



Clinical trial results: Effectiveness of Periocular drug Injection in CATaract surgery Summary

EudraCT number	2019-004890-21
Trial protocol	NL DE AT PT
Global end of trial date	13 August 2024

Results information

Result version number	v1 (current)
This version publication date	03 April 2025
First version publication date	03 April 2025

Trial information

Trial identification

Sponsor protocol code	NL72427.068.19
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Academic Hospital Maastricht (azM)
Sponsor organisation address	P. Debyelaan 25, Maastricht, Netherlands,
Public contact	Dr. N. Visser, MD, PhD, Academic Hospital Maastricht (azM), 0031 (0)433875347, nienke.visser@mumc.nl
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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 December 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 June 2024
Global end of trial reached?	Yes
Global end of trial date	13 August 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this study is to evaluate the effectiveness of different treatments to prevent CME after cataract surgery, using either topical drugs (control group) or intra-/periocular injections (intervention groups).

Protection of trial subjects:

All medicines used are registered for ophthalmic use in patients undergoing cataract surgery. Overall side effects are mild and uncommon and are described in the SPC's and IB.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 October 2021
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: 520
Country: Number of subjects enrolled	Portugal: 9
Country: Number of subjects enrolled	Austria: 85
Country: Number of subjects enrolled	Germany: 14
Worldwide total number of subjects	628
EEA total number of subjects	628

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)	126
From 65 to 84 years	488

85 years and over	14
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Subject disposition

Recruitment

Recruitment details:

Enrolment took place from 13-10-2021 until 13-08-2024 in The Netherlands, Germany, Austria and Portugal.

Pre-assignment

Screening details:

Diagnosis and main criteria for inclusion:

Patients aged 21 years or older who require cataract surgery in at least one eye.

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:

Control group: topical bromfenac 0.09% and topical dexamethasone disodium phosphate 0.1% started 2 days preoperatively and continued postoperatively

Arm type	Active comparator
Investigational medicinal product name	Yellox 0.9 mg/ml eye drops solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops
Routes of administration	Ocular use

Dosage and administration details:

Bromfenac 0.09% ophthalmic solution

Investigational medicinal product name	Dexamethason 1 mg/ml
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops
Routes of administration	Ocular use

Dosage and administration details:

Dexamethasone 0.1% ophthalmic suspension

Arm title	Intervention group 1
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Arm description:

Intervention group 1: subconjunctival injection of 10 mg triamcinolone acetonide (TA) during cataract surgery

Arm type	Experimental
Investigational medicinal product name	Triamcinolone Acetonide 40 mg/ml solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Subconjunctival use

Dosage and administration details:

subconjunctival injection of 10 mg triamcinolone acetonide (TA) during cataract surgery

Arm title	Intervention group 2
Arm description:	
Intervention group 2: intracameral injection of ketorolac tromethamine solution (Omidria; 0.023mg/mL) during cataract surgery	
Arm type	Experimental
Investigational medicinal product name	Ketorolac tromethamine (0.023mg/mL) solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intracameral use
Dosage and administration details:	
: intracameral injection of ketorolac tromethamine solution (Omidria; 0.023mg/mL) during cataract surgery	

Arm title	Intervention group 3
Arm description:	
Intervention group 3: subconjunctival injection of 10 mg TA and intracameral injection of ketorolac tromethamine solution (Omidria; 0.023mg/mL) during cataract surgery	
Arm type	Experimental
Investigational medicinal product name	Triamcinolone Acetonide 40 mg/ml solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Subconjunctival use
Dosage and administration details:	
subconjunctival injection of 10 mg triamcinolone acetonide (TA) during cataract surgery	
Investigational medicinal product name	Ketorolac tromethamine (0.023mg/mL) solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intracameral use
Dosage and administration details:	
: intracameral injection of ketorolac tromethamine solution (Omidria; 0.023mg/mL) during cataract surgery	

Number of subjects in period 1 ^[1]	Control group	Intervention group 1	Intervention group 2
Started	156	159	158
Completed	150	144	147
Not completed	6	15	11
study medication not available, excluded on... etc	6	15	11

Number of subjects in period 1 ^[1]	Intervention group 3
Started	153
Completed	136
Not completed	17
study medication not available, excluded on... etc	17

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 2 patients were excluded after enrollment, but before randomization

Baseline characteristics

Reporting groups

Reporting group title	Control group
Reporting group description: Control group: topical bromfenac 0.09% and topical dexamethasone disodium phosphate 0.1% started 2 days preoperatively and continued postoperatively	
Reporting group title	Intervention group 1
Reporting group description: Intervention group 1: subconjunctival injection of 10 mg triamcinolone acetonide (TA) during cataract surgery	
Reporting group title	Intervention group 2
Reporting group description: Intervention group 2: intracameral injection of ketorolac tromethamine solution (Omidria; 0.023mg/mL) during cataract surgery	
Reporting group title	Intervention group 3
Reporting group description: Intervention group 3: subconjunctival injection of 10 mg TA and intracameral injection of ketorolac tromethamine solution (Omidria; 0.023mg/mL) during cataract surgery	

Reporting group values	Control group	Intervention group 1	Intervention group 2
Number of subjects	156	159	158
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			
geometric mean	71	70	71
standard deviation	± 7.9	± 8.1	± 8.0
Gender categorical Units: Subjects			
Female	82	81	73
Male	74	78	85
Ethnicity Units: Subjects			
Caucasian	151	155	155
African	0	1	0
Asian	2	1	1
Other	1	2	1
Unknown	2	0	1
Hypertension			

Units: Subjects			
No	92	78	82
Yes	64	80	75
Unknown	0	1	1
Smoker			
Units: Subjects			
Non smoker	57	65	67
Current smoker	21	18	26
Former smoker	75	75	63
Unknown	3	1	2
Hypercholesterolemia			
Units: Subjects			
No	114	102	104
Yes	42	56	53
Unknown	0	1	1
Cataract type			
Units: Subjects			
Nuclear	65	47	59
Cortical	2	4	2
Capsular	0	1	1
Polar	0	0	0
Mature+Cortical+Nuclear	0	1	0
Phakic	0	1	0
Nuclear+Polar	0	0	1
Nuclear+Cortical+Capsular	14	14	10
Cortical+Capsular	1	2	1
Nuclear+Capsular	5	10	13
Nuclear+Cortical	68	77	67
Unknown	1	2	4
Cataract intensity LOCS III - Nuclear color			
Units: LOCS III			
geometric mean	3.24	3.08	3.08
standard deviation	± 0.98	± 0.96	± 0.90
Cataract intensity LOCS III - Nuclear opalescence			
Units: LOCS III			
geometric mean	2.76	2.76	2.76
standard deviation	± 0.82	± 0.87	± 0.79
Cataract intensity LOCS III - Cortical			
Units: LOCS III			
geometric mean	2.13	2.25	2.14
standard deviation	± 1.05	± 1.14	± 1.19
Cataract intensity LOCS III - Posterior			
Units: LOCS III			
geometric mean	1.34	1.44	1.55
standard deviation	± 0.83	± 0.95	± 1.12
Reporting group values	Intervention group 3	Total	
Number of subjects	153	626	

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			
geometric mean	70		
standard deviation	± 9.1	-	
Gender categorical Units: Subjects			
Female	75	311	
Male	78	315	
Ethnicity Units: Subjects			
Caucasian	152	613	
African	1	2	
Asian	0	4	
Other	0	4	
Unknown	0	3	
Hypertension Units: Subjects			
No	81	333	
Yes	69	288	
Unknown	3	5	
Smoker Units: Subjects			
Non smoker	51	240	
Current smoker	24	89	
Former smoker	75	288	
Unknown	3	9	
Hypercholesterolemia Units: Subjects			
No	98	418	
Yes	52	203	
Unknown	3	5	
Cataract type Units: Subjects			
Nuclear	59	230	
Cortical	3	11	
Capsular	1	3	
Polar	1	1	
Mature+Cortical+Nuclear	0	1	
Phakic	0	1	

Nuclear+Polar	0	1	
Nuclear+Cortical+Capsular	11	49	
Cortical+Capsular	1	5	
Nuclear+Capsular	9	37	
Nuclear+Cortical	65	277	
Unknown	3	10	
Cataract intensity LOCS III - Nuclear color Units: LOCS III geometric mean standard deviation	3.13 ± 0.89	-	
Cataract intensity LOCS III - Nuclear opalescence Units: LOCS III geometric mean standard deviation	2.72 ± 0.84	-	
Cataract intensity LOCS III - Cortical Units: LOCS III geometric mean standard deviation	2.17 ± 1.19	-	
Cataract intensity LOCS III - Posterior Units: LOCS III geometric mean standard deviation	1.42 ± 0.96	-	

End points

End points reporting groups

Reporting group title	Control group
Reporting group description: Control group: topical bromfenac 0.09% and topical dexamethasone disodium phosphate 0.1% started 2 days preoperatively and continued postoperatively	
Reporting group title	Intervention group 1
Reporting group description: Intervention group 1: subconjunctival injection of 10 mg triamcinolone acetonide (TA) during cataract surgery	
Reporting group title	Intervention group 2
Reporting group description: Intervention group 2: intracameral injection of ketorolac tromethamine solution (Omidria; 0.023mg/mL) during cataract surgery	
Reporting group title	Intervention group 3
Reporting group description: Intervention group 3: subconjunctival injection of 10 mg TA and intracameral injection of ketorolac tromethamine solution (Omidria; 0.023mg/mL) during cataract surgery	

Primary: CSMT 6 weeks

End point title	CSMT 6 weeks
End point description:	
End point type	Primary
End point timeframe: baseline to 6 weeks	

End point values	Control group	Intervention group 1	Intervention group 2	Intervention group 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	146	142	140	130
Units: μm				
arithmetic mean (standard deviation)	8.37 ($\pm$ 18.14)	6.90 ($\pm$ 18.46)	36.69 ($\pm$ 67.30)	7.26 ($\pm$ 11.30)

Statistical analyses

Statistical analysis title	Treatment effects
Statistical analysis description: Linear Mixed Model for calculating treatment effect between groups at 6 weeks. This is based on the mean values of CSMT at 6 weeks (not change score).	
Comparison groups	Control group v Intervention group 1 v Intervention group 2 v Intervention group 3

Number of subjects included in analysis	558
Analysis specification	Pre-specified
Analysis type	other ^[1]
P-value	≤ 0.05 ^[2]
Method	equality
Parameter estimate	Treatment effect
Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard error of the mean

Notes:

[1] - The fixed effects in the model consisted of time, time*treatment, center, center*time, and center*time*treatment.

[2] - A significance threshold of $P \leq 0.05$ was used, and following Bonferroni correction, a significance level of $P \leq 0.00833$ was applied for testing across 4 study groups.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From inclusion until 12 weeks after operation.

Assessment type	Systematic
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Dictionary used

Dictionary name	NA
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Dictionary version	0
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Reporting groups

Reporting group title	Control group
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Reporting group description:

Control group: topical bromfenac 0.09% and topical dexamethasone disodium phosphate 0.1% started 2 days preoperatively and continued postoperatively

Reporting group title	Intervention group 1
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Reporting group description:

Intervention group 1: subconjunctival injection of 10 mg triamcinolone acetonide (TA) during cataract surgery

Reporting group title	Intervention group 2
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Reporting group description:

Intervention group 2: intracameral injection of ketorolac tromethamine solution (Omidria; 0.023mg/mL) during cataract surgery

Reporting group title	Intervention group 3
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Reporting group description:

Intervention group 3: subconjunctival injection of 10 mg TA and intracameral injection of ketorolac tromethamine solution (Omidria; 0.023mg/mL) during cataract surgery

Serious adverse events	Control group	Intervention group 1	Intervention group 2
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 156 (2.56%)	2 / 159 (1.26%)	3 / 158 (1.90%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Fall	Additional description: Fall from roof		
subjects affected / exposed	0 / 156 (0.00%)	0 / 159 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Syncope	Additional description: Syncope during arterial hypotension of unknown origin		
subjects affected / exposed	1 / 156 (0.64%)	0 / 159 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Blood and lymphatic system disorders			
Acute myeloid leukaemia			
subjects affected / exposed	1 / 156 (0.64%)	0 / 159 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Eye disorders			
Retinal detachment			
Additional description: Retinal detachment with hospital admission			
subjects affected / exposed	1 / 156 (0.64%)	0 / 159 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic neuropathy			
Additional description: Non-Arteritic Anterior Ischemic Optic Neuropathy (NAION) non study eye			
subjects affected / exposed	0 / 156 (0.00%)	1 / 159 (0.63%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 156 (0.00%)	0 / 159 (0.00%)	1 / 158 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 156 (0.00%)	1 / 159 (0.63%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Urosepsis			
subjects affected / exposed	0 / 156 (0.00%)	0 / 159 (0.00%)	2 / 158 (1.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 156 (0.64%)	0 / 159 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Serious adverse events			
Intervention group 3			
Total subjects affected by serious			

adverse events			
subjects affected / exposed	1 / 153 (0.65%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Fall	Additional description: Fall from roof		
subjects affected / exposed	1 / 153 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Syncope	Additional description: Syncope during arterial hypotension of unknown origin		
subjects affected / exposed	0 / 153 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Acute myeloid leukaemia			
subjects affected / exposed	0 / 153 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Retinal detachment	Additional description: Retinal detachment with hospital admission		
subjects affected / exposed	0 / 153 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ischaemic neuropathy	Additional description: Non-Arteritic Anterior Ischemic Optic Neuropathy (NAION) non study eye		
subjects affected / exposed	0 / 153 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 153 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			

subjects affected / exposed	0 / 153 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Urosepsis			
subjects affected / exposed	0 / 153 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	0 / 153 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Control group	Intervention group 1	Intervention group 2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	33 / 156 (21.15%)	39 / 159 (24.53%)	74 / 158 (46.84%)
Eye disorders			
Dry eye			
subjects affected / exposed	27 / 156 (17.31%)	35 / 159 (22.01%)	49 / 158 (31.01%)
occurrences (all)	27	35	49
Corneal oedema			
subjects affected / exposed	5 / 156 (3.21%)	6 / 159 (3.77%)	14 / 158 (8.86%)
occurrences (all)	5	6	14
Conjunctival hyperaemia			
subjects affected / exposed	1 / 156 (0.64%)	3 / 159 (1.89%)	22 / 158 (13.92%)
occurrences (all)	1	3	22
Photophobia			
subjects affected / exposed	4 / 156 (2.56%)	7 / 159 (4.40%)	13 / 158 (8.23%)
occurrences (all)	4	7	13
Anterior chamber cells/Uveitis			
subjects affected / exposed	2 / 156 (1.28%)	0 / 159 (0.00%)	12 / 158 (7.59%)
occurrences (all)	2	0	12

Non-serious adverse events	Intervention group 3		
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Total subjects affected by non-serious adverse events			
subjects affected / exposed	41 / 153 (26.80%)		
Eye disorders			
Dry eye			
subjects affected / exposed	30 / 153 (19.61%)		
occurrences (all)	30		
Corneal oedema			
subjects affected / exposed	10 / 153 (6.54%)		
occurrences (all)	10		
Conjunctival hyperaemia			
subjects affected / exposed	7 / 153 (4.58%)		
occurrences (all)	7		
Photophobia			
subjects affected / exposed	1 / 153 (0.65%)		
occurrences (all)	1		
Anterior chamber cells/Uveitis			
subjects affected / exposed	1 / 153 (0.65%)		
occurrences (all)	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? No

Limitations and caveats

None reported