Type 1	2	4	6
Type 2	38	36	74
Visual acuity group Units: Subjects			
54-66 letters	22	21	43
67-78 letters	18	19	37
Lens status Units: Subjects			

Pseudophakic	13	13	26
Phakic	27	27	54

Duration of diabetes mellitus			
Units: years			
median	15	15	
inter-quartile range (Q1-Q3)	11 to 20	9 to 22.5	-
HbA1c			
Units: percent			
arithmetic mean	7.9	8.0	
standard deviation	± 1.2	± 1.4	-
Systolic BP			
Units: mmHg			
arithmetic mean	130.7	130.8	
standard deviation	± 16.6	± 16.0	-
Diastolic BP			
Units: mmHg			
arithmetic mean	72	76.1	
standard deviation	± 9.4	± 9.2	-
ETDRS BCVA			
Units: letters			
arithmetic mean	66.1	66.6	
standard deviation	± 7.3	± 7.7	-
Duration of CSMO			
Units: months			
median	25.5	41	
inter-quartile range (Q1-Q3)	7.5 to 40.5	23.5 to 83.5	-
number of prior macular laser therapies			
Units: number			
median	2	3	
inter-quartile range (Q1-Q3)	1 to 3	2 to 4	-

End points

End points reporting groups

Reporting group title	combination arm of Ozurdex and laser photocoagulation
Reporting group description:	
The patients randomised to the combination arm received two mandated doses of Ozurdex at baseline and at week 16. Further re-treatment occurred at 32 or 48 weeks with a combination of Ozurdex and macular laser if retreatment criteria were met.	
Reporting group title	Laser
Reporting group description:	
Patients randomized to the laser arm received modified ETDRS macular laser therapy at screening and again at 16, 32 or 48 weeks if clinically significant macula oedema was present.	

Primary: Difference in mean best corrected ETDRS visual acuity (BCVA) letter score at 56 weeks between the two study arms

End point title	Difference in mean best corrected ETDRS visual acuity (BCVA) letter score at 56 weeks between the two study arms
End point description:	
End point type	Primary
End point timeframe:	
56 weeks	

End point values	combination arm of Ozurdex and laser photocoagulation	Laser		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	40		
Units: ETDRS letters				
arithmetic mean (standard deviation)	-0.3 (± 11.4)	0.4 (± 9.5)		

Statistical analyses

Statistical analysis title	Intention to treat population
Statistical analysis description:	
Descriptive statistics	
Comparison groups	combination arm of Ozurdex and laser photocoagulation v Laser

Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.05
Method	t-test, 2-sided

Notes:

[1] - The primary analyses of efficacy parameters were performed for the ITT population. A per protocol (PP) population, including only all randomised patients that had 12-month visual acuity data, was also conducted. A sensitivity analysis was performed to estimate the effect of cataract surgery done as PP and otherwise, for patients who underwent cataract surgery during the study. Missing BCVA data were imputed with the method of last
observation carried forward.

Secondary: Patients gaining ≥10 ETDRS letters at 56 weeks from baseline

End point title	Patients gaining ≥10 ETDRS letters at 56 weeks from baseline

End point description:

End point type	Secondary

End point timeframe:

56 weeks

End point values	combination arm of Ozurdex and laser photocoagulation	Laser		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	39		
Units: number of participants/eyes	7	8		

Statistical analyses

No statistical analyses for this end point

Secondary: Patients gaining ≥15 ETDRS letters at 56 weeks from baseline

End point title	Patients gaining ≥15 ETDRS letters at 56 weeks from baseline

End point description:

End point type	Secondary

End point timeframe:

56 weeks

End point values	combination arm of Ozurdex and laser photocoagulation	Laser		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	39		
Units: number of participants/eyes	6	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Patients losing <15 ETDRS letters at 56 weeks from baseline,

End point title	Patients losing <15 ETDRS letters at 56 weeks from baseline,

End point description:

End point type	Secondary

End point timeframe:

56 weeks

End point values	combination arm of Ozurdex and laser photocoagulation	Laser		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	39		
Units: Number of participants/eyes	35	35		

Statistical analyses

No statistical analyses for this end point

Secondary: Patients losing ≥30 ETDRS letters at 56 weeks from baseline

End point title	Patients losing ≥30 ETDRS letters at 56 weeks from baseline

End point description:

End point type	Secondary

End point timeframe:

56 weeks

End point values	combination arm of Ozurdex and laser photocoagulation	Laser		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	39		
Units: number of participants/ eyes	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in ETDRS BCVA at 24 weeks from baseline

End point title	Change in ETDRS BCVA at 24 weeks from baseline

End point description:

End point type	Secondary

End point timeframe:

56 weeeks

End point values	combination arm of Ozurdex and laser photocoagulation	Laser		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	40		
Units: ETDRS letters				
arithmetic mean (standard deviation)	1.3 (± 8.8)	-0.7 (± 6.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in ETDRS BCVA at 40 weeks from baseline

End point title	Change in ETDRS BCVA at 40 weeks from baseline

End point description:

End point type	Secondary

End point timeframe:

56 weeks

End point values	combination arm of Ozurdex and laser photocoagulation	Laser		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	40		
Units: ETDRS letters				
arithmetic mean (standard deviation)	-1.1 (± 12.8)	-0.1 (± 6.8)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

56 weeks

Adverse event reporting additional description:

All adverse events (AEs) were recorded in the medical records and CRF until the patient completed their wk 56 visit. Severity, causality and expectedness were defined in the protocol and the SPC. All SAEs/SARs were recorded on the SAE form and reported to the sponsor within one working day unless otherwise specified in the protocol.

Assessment type	Non-systematic

Dictionary used

Dictionary name	None
Dictionary version	0.0

Reporting groups

Reporting group title	combination arm of Ozurdex and laser photocoagulation

Reporting group description:

The patients randomised to the combination arm received two mandated doses of Ozurdex at baseline and at week 16. Further re-treatment occurred at 32 or 48 weeks with a combination of Ozurdex and macular laser if retreatment criteria were met.

Reporting group title	Laser

Reporting group description:

Patients randomized to the laser arm received modified ETDRS macular laser therapy at screening and again at 16, 32 or 48 weeks if clinically significant macula oedema was present.

Serious adverse events	combination arm of Ozurdex and laser photocoagulation	Laser	
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 40 (37.50%)	3 / 40 (7.50%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Cardiac disorders			
Arrythmia			
subjects affected / exposed	0 / 40 (0.00%)	2 / 40 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac problem (unknown) with memory loss			
subjects affected / exposed	1 / 40 (2.50%)	0 / 40 (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 / 40 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Social circumstances			
Admitted to care home for rehabilitation			
subjects affected / exposed	0 / 40 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract surgery - study eye			
subjects affected / exposed	9 / 40 (22.50%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	5 / 9	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
cataract surgery - fellow eye			
subjects affected / exposed	3 / 40 (7.50%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endonasal dacryocystorhinostomy - fellow eye			
subjects affected / exposed	1 / 40 (2.50%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Raised intra-ocular pressure	Additional description: IOP >45 mmHg was defined as an SAE in the protocol		
subjects affected / exposed	1 / 40 (2.50%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ptosis repair			
subjects affected / exposed	1 / 40 (2.50%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vitreous haemorrhage			
subjects affected / exposed	0 / 40 (0.00%)	1 / 40 (2.50%)	
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			
Vaginal candidiasis			
subjects affected / exposed	0 / 40 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastric bypass			
subjects affected / exposed	1 / 40 (2.50%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis	Additional description: hospitalisation		
subjects affected / exposed	1 / 40 (2.50%)	0 / 40 (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			
Urinary tract infection			
subjects affected / exposed	1 / 40 (2.50%)	2 / 40 (5.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	0 / 40 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention	Additional description: Hospitalisation		
subjects affected / exposed	0 / 40 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Flank pain			
subjects affected / exposed	0 / 40 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Diabetic ketoacidosis	Additional description: Hospitalisation		

subjects affected / exposed	0 / 40 (0.00%)	1 / 40 (2.50%)	
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			
Osteomyelitis			
subjects affected / exposed	1 / 40 (2.50%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back surgery			
subjects affected / exposed	0 / 40 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amputation			
subjects affected / exposed	0 / 40 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture neck of femur	Additional description: Hospitalisation for surgery		
subjects affected / exposed	0 / 40 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device failure	Additional description: Fragmented implant/incomplete insertion		
subjects affected / exposed	3 / 40 (7.50%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Salmonella infection			
subjects affected / exposed	0 / 40 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	combination arm of Ozurdex and laser photocoagulation	Laser	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	35 / 40 (87.50%)	24 / 40 (60.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Melanoma			
subjects affected / exposed	0 / 40 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Intermittent pain			
subjects affected / exposed	0 / 40 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Respiratory infection			
subjects affected / exposed	2 / 40 (5.00%)	2 / 40 (5.00%)	
occurrences (all)	2	2	
Breathing difficulty and cough			
subjects affected / exposed	2 / 40 (5.00%)	0 / 40 (0.00%)	
occurrences (all)	2	0	
Product issues			
Device fault	Additional description: Drug packaging contained no drug		
subjects affected / exposed	1 / 40 (2.50%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Fluorescein angiography complications	Additional description: adverse reaction, extravasation of dye, difficult cannulation		
subjects affected / exposed	2 / 40 (5.00%)	2 / 40 (5.00%)	
occurrences (all)	2	2	
Cardiac disorders			
Raised blood pressure			
subjects affected / exposed	1 / 40 (2.50%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Cardiac failure			
subjects affected / exposed	1 / 40 (2.50%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			

Confusion and drowsiness			
subjects affected / exposed	1 / 40 (2.50%)	1 / 40 (2.50%)	
occurrences (all)	1	1	
Left sided weakness and dysphasia	Additional description: Residual sequelae of stroke		
subjects affected / exposed	0 / 40 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Amnesia			
subjects affected / exposed	0 / 40 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	1 / 40 (2.50%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Cataract progression - study eye			
subjects affected / exposed	21 / 40 (52.50%)	4 / 40 (10.00%)	
occurrences (all)	21	4	
Cataract progression non study eye			
subjects affected / exposed	5 / 40 (12.50%)	0 / 40 (0.00%)	
occurrences (all)	5	0	
Conjunctivitis			
subjects affected / exposed	1 / 40 (2.50%)	1 / 40 (2.50%)	
occurrences (all)	1	1	
Corneal adverse events	Additional description: Foreign body/abrasion/scar		
subjects affected / exposed	2 / 40 (5.00%)	0 / 40 (0.00%)	
occurrences (all)	3	0	
Progression of macular oedema - study eye			
subjects affected / exposed	1 / 40 (2.50%)	1 / 40 (2.50%)	
occurrences (all)	1	1	
Progression of macular oedema - fellow eye			
subjects affected / exposed	2 / 40 (5.00%)	2 / 40 (5.00%)	
occurrences (all)	2	2	
Floaters -study eye			
subjects affected / exposed	5 / 40 (12.50%)	0 / 40 (0.00%)	
occurrences (all)	6	0	
Raised intraocular pressure			

subjects affected / exposed	8 / 40 (20.00%)	1 / 40 (2.50%)	
occurrences (all)	9	1	
Eye pain			
subjects affected / exposed	5 / 40 (12.50%)	1 / 40 (2.50%)	
occurrences (all)	5	1	
Posterior capsular opacification - study eye			
subjects affected / exposed	0 / 40 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	0	
Progression to proliferative diabetic retinopathy- study eye			
subjects affected / exposed	1 / 40 (2.50%)	4 / 40 (10.00%)	
occurrences (all)	1	5	
Progression to proliferative diabetic retinopathy - fellow eye			
subjects affected / exposed	4 / 40 (10.00%)	4 / 40 (10.00%)	
occurrences (all)	5	5	
Ptosis			
subjects affected / exposed	3 / 40 (7.50%)	0 / 40 (0.00%)	
occurrences (all)	3	0	
Subconjunctival hemorrhage			
subjects affected / exposed	15 / 40 (37.50%)	0 / 40 (0.00%)	
occurrences (all)	20	0	
Post injection uveitis			
subjects affected / exposed	1 / 40 (2.50%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Blurred vision - study eye			
subjects affected / exposed	7 / 40 (17.50%)	0 / 40 (0.00%)	
occurrences (all)	7	0	
visual field defect			
subjects affected / exposed	0 / 40 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
vitreous hemorrhage - study eye			
subjects affected / exposed	2 / 40 (5.00%)	2 / 40 (5.00%)	
occurrences (all)	2	4	
Vitreous haemorrhage- fellow eye			

subjects affected / exposed	0 / 40 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	2	
Gastrointestinal disorders			
Nausea and vomiting			
subjects affected / exposed	1 / 40 (2.50%)	2 / 40 (5.00%)	
occurrences (all)	1	3	
Skin and subcutaneous tissue disorders			
Boils			
subjects affected / exposed	1 / 40 (2.50%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Nephrotic syndrome with kidney infection			
subjects affected / exposed	0 / 40 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Endocrine disorders			
Hypoglycemic episode	Additional description: Diabetic patient		
subjects affected / exposed	1 / 40 (2.50%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Fluctuating diabetic control			
subjects affected / exposed	0 / 40 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Infection	Additional description: Osteomyelitis, ulcer		
subjects affected / exposed	1 / 40 (2.50%)	1 / 40 (2.50%)	
occurrences (all)	2	1	
Infections and infestations			
Flu with gastroenteritis			
subjects affected / exposed	1 / 40 (2.50%)	1 / 40 (2.50%)	
occurrences (all)	1	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 October 2013	Amendment to the protocol, consent form and patient information sheet. The substantial amendment of the protocol, PIS and consent was a retrospective amendment to cover what was actually been undertaken for the study. This included the following: • Inclusion of cataract surgery within the study and clarification of referral for surgery • Definition of cataract • Amendment of the safety definitions and management of the study • Amendment of the SAP for the study

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

The study did not have an Ozurdex monotherapy arm to evaluate the effect of withholding MLT completely.
Under-reporting of AEs/SAEs was detected by QA and led to recognition of cataract as a SUSAR due to higher than expected frequency of occurrence.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/26472406