Clinical trial results:
The use of Ranibizumab (Lucentis ®) for the treatment of corneal neovascularisation

Summary

EudraCT number	2010-018673-37
Trial protocol	GB
Global end of trial date	12 April 2017

Results information

Result version number	v1 (current)
This version publication date	26 April 2018
First version publication date	26 April 2018

Trial information

Trial identification

Sponsor protocol code	10011

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	University of Nottingham
Sponsor organisation address	East atrium, Jubilee conference centre, Triumph road, Nottingham, United Kingdom, NG8 1DH
Public contact	Professor Harminder Dua, University of Nottingham, harminder.dua@nottingham.ac.uk
Scientific contact	Professor Harminder Dua, University of Nottingham, harminder.dua@nottingham.ac.uk

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	18 February 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 February 2013
Global end of trial reached?	Yes
Global end of trial date	12 April 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess the use of the drug in the treatment of active corneal new blood vessels.

Protection of trial subjects:

Subconjunctival injections were administered under topical anaesthesia and topical antibiotics were given as standard.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 March 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	United Kingdom: 6
Worldwide total number of subjects	6
EEA total number of subjects	6

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)	6
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

All participants were recruited from the 15th of March 2011 till the 18th of February 2013. They were all recruited in the UK from the cornea clinics of Queens Medical Centre, Nottingham.

Pre-assignment

Screening details:

Inclusion criteria
- Patients over the age of 18
- With corneal neovascularisation non responsive or non tolerant to conventional steroid therapy
- And capable of consenting

Exclusion criteria
- Patients under 18 years of age
- Patients unable to provide informed consent
- Patients who are needle phobic
- Patients refusing consent
- Pregna

Period 1

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

Blinding implementation details:

N/A

Arms

Arm title	Treatment group

Arm description:

Patients will receive subconjunctival injections around the limbus in the quadrant(s) affected (total volume of no more than 0.2ml of the 10mg/ml solution). The Subconjuctival injections will be administered in the treatment room under topical anaesthetics adjacent to the new corneal vessels and topical antibiotic will be given as standard after subconjunctival injection. Patient will be seen and assessed after two weeks and a second injection may be given if no effect is seen at the end of the second week but no more than a total of 2 injections will be given (for macular degeneration up to 4 injections per year are administered)

Arm type	Experimental
Investigational medicinal product name	Ranibizumab
Investigational medicinal product code	
Other name	Lucentis
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Subconjunctival use

Dosage and administration details:

Patients will receive subconjunctival injections around the limbus in the quadrant(s) affected (total volume of no more than 0.2ml of the 10mg/ml solution). The Subconjuctival injections will be administered in the treatment room under topical anaesthetics adjacent to the new corneal vessels and topical antibiotic will be given as standard after subconjunctival injection. Patient will be seen and assessed after two weeks and a second injection may be given if no effect is seen at the end of the second week but no more than a total of 2 injections will be given (for macular degeneration up to 4 injections per year are administered) Patients will be monitored fortnightly for the first month and then at months 2, 4 and 6.

Number of subjects in period 1	Treatment group
Started	6
Completed	6

Baseline characteristics

Reporting groups	
Reporting group title	Treatment group
Reporting group description:	
Patients will receive subconjunctival injections around the limbus in the quadrant(s) affected (total volume of no more than 0.2ml of the 10mg/ml solution). The Subconjuctival injections will be administered in the treatment room under topical anaesthetics adjacent to the new corneal vessels and topical antibiotic will be given as standard after subconjunctival injection. Patient will be seen and assessed after two weeks and a second injection may be given if no effect is seen at the end of the second week but no more than a total of 2 injections will be given (for macular degeneration up to 4 injections per year are administered)	

Reporting group values	Treatment group	Total	
Number of subjects	6	6	
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)	6	6	
From 65-84 years	0	0	
85 years and over	0	0	
Adult	0	0	
Gender categorical Units: Subjects			
Female	2	2	
Male	4	4	

End points

End points reporting groups

Reporting group title	Treatment group

Reporting group description:

Patients will receive subconjunctival injections around the limbus in the quadrant(s) affected (total volume of no more than 0.2ml of the 10mg/ml solution). The Subconjuctival injections will be administered in the treatment room under topical anaesthetics adjacent to the new corneal vessels and topical antibiotic will be given as standard after subconjunctival injection. Patient will be seen and assessed after two weeks and a second injection may be given if no effect is seen at the end of the second week but no more than a total of 2 injections will be given (for macular degeneration up to 4 injections per year are administered)

Subject analysis set title	Treatment group
Subject analysis set type	Full analysis

Subject analysis set description:

This single centre pilot study will include the identification of 10-20 patients from the routine corneal clinics presenting with corneal neovascularisation non responsive or not suitable for steroid therapy.

Primary: Cessation or reduction of corneal neovascularisation with Ranibizumab (Lucentis®) treatment

End point title	Cessation or reduction of corneal neovascularisation with Ranibizumab (Lucentis®) treatment

End point description:

Digital photographs of the cornea will be analysed by 2 blind observers and image analysis will be used to determine the area of
cornea covered by neovascularisation as a percentage of the total corneal area.

End point type	Primary

End point timeframe:

Patients will be monitored fortnightly for the first month
and then at months 2, 4 and 6.

End point values	Treatment group	Treatment group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	6	6		
Units: Area of neovascularisation	6	6		

Statistical analyses

Statistical analysis title	Descriptive analysis

Statistical analysis description:

The study was not completed, however some conclusions were drawn through descriptive analysis.

Comparison groups	Treatment group v Treatment group

Number of subjects included in analysis	12
Analysis specification	Post-hoc
Analysis type	other[1]
P-value	≤ 0.05 [2]
Method	t-test, 1-sided

Notes:

[1] - Lucentis has a short effect that can not be maintained with the presence of active corneal inflammation. As long as the stimulus for vascularisation is not addressed measures to reduce the vessels have only a temporary effect. One injection is not sufficient and several may be required during the course of the disease process. Subconjunctival use of Lucentis is safe and multiple injections can be given safely.
[2] - Statistical analysis was not performed as the study was not completed

Secondary: To determine whether established corneal vessels too would be influenced with Ranibizumab and whether there is any gain in visual acuity following 'regression' of corneal new vessels.

End point title	To determine whether established corneal vessels too would be influenced with Ranibizumab and whether there is any gain in visual acuity following 'regression' of corneal new vessels.

End point description:

On each visit relevant systemic and visual history will be taken then visual acuity, pupil reaction, anterior segment biomicroscopic examination, fundal examination and intraocular pressure measurement will be undertaken and a standard anterior eye segment photograph will be taken at each visit.

End point type	Secondary

End point timeframe:

Patients will be monitored fortnightly for the first month
and then at months 2, 4 and 6.

End point values	Treatment group	Treatment group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	6	6		
Units: LogMar units	6	6		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

All serious adverse events that fall or are suspected to fall within these criteria shall be treated as a SUSAR until deemed otherwise.
The event shall be reported immediately of knowledge of its occurrence to the Chief Investigator

Adverse event reporting additional description:

Participants will be asked to contact the study site immediately in the event of any serious adverse event. All adverse events will be recorded and closely monitored until resolution, stabilisation, or until it has been shown that the study medication or treatment is not the cause.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20

Reporting groups

Reporting group title	Treatment group

Reporting group description: -

Serious adverse events	Treatment group		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Treatment group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)		

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Only 6 patients were treated and there were no reported adverse events.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 June 2010	MHRA requested a justification for the dose of Lucentis and the protocol was changed accordingly

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 target was to recruit 20 participants however only 6 were recruited.

Notes: