EU Clinical Trials Register

Clinical trial results:

An exploratory study of ranibizumab (Lucentis) for treatment of uveitic patients with refractory cystoid macular oedema. 'The LIMO study'

Summary

EudraCT number	2011-001869-41
Trial protocol	GB
Global end of trial date	18 June 2014

Results information

Result version number	v1 (current)
This version publication date	02 June 2022
First version publication date	02 June 2022
Summary attachment (see zip file)	end of study report (end of study report LIMO.pdf)
	Explanation for the post-hoc analysis (Explanation of the post-hoc analysis.pdf)

Trial information

Trial identification

Sponsor protocol code	OKHN1005

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01564108
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, 020 72533411, moorfields.resadmin@nhs.net
Scientific contact	Tania West, Moorfields Eye Hospital, 020 72533411, moorfields.resadmin@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	03 November 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 June 2014
Global end of trial reached?	Yes
Global end of trial date	18 June 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Does ranibizumab improve visual outcome in patients with uveitic macular oedema refractory or ineligible for 'standard of care' therapy?

Protection of trial subjects:

Patients were reviewed at each visit and treatment for uveitis was allowed and instated in case of need.

Background therapy: -

Evidence for comparator:

No comparators included in the study

Actual start date of recruitment	04 July 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: 10
Worldwide total number of subjects	10
EEA total number of subjects	10

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)	7
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted in one single centre, Moorfields Eye Hospital NHS Foundation Trust. The first patient was recruited on the 21st of May 2012 and the last patient was enrolled on the 6th of June 2013.

Pre-assignment

Screening details:

Patients were identified through uveitis clinics. 21 patients were assessed for eligibility, 11 patients did not meet inclusion/exclusion criteria therefore 10 patients were enrolled in the study.

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

The study is not blinded - open-label

Arms

Arm title	ranibizumab for uveitic CMO

Arm description:

open-label. only arm in the study

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

Dosage and administration details:

intravitreal injection of a single dose of 0.05 ml containing 0.5 mg ranibizumab

Number of subjects in period 1	ranibizumab for uveitic CMO
Started	10
Completed	10

Baseline characteristics

Reporting groups

Reporting group title	overall trial

Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	10	10	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	7	7	
From 65-84 years	3	3	
85 years and over	0	0	
Gender categorical			
Gender for the full patients cohort			
Units: Subjects			
Female	5	5	
Male	5	5	

Subject analysis sets

Subject analysis set title	overall cohort
Subject analysis set type	Full analysis

Subject analysis set description:

Overall study cohort.

Reporting group values	overall cohort		
Number of subjects	10		
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)	7		
From 65-84 years	3		
85 years and over	0		

Gender categorical			
Gender for the full patients cohort			
Units: Subjects			
Female	5		
Male	5		

End points

End points reporting groups

Reporting group title	ranibizumab for uveitic CMO
Reporting group description:	
open-label. only arm in the study	
Subject analysis set title	overall cohort
Subject analysis set type	Full analysis
Subject analysis set description:	
Overall study cohort.	

Primary: the proportion of patients in whom by consensus, no further treatment is required at 6 month

End point title	the proportion of patients in whom by consensus, no further treatment is required at 6 month
End point description:	
the proportion of patients in whom by consensus, no further treatment is required at 6 month	
End point type	Primary
End point timeframe:	
baseline to 6 month	

End point values	ranibizumab for uveitic CMO	overall cohort		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	10	10		
Units: patient	3	3		

Statistical analyses

Statistical analysis title	Primary outcome measure 1 at 6 months
Comparison groups	ranibizumab for uveitic CMO v overall cohort
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	proportion
Point estimate	30
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.7
upper limit	65.2

Primary: the proportion of patients in whom by consensus, no further treatment is

required at 12 month

End point title	the proportion of patients in whom by consensus, no further treatment is required at 12 month
End point description:	
the proportion of patients in whom by consensus, no further treatment is required at 12 month	
End point type	Primary
End point timeframe:	
baseline to 12 month	

End point values	ranibizumab for uveitic CMO	overall cohort		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	10	10		
Units: patient	5	5		

Statistical analyses

Statistical analysis title	No further treatment required at 12 month
Comparison groups	ranibizumab for uveitic CMO v overall cohort
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	proportion
Point estimate	50
Confidence interval	
level	95 %
sides	2-sided
lower limit	18.7
upper limit	81.3

Primary: Change in central retinal thickness as measured by Spectralis spectral domain optical coherence tomography in the study eye from baseline to 6 months

End point title	Change in central retinal thickness as measured by Spectralis spectral domain optical coherence tomography in the study eye from baseline to 6 months[1]
End point description:	
End point type	Primary
End point timeframe:	
baseline to 6 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: The number and proportion of patients in whom resolution is achieved will be reported and a 95% confidence interval for the proportion will be computed by the exact binomial method. Summary data will be provided for all other study variables using means and SDs or non-parametric equivalents.

End point values	ranibizumab for uveitic CMO			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: μm				
median (inter-quartile range (Q1-Q3))	-42.5 (-140 to 4)			

Statistical analyses

No statistical analyses for this end point

Primary: Change in central retinal thickness as measured by Spectralis spectral domain optical coherence tomography in the study eye from baseline to 12 months

End point title	Change in central retinal thickness as measured by Spectralis spectral domain optical coherence tomography in the study eye from baseline to 12 months[2]

End point description:

End point type	Primary

End point timeframe:

baseline to 12 months

Notes:

[2] - 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: The number and proportion of patients in whom resolution is achieved will be reported and a 95% confidence interval for the proportion will be computed by the exact binomial method. Summary data will be provided for all other study variables using means and SDs or non-parametric equivalents.

End point values	ranibizumab for uveitic CMO			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: μm				
median (inter-quartile range (Q1-Q3))	-5 (-183 to 100)			

Statistical analyses

No statistical analyses for this end point

Post-hoc: The proportion of patients in whom by consensus, no further treatment is required at 6 months

End point title	The proportion of patients in whom by consensus, no further treatment is required at 6 months

End point description:

The proportion of patients in whom by consensus, no further treatment is required at 6 months.

End point type	Post-hoc

End point timeframe:

Baseline to 6 months

End point values	ranibizumab for uveitic CMO	overall cohort		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	10	10		
Units: Patients	6	6		

Statistical analyses

No statistical analyses for this end point

Post-hoc: The proportion of patients in whom by consensus, no further treatment is required at 12 months

End point title	The proportion of patients in whom by consensus, no further treatment is required at 12 months

End point description:

The proportion of patients in whom by consensus, no further treatment is required at 12 months

End point type	Post-hoc

End point timeframe:

Baseline to 12 months

End point values	ranibizumab for uveitic CMO	overall cohort		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	10	10		
Units: Patients	9	9		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:	
One year	
Assessment type	Systematic

Dictionary used

Dictionary name	none specific used
Dictionary version	0

Reporting groups

Reporting group title	All cohort
Reporting group description:	
All the patients enrolled in the study have been included in this group	

Serious adverse events	All cohort		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 0.05 %

Non-serious adverse events	All cohort		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 10 (100.00%)		
General disorders and administration site conditions			
Eye pain post injection			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	3		
Eye redness post injection			
subjects affected / exposed	8 / 10 (80.00%)		
occurrences (all)	9		
Headache post injection			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Wisdom tooth pain			

subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Decreased hearing acuity			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Eye disorders			
Relapse of Uveitis			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	7		
Itchy sensation around eye (skin)			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Cystoid macular oedema (CMO)			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	4		
Bilateral dry eye			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Poor visual acuity			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Floaters			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Twitches - eye			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Blepharitis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Pain - eye			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			

Coughing of unidentified origin			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Chest Infection			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Sore throat			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Axillary Pain			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Dislocated fingers			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Back pain			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Leg pain			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Knee pain			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Hip and knee pain			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
back pain / cyst			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Infections and infestations			

Lung infection			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Gum infection			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 January 2013	Inclusion criteria to be changed: a 3 month period post cataract surgery before recruitment rather than 6 months. RATIONALE: 3 months is the standard period following cataract surgery one would wait in clinical practice before undertaking a further non-urgent intraocular procedure e.g. YAG laser capsulotomy. In addition, waiting 3 months following any intraocular surgery is the period of time now commonly used in studies investigating intravitreal agents, such as this study. Furthermore, macular oedema directly related to surgery would be expected to have resolved within 3 months.
18 June 2014	Amendment to CI of the study This amendment was submitted before the end of the study (submitted to MHRA on the 14th of May 2014) and was pending when last visit was conducted on the 18th of June 2014. The MHRA was aware of this last visit date, and they approved the substantial amendment on the 31st of July 2014.

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.

A limitation for this study was the limited number of subjects enrolled in the study

Notes: