



Clinical trial results:

Evaluation of inflammatory markers in patients on topical anti-glaucoma drop therapy; a comparative trial of preserved and non-preserved primary medical treatment (eye drops) in patients with glaucoma and ocular hypertension – a pilot study.

Summary

EudraCT number	2013-000581-10
Trial protocol	GB
Global end of trial date	02 November 2018

Results information

Result version number	v1 (current)
This version publication date	30 May 2020
First version publication date	30 May 2020
Summary attachment (see zip file)	Ocular Surface Study - End of Study report (AK - OS Study End of Study Report 08-07-19 updated(2).docx)

Trial information

Trial identification

Sponsor protocol code	12OY006
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Nottingham University NHS Hospitals Trust
Sponsor organisation address	Queens Medical Centre, Derby Road, Nottingham, United Kingdom, NG7 2UH
Public contact	R&I, Nottingham University Hospitals NHS Trust, +44 115 9249924, researchsponsor@nuh.nhs.uk
Scientific contact	R&I, Nottingham University NHS Hospitals Trust, +44 115 9249924 , researchsponsor@nuh.nhs.uk

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	31 August 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 August 2018
Global end of trial reached?	Yes
Global end of trial date	02 November 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary outcome:

To evaluate the expression of inflammatory markers in the tear film and on the ocular surface of patients undergoing treatment for glaucoma and ocular hypertension using drops containing different types of preservative or no preservative.

Secondary Outcome: Trabecular Meshwork (TMW) endothelium cell health following exposure to different preservative regimes

Clinical Outcomes: Ocular surface disease index (OSDI) assessment

Biomarker outcomes:

1.identification of tear, ocular surface and tissue expression of biomarkers of inflammation between patients using preserved and preservative free medical treatment for glaucoma and the control participants

2.quantification of changes in biomarker expression between different treatment modalities.

3.quantification and identification of profile changes in inflammatory biomarker expression over time and with different drop regimes

Protection of trial subjects:

None.

Background therapy:

None.

Evidence for comparator:

Treatment-naïve glaucoma patients requiring topical hypotensive medication were enrolled and randomized into three groups each receiving benzalkonium chloride (BAK), polyquad (PQ) or preservative free (PF).

Actual start date of recruitment	01 May 2013
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	United Kingdom: 38
Worldwide total number of subjects	38
EEA total number of subjects	38

Notes:

Subjects enrolled per age group

In utero	0
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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)	13
From 65 to 84 years	24
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Potential trial participants with ocular hypertension or glaucoma requiring drop treatment were recruited from the glaucoma service at Nottingham University Hospitals from 09/07/2014 to 31/01/2017.

Pre-assignment

Screening details:

Newly diagnosed patients with glaucoma and ocular hypertension attending the glaucoma service were sent an invitation letter over a 12 month period.

Period 1

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

Blinding implementation details:

Masking of patients or clinicians to treatment was not possible. However, IC and tear samples were masked to group allocation and the analysis of biomarkers was undertaken in a masked fashion.

Arms

Are arms mutually exclusive?	Yes
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Arm title	Benzalkonium chloride (BAK)
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Arm description:

Benzalkonium chloride arm - preserved eye drops

Arm type	Active comparator
Investigational medicinal product name	Bimatoprost
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops
Routes of administration	Ocular use

Dosage and administration details:

xxx

Arm title	Polyquad (PQ)
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Arm description:

Polyquad preservative arm

Arm type	Active comparator
Investigational medicinal product name	Travaprost
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops
Routes of administration	Ocular use

Dosage and administration details:

0.04% Once daily preferably in the evening

Investigational medicinal product name	Travaprost + Timolol (Duotrav)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops
Routes of administration	Ocular use

Dosage and administration details:

0.04%/ml plus 0.5%/ml Once daily

Investigational medicinal product name	Travaprost
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops
Routes of administration	Ocular use
Dosage and administration details: 0.04% once daily preferably in the evening.	
Arm title	Preservative free

Arm description:

Preservative free arm

Arm type	Active comparator
Investigational medicinal product name	Latanoprost
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops
Routes of administration	Ocular use

Dosage and administration details:

0.005% Once daily preferably in the evening

Number of subjects in period 1^[1]	Benzalkonium chloride (BAK)	Polyquad (PQ)	Preservative free
Started	7	8	8
Baseline	7	8	8
1 month	7	8	8
3 months	7	8	8
6 months	7	8	8
12 months	7	8	8
24 months	7	8	8
Completed	7	8	8

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: Please see end of study report.

Baseline characteristics

Reporting groups

Reporting group title	Benzalkonium chloride (BAK)
Reporting group description: Benzalkonium chloride arm - preserved eye drops	
Reporting group title	Polyquad (PQ)
Reporting group description: Polyquad preservative arm	
Reporting group title	Preservative free
Reporting group description: Preservative free arm	

Reporting group values	Benzalkonium chloride (BAK)	Polyquad (PQ)	Preservative free
Number of subjects	7	8	8
Age categorical			
Of the 38 original participants 13 participants were between the ages of 18 and 64. The youngest of these was 46 years of age, 24 participants were between the ages of 65 and 84 and there was just one patient who was 85 and over. The oldest participant in this study was 86 years of age.			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	3	2	4
From 65-84 years	4	5	4
85 years and over	0	1	0
Age continuous			
Units: years			
arithmetic mean	61	68	65
full range (min-max)	46 to 76	50 to 86	56 to 74
Gender categorical			
See End of study report			
Units: Subjects			
Female	3	6	3
Male	4	2	5

Reporting group values	Total		
Number of subjects	23		
Age categorical			
Of the 38 original participants 13 participants were between the ages of 18 and 64. The youngest of these was 46 years of age, 24 participants were between the ages of 65 and 84 and there was just one patient who was 85 and over. The oldest participant in this study was 86 years of age.			
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)	9		
From 65-84 years	13		
85 years and over	1		
Age continuous			
Units: years			
arithmetic mean			
full range (min-max)	-		
Gender categorical			
See End of study report			
Units: Subjects			
Female	12		
Male	11		

Subject analysis sets

Subject analysis set title	Benzalkonium (BAK)
Subject analysis set type	Full analysis
Subject analysis set description:	
Benzalkonium preserved eyedrops	
Subject analysis set title	Polyquad (PQ)
Subject analysis set type	Full analysis
Subject analysis set description:	
Preserved eye drop	
Subject analysis set title	Preservative free
Subject analysis set type	Full analysis
Subject analysis set description:	
Preservative free eyedrop	

Reporting group values	Benzalkonium (BAK)	Polyquad (PQ)	Preservative free
Number of subjects	7	8	8
Age categorical			
Of the 38 original participants 13 participants were between the ages of 18 and 64. The youngest of these was 46 years of age, 24 participants were between the ages of 65 and 84 and there was just one patient who was 85 and over. The oldest participant in this study was 86 years of age.			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	3	2	4
From 65-84 years	4	5	4
85 years and over	0	1	0

Age continuous			
Units: years			
arithmetic mean	65	61	68
full range (min-max)	56 to 74	46 to 76	50 to 86
Gender categorical			
See End of study report			
Units: Subjects			
Female	3	6	3
Male	4	2	5

End points

End points reporting groups

Reporting group title	Benzalkonium chloride (BAK)
Reporting group description: Benzalkonium chloride arm - preserved eye drops	
Reporting group title	Polyquad (PQ)
Reporting group description: Polyquad preservative arm	
Reporting group title	Preservative free
Reporting group description: Preservative free arm	
Subject analysis set title	Benzalkonium (BAK)
Subject analysis set type	Full analysis
Subject analysis set description: Benzalkonium preserved eyedrops	
Subject analysis set title	Polyquad (PQ)
Subject analysis set type	Full analysis
Subject analysis set description: Preserved eye drop	
Subject analysis set title	Preservative free
Subject analysis set type	Full analysis
Subject analysis set description: Preservative free eyedrop	

Primary: Cytokine Results

End point title	Cytokine Results ^[1]
End point description: The expression of inflammatory markers in the tear film, on the ocular surface and on the conjunctiva and Tenons' tissue of patients undergoing treatment for glaucoma using drops containing different types of preservative or no preservative.	
End point type	Primary
End point timeframe: 24 months	

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: Full statistical analysis can be found in the attached End of Study report.

End point values	Benzalkonium (BAK)	Polyquad (PQ)	Preservative free	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed				
Units: decimals				
arithmetic mean (standard deviation)	83.34 (± 55.63)	1119.40 (± 674.68)	2.06 (± 5.65)	

Statistical analyses

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Non serious adverse events did not have a specified timeframe for reporting. Serious adverse events were required to be reported within 24 hours of participating site becoming aware of the event.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16
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Frequency threshold for reporting non-serious adverse events: 5 %

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 of any kind were reported please see attached end of study report.

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.

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| <ol style="list-style-type: none">1. Recruitment was not to time and target and therefore the study may be underpowered to show affect.2. Neither the patients nor the clinicians were masked to treatment allocation.3 Significant number of samples were not adequate for analysis |
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Notes: