



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
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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, +31 10 4023449, roi@oogziekenhuis.nl
Scientific contact	Rotterdam Ophthalmic Institute, The Rotterdam Eye Hospital, +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
Arm title	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.

Arm title	Active substances
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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.

Number of subjects in period 1	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: 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.	

Reporting group values	Placebo group	Active substances	Total
Number of subjects	10	15	25
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 Units: years			
arithmetic mean	66	68	
standard deviation	± 13	± 8	-
Gender categorical Units: Subjects			
Female	4	9	13
Male	6	6	12

End points

End points 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.	

Primary: Letters gained.

End point title	Letters gained. ^[1]
End point description: Letters gained (ETDRS chart) at last FU visit.	
End point type	Primary
End point timeframe: 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
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	10
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Reporting groups

Reporting group title	Placebo group
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Reporting group description:

Placebo eyedrops in two separate phials.

Reporting group title	Active substances
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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

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: