



Clinical trial results:

Clonidine as an adjuvant to prolong local anaesthesia in ophthalmic surgery with cryocoagulation. A randomized, controlled, patient-masked trial.

Summary

EudraCT number	2010-024100-10
Trial protocol	NL
Global end of trial date	03 May 2013

Results information

Result version number	v1 (current)
This version publication date	01 February 2016
First version publication date	20 November 2014

Trial information

Trial identification

Sponsor protocol code	OZR-2010-17
-----------------------	-------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	Nederlands Trial Register: NTR2820

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	02 September 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 May 2013
Global end of trial reached?	Yes
Global end of trial date	03 May 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the beneficial effect of a single dose of 150 µg clonidine as an adjuvant to chirocaine in retrobulbar block.

Protection of trial subjects:

Blood pressure monitored during surgery.

Background therapy:

Clonidine, an α_2 -adrenergic receptor agonist, appears to mediate sedation, anxiolysis and analgesia. Its working mechanism, however, is still a matter of debate (Hoffman 2001; Bergendahl 2002). As an adjuvant in neuraxial local anaesthesia, clonidine is generally recognized to prolong motor block and analgesia (e.g. see Elia et al. 2008). Besides, it has been suggested that the effect of local anaesthetics on peripheral nerves blockade can also be prolonged by the use of clonidine as an adjuvant. Thus, it might help to reduce both post-operative pain and the post-operative use of rescue analgesics.

Evidence for comparator: -

Actual start date of recruitment	06 July 2011
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: 101
Worldwide total number of subjects	101
EEA total number of subjects	101

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)	83
From 65 to 84 years	18

85 years and over	0
-------------------	---

Subject disposition

Recruitment

Recruitment details:

Patients scheduled for retinal detachment surgery with cryocoagulation and episcleral explant were asked to participate (age > 18 yrs; n=120).

Pre-assignment

Screening details:

Hypersensitivity to clonidine, oral use of clonidine, severe bradyarrhythmia, bipolar disorder, and history of renal insufficiency.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Control group

Arm description:

Retrobulbar, Chirocaine 7.5 mg/ml: 3-5 ml.

Arm type	No intervention
No investigational medicinal product assigned in this arm	

Arm title	Clonidine group
------------------	-----------------

Arm description:

Retrobulbar, Chirocaine 7.5 mg/ml: 3-5 ml + clonidine 150 µg in 1 ml.

Arm type	Experimental
Investigational medicinal product name	clonidine
Investigational medicinal product code	RVG 06055
Other name	Catapresan
Pharmaceutical forms	Solution for injection
Routes of administration	Retrobulbar use

Dosage and administration details:

150 µg (micrograms)

Number of subjects in period 1	Control group	Clonidine group
Started	52	49
Completed	52	49

Baseline characteristics

Reporting groups

Reporting group title	Control group
Reporting group description: Retrobulbar, Chirocaine 7.5 mg/ml: 3-5 ml.	
Reporting group title	Clonidine group
Reporting group description: Retrobulbar, Chirocaine 7.5 mg/ml: 3-5 ml + clonidine 150 µg in 1 ml.	

Reporting group values	Control group	Clonidine group	Total
Number of subjects	52	49	101
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	55.5	55.5	
standard deviation	± 11.2	± 11.1	-
Gender categorical Units: Subjects			
Female	22	19	41
Male	30	30	60

End points

End points reporting groups

Reporting group title	Control group
Reporting group description: Retrobulbar, Chirocaine 7.5 mg/ml: 3-5 ml.	
Reporting group title	Clonidine group
Reporting group description: Retrobulbar, Chirocaine 7.5 mg/ml: 3-5 ml + clonidine 150 µg in 1 ml.	
Subject analysis set title	Mixed model analysis for pain score
Subject analysis set type	Full analysis
Subject analysis set description: Mixed model analysis for repeated measurements	

Primary: Pain score on 10 cm Visual Analogue Scale (VAS) at postoperative day 1.

End point title	Pain score on 10 cm Visual Analogue Scale (VAS) at postoperative day 1.
End point description:	
End point type	Primary
End point timeframe: Postoperative day 1.	

End point values	Control group	Clonidine group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	49		
Units: percentage				
VAS-0: score = 0	24	23		
VAS-1: score < 1	14	13		
VAS-2: score > 1	14	13		

Statistical analyses

Statistical analysis title	Mixed model analysis pain score.
Statistical analysis description: Mixed model analysis for repeated measurements.	
Comparison groups	Control group v Clonidine group
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.05
Method	Mixed models analysis
Parameter estimate	Cox proportional hazard

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Day of surgery.

Adverse event reporting additional description:

Monitoring of blood pressure.

Assessment type	Systematic
-----------------	------------

Dictionary used

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

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

Reporting groups

Reporting group title	Control group
-----------------------	---------------

Reporting group description:

Retrobulbar, Chirocaine 7.5 mg/ml: 3-5 ml.

Reporting group title	Clonidine group
-----------------------	-----------------

Reporting group description:

Retrobulbar, Chirocaine 7.5 mg/ml: 3-5 ml + clonidine 150 µg in 1 ml.

Serious adverse events	Control group	Clonidine group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 52 (0.00%)	0 / 49 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Control group	Clonidine group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 52 (0.00%)	0 / 49 (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: Five patients of each group had postoperative diastolic pressure below 60 mm Hg. As systolic pressure was > 100 mm Hg for all 10 patients, this was not considered to be an adverse event.

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

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/25188774>