



## Clinical trial results:

**Treatment of Cystoid Macular Edema following cataract surgery.  
A randomized, double-masked, placebo-controlled, clinical trial.**

### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2009-017031-18 |
| Trial protocol           | NL             |
| Global end of trial date | 08 June 2015   |

### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 17 February 2016 |
| First version publication date | 17 February 2016 |

### Trial information

#### Trial identification

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | OZR-2009-06 |
|-----------------------|-------------|

#### Additional study identifiers

|                                    |                                    |
|------------------------------------|------------------------------------|
| ISRCTN number                      | -                                  |
| ClinicalTrials.gov id (NCT number) | -                                  |
| WHO universal trial number (UTN)   | -                                  |
| Other trial identifiers            | Nederlands Trial Register: NTR2280 |

Notes:

### Sponsors

|                              |                                                                                                     |
|------------------------------|-----------------------------------------------------------------------------------------------------|
| Sponsor organisation name    | The Rotterdam Eye Hospital                                                                          |
| Sponsor organisation address | PO Box 70030, Rotterdam, Netherlands, 3000LM                                                        |
| Public contact               | Rotterdam Ophthalmic Institute, The Rotterdam Eye Hospital,<br>+31 10 4023449, roi@oogziekenhuis.nl |
| Scientific contact           | Rotterdam Ophthalmic Institute, The Rotterdam Eye Hospital,<br>+31 10 4023449, roi@oogziekenhuis.nl |

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                       | 29 January 2016 |
| Is this the analysis of the primary completion data? | Yes             |
| Primary completion date                              | 08 June 2015    |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 08 June 2015    |
| Was the trial ended prematurely?                     | Yes             |

Notes:

## General information about the trial

Main objective of the trial:

To study the efficacy of treatment with Nevanac in combination with Pred Forte of acute clinical inflammation resulting in Cystoid Macular Edema after phacoemulsification.

Protection of trial subjects:

With respect to the repetitive use of NSAIDs, patients were encouraged to seek early medical attention if symptoms of possible corneal problems were present; signs of corneal melting were checked during all follow-up visits to the outpatient clinic. Furthermore previous corneal problems were part of the exclusion criteria.

Background therapy:

Cataract extraction is the most frequently performed surgical intervention. One of the most common causes of poor visual acuity after cataract surgery is the development of postoperative clinical (cystoid) macular edema ((C)ME). Several treatment options have been investigated, but a uniform treatment protocol does not exist.

Current treatment strategies range from none to very intensive treatment with no strategy showing unambiguous benefits. However, based on our experience and extensive literature review, it is likely that a treatment using local application of a corticosteroid and a nonsteroidal anti-inflammatory drug will be optimal. Therefore, the aim of this study was to investigate the efficacy of treatment of CME with a combination of these types of drug.

Evidence for comparator: -

|                                                           |              |
|-----------------------------------------------------------|--------------|
| Actual start date of recruitment                          | 23 July 2010 |
| 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 | Netherlands: 25 |
| Worldwide total number of subjects   | 25              |
| EEA total number of subjects         | 25              |

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          | 0 |

|                           |    |
|---------------------------|----|
| months)                   |    |
| Children (2-11 years)     | 0  |
| Adolescents (12-17 years) | 0  |
| Adults (18-64 years)      | 11 |
| From 65 to 84 years       | 13 |
| 85 years and over         | 1  |

## Subject disposition

### Recruitment

Recruitment details:

Patients diagnosed with clinical CME within three months after phacoemulsification were invited to participate.

### Pre-assignment

Screening details:

Clinical CME in our study is defined as optical coherence tomography-evident (cystoid) macular edema in combination with reduced visual acuity.

### Period 1

|                              |                                          |
|------------------------------|------------------------------------------|
| Period 1 title               | Overall trial (overall period)           |
| Is this the baseline period? | Yes                                      |
| Allocation method            | Randomised - controlled                  |
| Blinding used                | Double blind                             |
| Roles blinded                | Subject, Investigator, Monitor, Assessor |

### Arms

|                              |               |
|------------------------------|---------------|
| Are arms mutually exclusive? | Yes           |
| <b>Arm title</b>             | Placebo group |

Arm description:

Placebo eyedrops in two separate phials.

|                                        |                |
|----------------------------------------|----------------|
| Arm type                               | Placebo        |
| Investigational medicinal product name | Placebo        |
| Investigational medicinal product code |                |
| Other name                             |                |
| Pharmaceutical forms                   | Eye drops      |
| Routes of administration               | Ophthalmic use |

Dosage and administration details:

Placebo eye drops, 3 times a day, during 6 weeks.

|                  |                   |
|------------------|-------------------|
| <b>Arm title</b> | Active substances |
|------------------|-------------------|

Arm description:

Treatment with nepafenac 0.1% eye drops & prednisolone acetate 1% eye drops.

|                                        |                 |
|----------------------------------------|-----------------|
| Arm type                               | Experimental    |
| Investigational medicinal product name | nepafenac       |
| Investigational medicinal product code | EU/1/07/433/001 |
| Other name                             | Nevanac         |
| Pharmaceutical forms                   | Eye drops       |
| Routes of administration               | Ophthalmic use  |

Dosage and administration details:

0.1% eye drops, 3 times a day, during 6 weeks.

|                                        |                      |
|----------------------------------------|----------------------|
| Investigational medicinal product name | prednisolone acetate |
| Investigational medicinal product code | RVG11271             |
| Other name                             | PredForte            |
| Pharmaceutical forms                   | Eye drops            |
| Routes of administration               | Ophthalmic use       |

Dosage and administration details:

1% eye drops, 3 times a day, during 6 weeks.

| <b>Number of subjects in period 1</b> | Placebo group | Active substances |
|---------------------------------------|---------------|-------------------|
| Started                               | 10            | 15                |
| Completed                             | 2             | 6                 |
| Not completed                         | 8             | 9                 |
| Lost to follow-up                     | 8             | 9                 |

## Baseline characteristics

### Reporting groups

|                                                                                                              |                   |
|--------------------------------------------------------------------------------------------------------------|-------------------|
| Reporting group title                                                                                        | Placebo group     |
| Reporting group description:<br>Placebo eyedrops in two separate phials.                                     |                   |
| Reporting group title                                                                                        | Active substances |
| Reporting group description:<br>Treatment with nepafenac 0.1% eye drops & prednisolone acetate 1% eye drops. |                   |

| Reporting group values                                | Placebo group | Active substances | Total |
|-------------------------------------------------------|---------------|-------------------|-------|
| Number of subjects                                    | 10            | 15                | 25    |
| Age categorical<br>Units: Subjects                    |               |                   |       |
| In utero                                              |               |                   | 0     |
| Preterm newborn infants<br>(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<br>Units: years                        |               |                   |       |
| arithmetic mean                                       | 66            | 68                |       |
| standard deviation                                    | ± 13          | ± 8               | -     |
| Gender categorical<br>Units: Subjects                 |               |                   |       |
| Female                                                | 4             | 9                 | 13    |
| Male                                                  | 6             | 6                 | 12    |

## End points

### End points reporting groups

|                                                                                                              |                   |
|--------------------------------------------------------------------------------------------------------------|-------------------|
| Reporting group title                                                                                        | Placebo group     |
| Reporting group description:<br>Placebo eyedrops in two separate phials.                                     |                   |
| Reporting group title                                                                                        | Active substances |
| Reporting group description:<br>Treatment with nepafenac 0.1% eye drops & prednisolone acetate 1% eye drops. |                   |

### Primary: Letters gained.

|                                                                          |                                |
|--------------------------------------------------------------------------|--------------------------------|
| End point title                                                          | Letters gained. <sup>[1]</sup> |
| End point description:<br>Letters gained (ETDRS chart) at last FU visit. |                                |
| End point type                                                           | Primary                        |
| End point timeframe:<br>Last follow up visit.                            |                                |

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 of subjects included in this study did not warrant any further statistical analysis.

| End point values                     | Placebo group   | Active substances |  |  |
|--------------------------------------|-----------------|-------------------|--|--|
| Subject group type                   | Reporting group | Reporting group   |  |  |
| Number of subjects analysed          | 9               | 9                 |  |  |
| Units: Letters                       |                 |                   |  |  |
| arithmetic mean (standard deviation) | 11 ( $\pm$ 15)  | 12 ( $\pm$ 6)     |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

One year after diagnosis of CME.

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |    |
|--------------------|----|
| Dictionary version | 10 |
|--------------------|----|

### Reporting groups

|                       |               |
|-----------------------|---------------|
| Reporting group title | Placebo group |
|-----------------------|---------------|

Reporting group description:

Placebo eyedrops in two separate phials.

|                       |                   |
|-----------------------|-------------------|
| Reporting group title | Active substances |
|-----------------------|-------------------|

Reporting group description:

Treatment with nepafenac 0.1% eye drops & prednisolone acetate 1% eye drops.

| Serious adverse events                            | Placebo group  | Active substances |  |
|---------------------------------------------------|----------------|-------------------|--|
| Total subjects affected by serious adverse events |                |                   |  |
| subjects affected / exposed                       | 0 / 10 (0.00%) | 0 / 15 (0.00%)    |  |
| number of deaths (all causes)                     | 0              | 0                 |  |
| number of deaths resulting from adverse events    |                |                   |  |

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

| Non-serious adverse events                            | Placebo group  | Active substances |  |
|-------------------------------------------------------|----------------|-------------------|--|
| Total subjects affected by non-serious adverse events |                |                   |  |
| subjects affected / exposed                           | 0 / 10 (0.00%) | 1 / 15 (6.67%)    |  |
| General disorders and administration site conditions  |                |                   |  |
| Allergic keratitis                                    |                |                   |  |
| subjects affected / exposed                           | 0 / 10 (0.00%) | 1 / 15 (6.67%)    |  |
| occurrences (all)                                     | 0              | 1                 |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date         | Interruption                        | Restart date |
|--------------|-------------------------------------|--------------|
| 08 June 2015 | Premature termination of the trial. | -            |

Notes:

### Limitations and caveats

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

This trial was designed as RCT with two arms of 60 subjects each. It was prematurely terminated after inclusion of 10 subject in the placebo arm and 15 in the experimental arm. No further statistical analysis was performed.

Notes: