Clinical trial results:
The post-cataract inflammatory reaction with combination therapy of topical steroid and NSAID.

Summary

EudraCT number	2011-006066-40
Trial protocol	NL
Global end of trial date	31 December 2014

Results information

Result version number	v1 (current)
This version publication date	01 February 2016
First version publication date	29 April 2015

Trial information

Trial identification

Sponsor protocol code	OZR-2011-23

Additional study identifiers

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

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 4023449, roi@oogziekenhuis.nl
Scientific contact	Rotterdam Ophthalmic Institute, The Rotterdam Eye Hospital, 31 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	03 April 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 December 2014
Global end of trial reached?	Yes
Global end of trial date	31 December 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluation of the inflammatory reaction with NSAID and steroid prophylaxis.

Protection of trial subjects:

No specific measures.

Background therapy:

After cataract extraction, ocular inflammation may be observed. A rapid decline of inflammation and minimal irritation of the eye during the early postoperative period may prevent cystoid macular edema and other postoperative complications. The inflammatory response has been frequently measured during the first 3 months after cataract extraction. Three types of prophylaxis were compared: 1) subconjunctival depot of betamethasone, 2) dexamethasone eye drops, and 3) combination of dexamethasone + nepafenac eye drops.

[Arms 1) and 2) have been performed as an addendum to study OZR-2006-01 (EudraCT 2006-001486-41); arm 3) was submitted for ethical approval as a separate protocol OZR-2011-23 (EudraCT 2011-006066-40). Here, results are summarized for all three study arms.]

Evidence for comparator: -

Actual start date of recruitment	01 March 2012
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	Netherlands: 29
Worldwide total number of subjects	29
EEA total number of subjects	29

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	21
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Patients indicated for cataract surgery.

Pre-assignment

Screening details:

Subcapsular posterior cataract (very soft, short phaco time).
Brunescens or mature cataract (hard, long phaco time).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm 1

Arm description:

Subconjunctival depot of betamethasone

Arm type	Experimental
Investigational medicinal product name	Betamehtasone
Investigational medicinal product code	RVG05399
Other name	Celestone chronodose
Pharmaceutical forms	Suspension for injection
Routes of administration	Subconjunctival use

Dosage and administration details:

Single perioperative subconjunctival injection, 2.7 mg (1 ml).

Arm title	Arm 2

Arm description:

Eye drops dexamethasone

Arm type	Active comparator
Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	RVG56003
Other name	
Pharmaceutical forms	Eye drops
Routes of administration	Topical use

Dosage and administration details:

Dexamethasone eye drops (0,1%, 1mg/ml), 3 times a day: postop days 1-28.

Arm title	Arm 3

Arm description:

Combination of dexamethasone and nepafenac drops.

Arm type	Experimental
Investigational medicinal product name	Nepafenac
Investigational medicinal product code	EU/1/07/433/001
Other name	Nevanac ophthalmic
Pharmaceutical forms	Eye drops
Routes of administration	Topical use

Dosage and administration details: Nevanac eye drops (0,1%, 1mg/ml), 3 times a day: one day preop, day of surgery and postop days 1-28.	
Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	RVG56003
Other name	
Pharmaceutical forms	Eye drops
Routes of administration	Topical use
Dosage and administration details: Dexamethasone eye drops (0,1%, 1mg/ml), 3 times a day: postop days 1-28.	

Number of subjects in period 1	Arm 1	Arm 2	Arm 3
Started	9	10	10
Completed	9	10	10

Baseline characteristics

Reporting groups	
Reporting group title	Arm 1
Reporting group description:	
Subconjunctival depot of betamethasone	
Reporting group title	Arm 2
Reporting group description:	
Eye drops dexamethasone	
Reporting group title	Arm 3
Reporting group description:	
Combination of dexamethasone and nepafenac drops.	

Reporting group values	Arm 1	Arm 2	Arm 3
Number of subjects	9	10	10
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous Units: years			
arithmetic mean	72.2	70.9	70.3
standard deviation	± 7.7	± 7.7	± 10
Gender categorical Units: Subjects			
Female	4	5	6
Male	5	5	4
Flare at baseline Units: Arbitrary			
arithmetic mean	1.54	1.7	1.8
standard deviation	± 0.89	± 0.46	± 0.38

Reporting group values	Total		
Number of subjects	29		
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			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	15		
Male	14		
Flare at baseline			
Units: Arbitrary			
arithmetic mean			
standard deviation	-		

End points

End points reporting groups

Reporting group title	Arm 1
Reporting group description: Subconjunctival depot of betamethasone	
Reporting group title	Arm 2
Reporting group description: Eye drops dexamethasone	
Reporting group title	Arm 3
Reporting group description: Combination of dexamethasone and nepafenac drops.	
Subject analysis set title	Repeated flare measurements
Subject analysis set type	Full analysis
Subject analysis set description: Flare measurements comparison in three arms.	

Primary: Flare at day 1

End point title	Flare at day 1
End point description:	
End point type	Primary
End point timeframe: Postoperative	

End point values	Arm 1	Arm 2	Arm 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	10	10	
Units: Arbitrary				
arithmetic mean (standard deviation)	2.62 (± 0.72)	2.76 (± 0.69)	2.88 (± 0.46)	

Statistical analyses

Statistical analysis title	Repeated measurements analysis
Comparison groups	Arm 2 v Arm 3 v Arm 1
Number of subjects included in analysis	29
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Mixed models analysis

Primary: Flare at day 3

End point title	Flare at day 3[1]

End point description:

End point type	Primary

End point timeframe:

Postoperative

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: Mixed model analysis (see end point 'Flare at day 1').

End point values	Arm 1	Arm 2	Arm 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	10	10	
Units: Arbitrayr				
arithmetic mean (standard deviation)	2.97 (± 0.76)	3.06 (± 0.73)	2.77 (± 0.38)	

Statistical analyses

No statistical analyses for this end point

Primary: Flare at day 5

End point title	Flare at day 5[2]

End point description:

End point type	Primary

End point timeframe:

Postoperative

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: Mixed model analysis (see end point 'Flare at day 1').

End point values	Arm 1	Arm 2	Arm 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	10	10	
Units: Arbitrary				
arithmetic mean (standard deviation)	3.04 (± 1)	2.91 (± 0.66)	2.53 (± 0.5)	

Statistical analyses

No statistical analyses for this end point

Primary: Flare at day 7

End point title	Flare at day 7[3]

End point description:

End point type	Primary

End point timeframe:

Postoperativ

Notes:

[3] - 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: Mixed model analysis (see end point 'Flare at day 1').

End point values	Arm 1	Arm 2	Arm 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	10	10	
Units: Arbitrary				
arithmetic mean (standard deviation)	2.96 (± 1.09)	2.5 (± 0.37)	2.39 (± 0.6)	

Statistical analyses

No statistical analyses for this end point

Primary: Flare at day 10

End point title	Flare at day 10[4]

End point description:

End point type	Primary

End point timeframe:

Postoperative

Notes:

[4] - 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: Mixed model analysis (see end point 'Flare at day 1').

End point values	Arm 1	Arm 2	Arm 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	10	10	
Units: Arbitrary				
arithmetic mean (standard deviation)	3.07 (± 0.76)	2.5 (± 0.41)	2.46 (± 0.34)	

Statistical analyses

No statistical analyses for this end point

Primary: Flare at day 14

End point title	Flare at day 14[5]

End point description:

End point type	Primary

End point timeframe:

Postoperative

Notes:

[5] - 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: Mixed model analysis (see end point 'Flare at day 1').

End point values	Arm 1	Arm 2	Arm 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	10	10	
Units: Arbitrary				
arithmetic mean (standard deviation)	2.9 (± 0.84)	2.38 (± 0.35)	2.34 (± 0.31)	

Statistical analyses

No statistical analyses for this end point

Primary: Flare at day 21

End point title	Flare at day 21[6]

End point description:

End point type	Primary

End point timeframe:

Postoperative

Notes:

[6] - 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: Mixed model analysis (see end point 'Flare at day 1').

End point values	Arm 1	Arm 2	Arm 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	10	10	
Units: Arbitrary				
arithmetic mean (standard deviation)	2.62 (± 0.76)	2.19 (± 0.47)	2.21 (± 0.48)	

Statistical analyses

No statistical analyses for this end point

Primary: Flare at day 30

End point title	Flare at day 30[7]

End point description:

End point type	Primary

End point timeframe:

Postoperativ

Notes:

[7] - 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: Mixed model analysis (see end point 'Flare at day 1').

End point values	Arm 1	Arm 2	Arm 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	10	10	
Units: Arbitrary				
arithmetic mean (standard deviation)	2.48 (± 0.62)	2.29 (± 0.57)	2.2 (± 0.59)	

Statistical analyses

No statistical analyses for this end point

Primary: Flare at day 60

End point title	Flare at day 60[8]

End point description:

End point type	Primary

End point timeframe:

Postoperative

Notes:

[8] - 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: Mixed model analysis (see end point 'Flare at day 1').

End point values	Arm 1	Arm 2	Arm 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	10	10	
Units: Arbitrary				
arithmetic mean (standard deviation)	2.28 (± 0.73)	1.99 (± 0.31)	2.19 (± 0.5)	

Statistical analyses

No statistical analyses for this end point

Primary: Flare at day 90

End point title	Flare at day 90[9]

End point description:

End point type	Primary

End point timeframe:

Postoperative

Notes:

[9] - 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: Mixed model analysis (see end point 'Flare at day 1').

End point values	Arm 1	Arm 2	Arm 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	10	10	
Units: Arbitrary				
arithmetic mean (standard deviation)	2.19 (± 0.67)	1.95 (± 0.45)	2.13 (± 0.34)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: Three months postoperative.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	10

Reporting groups	
Reporting group title	All study patients
Reporting group description: -	

Serious adverse events	All study patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 29 (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	All study patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 29 (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: No adverse events were reported.

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? No

Limitations and caveats

None reported