Clinical trial results:
Efficacy and tolerability of brinzolamide in patients with elevated intraocular pressure: a double-blind, randomized, parallel, verum-controlled trial.

Summary

EudraCT number	2013-001793-21
Trial protocol	HU GR
Global end of trial date	16 April 2014

Results information

Result version number	v1 (current)
This version publication date	25 April 2022
First version publication date	25 April 2022

Trial information

Trial identification

Sponsor protocol code	CPA12001

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Pharmathen S.A
Sponsor organisation address	Dervenakion 6 , Pallini, Athens , Greece, 15351
Public contact	Lida Kalantzi, PhD Director of Scientific Affairs Pharmaceutical Research Operations / Finished Fo, PHARMATHEN S.A., +30 210 66 04 300, lkalantzi@pharmathen.com
Scientific contact	Lida Kalantzi, PhD Director of Scientific Affairs Pharmaceutical Research Operations / Finished Fo, PHARMATHEN S.A., +30 210 66 04 300, lkalantzi@pharmathen.com

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	21 July 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 April 2014
Global end of trial reached?	Yes
Global end of trial date	16 April 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the non-inferiority of eye drops containing brinzolamide 10 mg/ml (Brinzolamide Ophthalmic Suspension) as compared to a reference product (AZOPT® 10 mg/ml eye drops suspension) for the treatment of elevated intraocular pressure or open angle glaucoma.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial participants were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 September 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	Greece: 9
Country: Number of subjects enrolled	Hungary: 160
Worldwide total number of subjects	169
EEA total number of subjects	169

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)	67
From 65 to 84 years	102
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Greece : 2 Sites
Hungary : 10 sites

Pre-assignment

Screening details:

Study has been conducted in sites in Greece and Hungary. For both countries : Number of subjects screened: 177 Number of screening failures: 8

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer

Blinding implementation details:

The study was double blind. The subjects, the investigator(s) (the study team, monitors and CRO), and the central bioanalytical laboratory were held blind during the study. CROs personnel, including the trial biostatistician, were blind with respect to treatment allocation. Biostatisticians were informed on the unblinded treatment allocation following the database lock and statistical analysis.
To achieve blinding, both products were identical in their appearance.

Arms

Are arms mutually exclusive?	Yes
Arm title	Test

Arm description:

Brinzolamide Ophthalmic Suspension10 mg/ml, PHARMATHEN S.A., Greece

Arm type	Test
Investigational medicinal product name	Brinzolamide Ophthalmic Suspension
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops, suspension
Routes of administration	Intraocular use

Dosage and administration details:

One drop into the conjunctival sac: once in the morning and once in the evening, approximately 12 hours (between 8 and 14 hours) apart

Arm title	Reference

Arm description:

AZOPT 10 mg/ml eye drops suspension, Alcon Laboratories (UK) Ltd

Arm type	Reference
Investigational medicinal product name	AZOPT
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops, suspension
Routes of administration	Intraocular use

Dosage and administration details:

One drop into the conjunctival sac: once in the morning and once in the evening, approximately 12 hours (between 8 and 14 hours) apart

Number of subjects in period 1	Test	Reference
Started	88	81
Completed	80	58
Not completed	8	23
Adverse event, serious fatal	-	1
Consent withdrawn by subject	4	7
Adverse event, non-fatal	-	1
Protocol deviation	4	14

Baseline characteristics

Reporting groups	
Reporting group title	Test
Reporting group description:	
Brinzolamide Ophthalmic Suspension10 mg/ml, PHARMATHEN S.A., Greece	
Reporting group title	Reference
Reporting group description:	
AZOPT 10 mg/ml eye drops suspension, Alcon Laboratories (UK) Ltd	

Reporting group values	Test	Reference	Total
Number of subjects	88	81	169
Age categorical			
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)	35	32	67
From 65-84 years	53	49	102
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	63.1	63.2	
standard deviation	± 11.3	± 13	-
Gender categorical			
Units: Subjects			
Female	53	51	104
Male	35	30	65

Subject analysis sets	
Subject analysis set title	PP
Subject analysis set type	Per protocol
Subject analysis set description:	
The per protocol (PP) population includes all those of the patients who had no major protocol violations, who completed IOP measurements within the allowed time frames, who completed 12 weeks of treatment and who did not take prohibited concurrent medication.	

Reporting group values	PP		
Number of subjects	138		
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	58		
85 years and over	80		
Age continuous			
Units: years			
arithmetic mean	62.58		
standard deviation	± 12.25		
Gender categorical			
Units: Subjects			
Female	82		
Male	56		

End points

End points reporting groups

Reporting group title	Test
Reporting group description:	
Brinzolamide Ophthalmic Suspension10 mg/ml, PHARMATHEN S.A., Greece	
Reporting group title	Reference
Reporting group description:	
AZOPT 10 mg/ml eye drops suspension, Alcon Laboratories (UK) Ltd	
Subject analysis set title	PP
Subject analysis set type	Per protocol
Subject analysis set description:	
The per protocol (PP) population includes all those of the patients who had no major protocol violations, who completed IOP measurements within the allowed time frames, who completed 12 weeks of treatment and who did not take prohibited concurrent medication.	

Primary: Primary : Change in IOP at 8:00am in study eye from baseline (week 0) to end of treatment (week 12)

End point title	Primary : Change in IOP at 8:00am in study eye from baseline (week 0) to end of treatment (week 12)
End point description:	
Comparison of reductions in IOP at 8:00 a.m. in subjects treated with the test or reference product, characterised as an intra-individual difference in the target eye from baseline (week 0) to the end of the treatment period (12 weeks).	
End point type	Primary
End point timeframe:	
Week 0 (baseline) to end of treatment (week 12)	

End point values	Test	Reference	PP	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	80	58	138	
Units: mmHg				
arithmetic mean (confidence interval 95%)	7.8 (7.011 to 8.59)	7.3 (6.27 to 8.33)	0.54 (-0.75 to 1.83)	

Statistical analyses

Statistical analysis title	IOP change
Comparison groups	Test v Reference
Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Mean difference (final values)
Point estimate	0.54

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.75
upper limit	1.83

Notes:

[1] - Δ0 is the non–inferiority margin, which was set to 1.5 mmHg.

Secondary: Secondary: Change in IOP at 8:00am in study eye from baseline (week 0) to week 2

End point title	Secondary: Change in IOP at 8:00am in study eye from baseline (week 0) to week 2

End point description:

Comparison of reductions in IOP at 8:00 a.m. in subjects treated with the test or reference product, characterised as an intra-individual difference in the target eye from baseline (week 0) to week 2 of treatment period.

End point type	Secondary

End point timeframe:

Week 0 (baseline) to Week 2

End point values	Test	Reference		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	58		
Units: mmHg				
arithmetic mean (confidence interval 98.3%)	6.7 (5.84 to 7.56)	6.0 (4.8 to 7.19)		

Statistical analyses

Statistical analysis title	change in IOP at 8.00a.m from week 0 to week 2
Comparison groups	Test v Reference
Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Mean difference (final values)
Point estimate	0.71
Confidence interval	
level	Other: 98.3 %
sides	2-sided
lower limit	-0.79
upper limit	2.2

Secondary: Secondary : Change in IOP at 12.00 noon in study eye from baseline (week 0) to week 2

End point title	Secondary : Change in IOP at 12.00 noon in study eye from baseline (week 0) to week 2

End point description:

Comparison of reductions in IOP at 12.00 noon in subjects treated with the test or reference product, characterized as an intra-individual difference in the target eye from baseline (week 0) to week 2 of treatment period.

End point type	Secondary

End point timeframe:

Week 0 (baseline) to week 2

End point values	Test	Reference		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	58		
Units: mmHg				
arithmetic mean (confidence interval 98.3%)	7.3 (6.49 to 8.11)	7.1 (6.12 to 8.08)		

Statistical analyses

Statistical analysis title	change in IOP at 12:00pm from week 0 to week 2
Comparison groups	Test v Reference
Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Mean difference (final values)
Point estimate	0.21
Confidence interval	
level	Other: 98.3 %
sides	2-sided
lower limit	-1.12
upper limit	1.52

Secondary: Secondary : Change in IOP at 4.00pm in study eye from baseline (week 0) to week 2

End point title	Secondary : Change in IOP at 4.00pm in study eye from baseline (week 0) to week 2

End point description:

Comparison of reductions in IOP at 4.00 pm. in subjects treated with the test or reference product, characterized as an intra-individual difference in the target eye from baseline (week 0) to week 2 of treatment period.

End point type	Secondary

End point timeframe:

Week 0 (baseline) to Week 2

End point values	Test	Reference		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	58		
Units: mmHg				
arithmetic mean (confidence interval 98.3%)	7.0 (6.17 to 7.83)	6.9 (5.7 to 8.09)		

Statistical analyses

Statistical analysis title	change in IOP at 4.00 pm from week 0 to week 2
Comparison groups	Test v Reference
Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Mean difference (final values)
Point estimate	0.13
Confidence interval	
level	Other: 98.3 %
sides	2-sided
lower limit	-1.33
upper limit	1.59

Secondary: Secondary : Change in IOP at 8:00am in study eye from baseline (week 0) to week 6

End point title	Secondary : Change in IOP at 8:00am in study eye from baseline (week 0) to week 6

End point description:

Comparison of reductions in IOP at 8:00 a.m. in subjects treated with the test or reference product, characterized as an intra-individual difference in the target eye from baseline (week 0) to week 6 of treatment period.

End point type	Secondary

End point timeframe:

Week 0 (baseline) to week 6

End point values	Test	Reference		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	58		
Units: mmHg				
arithmetic mean (confidence interval 98.3%)	7.5 (6.53 to 8.46)	7.1 (5.81 to 8.39)		

Statistical analyses

Statistical analysis title	change in IOP at 8.00 a.m from week 0 to week 6
Comparison groups	Test v Reference
Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Mean difference (final values)
Point estimate	0.46
Confidence interval	
level	Other: 98.3 %
sides	2-sided
lower limit	-1.17
upper limit	2.09

Secondary: Secondary : Change in IOP at 12.00 noon in study eye from baseline (week 0) to week 6

End point title	Secondary : Change in IOP at 12.00 noon in study eye from baseline (week 0) to week 6

End point description:

Comparison of reductions in IOP at 12.00 noon . in subjects treated with the test or reference product, characterized as an intra-individual difference in the target eye from baseline (week 0) to week 6 of treatment period.

End point type	Secondary

End point timeframe:

Week 0 (baseline) to Week 6

End point values	Test	Reference		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	58		
Units: mmHg				
arithmetic mean (confidence interval 98.3%)	8.1 (7.32 to 8.88)	8 (6.99 to 9)		

Statistical analyses

Statistical analysis title	change in IOP at 12:00pm from week 0 to week 6
Comparison groups	Test v Reference

Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Mean difference (final values)
Point estimate	0.05
Confidence interval	
level	Other: 98.3 %
sides	2-sided
lower limit	-1.25
upper limit	1.34

Secondary: Secondary : Change in IOP at 4.00 p.m in study eye from baseline (week 0) to week 6

End point title	Secondary : Change in IOP at 4.00 p.m in study eye from baseline (week 0) to week 6

End point description:

Comparison of reductions in IOP at 8:00 a.m. in subjects treated with the test or reference product, characterized as an intra-individual difference in the target eye from baseline to week 6 of treatment period.

End point type	Secondary

End point timeframe:

Baseline (Week 0) to Week 6

End point values	Test	Reference		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	58		
Units: mmHg				
arithmetic mean (confidence interval 98.3%)	7.8 (6.94 to 8.66)	8.1 (7.09 to 9.1)		

Statistical analyses

Statistical analysis title	Change in IOP at 4.00p.m from week0 to week 6
Comparison groups	Test v Reference
Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Mean difference (final values)
Point estimate	-0.31

Confidence interval	
level	Other: 98.3 %
sides	2-sided
lower limit	-1.68
upper limit	1.07

Secondary: Secondary : Change in IOP at 12.00 noon in study eye from baseline (week 0) to end of treatment (week 12)

End point title	Secondary : Change in IOP at 12.00 noon in study eye from baseline (week 0) to end of treatment (week 12)

End point description:

Comparison of reductions in IOP at 12.00 noon in subjects treated with the test or reference product, characterized as an intra-individual difference in the target eye from baseline (week 0) to the end of the treatment period (12 weeks).

End point type	Secondary

End point timeframe:

Week 0 (baseline) to Week 12

End point values	Test	Reference		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	58		
Units: mmHg				
arithmetic mean (confidence interval 98.3%)	8.2 (7.41 to 8.98)	7.8 (6.76 to 8.84)		

Statistical analyses

Statistical analysis title	change in IOP at 12:00pm from week 0 to week 12
Comparison groups	Test v Reference
Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Mean difference (final values)
Point estimate	0.32
Confidence interval	
level	Other: 98.3 %
sides	2-sided
lower limit	-1.01
upper limit	1.66

Secondary: Secondary : Change in IOP at 4.00 p.m in study eye from baseline (week 0) to the end of the treatment (week 12)

End point title	Secondary : Change in IOP at 4.00 p.m in study eye from baseline (week 0) to the end of the treatment (week 12)

End point description:

Comparison of reductions in IOP at 8:00 a.m. in subjects treated with the test or reference product, characterized as an intra-individual difference in the target eye from baseline (week 0) to the end of the treatment period (12 weeks).

End point type	Secondary

End point timeframe:

Week 0 (Baseline) to week 12

End point values	Test	Reference		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	58		
Units: mmHg				
arithmetic mean (confidence interval 98.3%)	8.1 (7.24 to 8.95)	8.1 (6.99 to 9.2)		

Statistical analyses

Statistical analysis title	change in IOP at 4.00 p.m from week 0 to week 12
Comparison groups	Test v Reference
Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Mean difference (final values)
Point estimate	0.01
Confidence interval	
level	Other: 98.3 %
sides	2-sided
lower limit	-1.41
upper limit	1.43

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Week 0 to end of treatment (12 weeks)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	Test
Reporting group description: -	
Reporting group title	Reference

Reporting group description: -

Serious adverse events	Test	Reference	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 88 (0.00%)	2 / 81 (2.47%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	1	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung neoplasm			
subjects affected / exposed	0 / 88 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metastasis			
subjects affected / exposed	0 / 88 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Surgical and medical procedures			
Carpal tunnel decompression			
subjects affected / exposed	0 / 88 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Test	Reference	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 88 (28.41%)	11 / 81 (13.58%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 88 (0.00%)	2 / 81 (2.47%)	
occurrences (all)	0	2	
Surgical and medical procedures			
Maxillofacial operation			
subjects affected / exposed	1 / 88 (1.14%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Drug intolerance			
subjects affected / exposed	2 / 88 (2.27%)	3 / 81 (3.70%)	
occurrences (all)	2	4	
Product taste abnormal			
subjects affected / exposed	1 / 88 (1.14%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Asthenia			
subjects affected / exposed	0 / 88 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Bartholin's cyst			
subjects affected / exposed	1 / 88 (1.14%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 88 (2.27%)	0 / 81 (0.00%)	
occurrences (all)	2	0	
Cough			
subjects affected / exposed	1 / 88 (1.14%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Investigations			
Blood glucose increased			
subjects affected / exposed	3 / 88 (3.41%)	1 / 81 (1.23%)	
occurrences (all)	3	1	
Gamma-glutamyltransferase			

increased			
subjects affected / exposed	3 / 88 (3.41%)	1 / 81 (1.23%)	
occurrences (all)	3	1	
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 88 (2.27%)	0 / 81 (0.00%)	
occurrences (all)	2	0	
Alanine aminotransferase increased			
subjects affected / exposed	1 / 88 (1.14%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 88 (1.14%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Blood pressure increased			
subjects affected / exposed	1 / 88 (1.14%)	1 / 81 (1.23%)	
occurrences (all)	1	1	
Blood uric acid increased			
subjects affected / exposed	1 / 88 (1.14%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 88 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	2	
Injury			
subjects affected / exposed	0 / 88 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 88 (1.14%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Bradycardia			
subjects affected / exposed	0 / 88 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Palpitations			
subjects affected / exposed	0 / 88 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Nervous system disorders			

Headache			
subjects affected / exposed	1 / 88 (1.14%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Dysgeusia			
subjects affected / exposed	0 / 88 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Visual field defect			
subjects affected / exposed	0 / 88 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 88 (2.27%)	0 / 81 (0.00%)	
occurrences (all)	2	0	
Thrombocytopenia			
subjects affected / exposed	1 / 88 (1.14%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 88 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Eye disorders			
Foreign body sensation in eyes			
subjects affected / exposed	2 / 88 (2.27%)	0 / 81 (0.00%)	
occurrences (all)	3	0	
Eye pain			
subjects affected / exposed	1 / 88 (1.14%)	2 / 81 (2.47%)	
occurrences (all)	2	2	
Ocular hyperaemia			
subjects affected / exposed	2 / 88 (2.27%)	1 / 81 (1.23%)	
occurrences (all)	2	1	
Eye swelling			
subjects affected / exposed	1 / 88 (1.14%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Keratitis			
subjects affected / exposed	1 / 88 (1.14%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Ocular discomfort			

subjects affected / exposed	1 / 88 (1.14%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Vision blurred			
subjects affected / exposed	0 / 88 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	3	
Eye discharge			
subjects affected / exposed	0 / 88 (0.00%)	2 / 81 (2.47%)	
occurrences (all)	0	2	
Eye irritation			
subjects affected / exposed	0 / 88 (0.00%)	2 / 81 (2.47%)	
occurrences (all)	0	2	
Conjunctival hyperaemia			
subjects affected / exposed	0 / 88 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Corneal thickening			
subjects affected / exposed	0 / 88 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Hypoaesthesia eye			
subjects affected / exposed	0 / 88 (0.00%)	1 / 81 (1.23%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 88 (1.14%)	0 / 81 (0.00%)	
occurrences (all)	2	0	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 88 (1.14%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	1 / 88 (1.14%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Laryngitis			
subjects affected / exposed	2 / 88 (2.27%)	0 / 81 (0.00%)	
occurrences (all)	2	0	

Hordeolum			
subjects affected / exposed	1 / 88 (1.14%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			
subjects affected / exposed	1 / 88 (1.14%)	0 / 81 (0.00%)	
occurrences (all)	1	0	
Pneumonia			
subjects affected / exposed	1 / 88 (1.14%)	0 / 81 (0.00%)	
occurrences (all)	1	0	

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