Clinical trial results:
Effects of post-operative topical steroid versus intraoperative subconjunctival steroid injection and postoperative miotic on intraocular inflammation following cataract extraction.

Summary

EudraCT number	2006-001486-41
Trial protocol	NL
Global end of trial date	30 November 2010

Results information

Result version number	v1
This version publication date	02 February 2016
First version publication date	28 December 2014

Trial information

Trial identification

Sponsor protocol code	OZR-2006-01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	Nederlands Trial Register: NTR779

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 April 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 November 2010
Global end of trial reached?	Yes
Global end of trial date	30 November 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Comparison of incidence of post-cataract extraction ocular inflammation with subconjunctival steroid injection versus traditional eye drops.

Protection of trial subjects:

No specific measures.

Background therapy:

Cataract extraction is the most frequently performed surgical intervention. A relatively high prevalence of post-op ocular inflammation, needing additional treatment and visits, has prompted the search for a treatment to replace the traditionally prescribed topical steroids. A subconjunctival steroid depot was compared with traditional prophylaxis.
(Dieleman M, Wubbels RJ, van Kooten-Noordzij M, de Waard PWT. Single perioperative subconjunctival steroid depot versus postoperative steroid eyedrops to prevent intraocular inflammation and macular edema after cataract surgery. J Cataract Refract Surg, 37, 1589-1597.)

The use of miotics after cataract extraction appears to have lost its rationale. Therefore, as a secondary objective of this study, the efficacy of Eserine has been evaluated.
(Dieleman M, Wubbels RJ, de Waard PWT. Miotics after modern cataract surgery are history. J Ocul Pharmacol Ther, 28, 98-101.)

Evidence for comparator: -

Actual start date of recruitment	29 January 2007
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: 400
Worldwide total number of subjects	400
EEA total number of subjects	400

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)	97
From 65 to 84 years	281
85 years and over	22

Subject disposition

Recruitment

Recruitment details:

Patients indicated for cataract surgery (age > 18 years).

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 trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Subconjunctival betamethasone

Arm description:

Subconjunctival betamethasone

Arm type	Experimental
Investigational medicinal product name	Betamethasone
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	Eye drops dexamethasone

Arm description:

Eye drops dexamethasone

Arm type	Active comparator
Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	RVG56003
Other name	Dexamethason ratiopharm
Pharmaceutical forms	Ear/eye drops, solution
Routes of administration	Topical use

Dosage and administration details:

Eye drops, 3X per day, 3 weeks postop (1 mg/mlo).

Number of subjects in period 1	Subconjunctival betamethasone	Eye drops dexamethasone
Started	200	200
Completed	200	200

Baseline characteristics

Reporting groups	
Reporting group title	Subconjunctival betamethasone
Reporting group description: Subconjunctival betamethasone	
Reporting group title	Eye drops dexamethasone
Reporting group description: Eye drops dexamethasone	

Reporting group values	Subconjunctival betamethasone	Eye drops dexamethasone	Total
Number of subjects	200	200	400
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	72.3	69.3	
standard deviation	± 9.6	± 9.2	-
Gender categorical Units: Subjects			
Female	127	115	242
Male	73	85	158

End points

End points reporting groups

Reporting group title	Subconjunctival betamethasone
Reporting group description: Subconjunctival betamethasone	
Reporting group title	Eye drops dexamethasone
Reporting group description: Eye drops dexamethasone	
Subject analysis set title	Mann-Whitney U test for flare measurements
Subject analysis set type	Full analysis
Subject analysis set description: Mann-Whitney U test for flare measurements	

Primary: Flare count (photons/ms) at 4 weeks postop.

End point title	Flare count (photons/ms) at 4 weeks postop.
End point description:	
End point type	Primary
End point timeframe: 4 weeks postop.	

End point values	Subconjunctival betamethasone	Eye drops dexamethasone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	200	200		
Units: photons per ms				
arithmetic mean (standard deviation)	10.8 (± 7.2)	9.9 (± 9.5)		

Statistical analyses

Statistical analysis title	Mann-Whitney U
Comparison groups	Subconjunctival betamethasone v Eye drops dexamethasone
Number of subjects included in analysis	400
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Four weeks postop.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	10

Reporting groups	
Reporting group title	Subconjunctival betamehtasone
Reporting group description: -	
Reporting group title	Eye drops dexamethasone
Reporting group description: -	

Serious adverse events	Subconjunctival betamehtasone	Eye drops dexamethasone	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 200 (0.00%)	0 / 200 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Subconjunctival betamehtasone	Eye drops dexamethasone	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 200 (11.00%)	27 / 200 (13.50%)	
Eye disorders			
Clinical significant macular edema			
subjects affected / exposed	4 / 200 (2.00%)	7 / 200 (3.50%)	
occurrences (all)	4	7	
Intraocular pressure > 30 mm Hg			
subjects affected / exposed	2 / 200 (1.00%)	3 / 200 (1.50%)	
occurrences (all)	2	3	
Subconjunctival hemorrhage			
subjects affected / exposed	16 / 200 (8.00%)	17 / 200 (8.50%)	
occurrences (all)	16	17	

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

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

The reported difference between the flare counts of both groups is statistically significant but "the question remains as to whether this reflects a clinically significant difference."

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/21855759

http://www.ncbi.nlm.nih.gov/pubmed/2202957