# 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<br>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<br>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: