Clinical trial results:
A phase II, observer masked, active controlled study of SYL040012 for the treatment of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension (SYLTAG)

Summary

EudraCT number	2013-002947-27
Trial protocol	EE DE ES
Global end of trial date	05 August 2015

Results information

Result version number	v1 (current)
This version publication date	01 March 2017
First version publication date	01 March 2017

Trial information

Trial identification

Sponsor protocol code	SYL040012_IV

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Sylentis SAU - Grupo PharmaMar
Sponsor organisation address	Parque Tecnológico de Madrid C/Santiago Grisolía nº 2, Tres Cantos, Madrid, Spain, 28760
Public contact	Head of Regulatory Affairs & QP, Sylentis S.A.U., 0034 918047667, info@sylentis.com
Scientific contact	Head of Regulatory Affairs & QP, Sylentis S.A.U., 0034 918047667, info@sylentis.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	20 January 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 August 2015
Global end of trial reached?	Yes
Global end of trial date	05 August 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the most effective drug concentration of SYL040012 in the reduction of the intraocular pressure (IOP) after 28 days of treatment.

Protection of trial subjects:

This study was conducted in compliance with ICH-GCP Guidelines, the Declaration of Helsinki (18th World Medical Assembly, 1964) and its last revision (Fortaleza, October 2013), and local laws and regulations of the countries where the study was performed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 October 2014
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	Spain: 80
Country: Number of subjects enrolled	Estonia: 78
Country: Number of subjects enrolled	Germany: 17
Country: Number of subjects enrolled	United States: 100
Worldwide total number of subjects	275
EEA total number of subjects	175

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)	200
From 65 to 84 years	75

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

275 patients were screened from 28 October 2014 to 06 July 2015 in 19 centers in Spain, Germany, Estonia and the USA. 91 patients were finally not included in the study. 184 (66.9%) were randomized to 5 different groups: bamosiran 0.375%, bamosiran 0.75%, bamosiran 1.125%, bamosiran 1.5% and 0.5 Timolol solution

Pre-assignment

Screening details:

Age≥18 years;Signed IC;OAG or OHT;IOP≥23 mmHg;BCVA=1.0 logMAR;Stable visual field;Central corneal thickness 480-620 µm;Shaffer gonioscopic grade of ≥ 3 (in at least 3 quadrants) in both eyes

Period 1

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

Blinding implementation details:

The study was double-masked by definition for the different doses of bamosiran; but as the timolol group was dosed with a different dosage form and regimen, in order to keep a masked assessment of the study parameters, the principal investigator defined, if necessary, a different investigational staff for the treatment handling and support and for the study assessments (masked) at each site, so also the comparisons vs timolol could be considered at least masked to the assessment

Arms

Are arms mutually exclusive?	Yes
Arm title	0.375% Bamosiran

Arm description:

Bamosiran, a 21-nucleotide siRNA for ocular administration (eye drops) once daily in each eye over a period of 28 days at a dose of 0.375%

Arm type	Experimental
Investigational medicinal product name	Bamosiran
Investigational medicinal product code	SYL040012
Other name	
Pharmaceutical forms	Eye drops
Routes of administration	Ophthalmic use

Dosage and administration details:

Bamosiran, a 21-nucleotide siRNA for ocular administration (eye drops) once daily in each eye over a period of 28 days

Arm title	0.75% Bamosiran

Arm description:

Bamosiran, a 21-nucleotide siRNA for ocular administration (eye drops) once daily in each eye over a period of 28 days at a dose of 0.75%

Arm type	Experimental
Investigational medicinal product name	Bamosiran
Investigational medicinal product code	SYL040012
Other name	
Pharmaceutical forms	Eye drops, solution
Routes of administration	Ophthalmic use

Dosage and administration details:

Bamosiran, a 21-nucleotide siRNA for ocular administration (eye drops) once daily in each eye over a period of 28 days

Arm title	1.125% Bamosiran

Arm description:

Bamosiran, a 21-nucleotide siRNA for ocular administration (eye drops) once daily in each eye over a period of 28 days at a dose of 1.125%

Arm type	Experimental
Investigational medicinal product name	Bamosiran
Investigational medicinal product code	SYL040012
Other name	
Pharmaceutical forms	Eye drops, solution
Routes of administration	Ophthalmic use

Dosage and administration details:

Bamosiran, a 21-nucleotide siRNA for ocular administration (eye drops) once daily in each eye over a period of 28 days

Arm title	1.5% Bamosiran

Arm description:

Bamosiran, a 21-nucleotide siRNA for ocular administration (eye drops) once daily in each eye over a period of 28 days at a dose of 1.5%

Arm type	Experimental
Investigational medicinal product name	Bamosiran
Investigational medicinal product code	SYL040012
Other name	
Pharmaceutical forms	Eye drops, solution
Routes of administration	Ophthalmic use

Dosage and administration details:

Bamosiran, a 21-nucleotide siRNA for ocular administration (eye drops) once daily in each eye over a period of 28 days

Arm title	0.5% Timolol

Arm description:

Timolol maleate for ocular administration (eye drops) bid in each eye over a period of 28 days at a dose of 0.5%.

Arm type	Active comparator
Investigational medicinal product name	Timolol maleate
Investigational medicinal product code	Timolol
Other name	
Pharmaceutical forms	Eye drops, solution
Routes of administration	Ophthalmic use

Dosage and administration details:

Timolol maleate for ocular administration (eye drops) bid in each eye over a period of 28 days at a dose of 0.5%.

Number of subjects in period 1[1]	0.375% Bamosiran	0.75% Bamosiran	1.125% Bamosiran
Started	37	40	37
Completed	36	38	35
Not completed	1	2	2
Consent withdrawn by subject	-	-	-
Red and purulent eye	-	1	-
Forbidden medication	-	-	1

IOP>35 mmHg	-	1	-
Protocol deviation	1	-	1

Number of subjects in period 1[1]	1.5% Bamosiran	0.5% Timolol
Started	33	37
Completed	33	36
Not completed	0	1
Consent withdrawn by subject	-	1
Red and purulent eye	-	-
Forbidden medication	-	-
IOP>35 mmHg	-	-
Protocol deviation	-	-

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: A total of 91 patients were finally not included in the study due to the following reasons: Inclusion/Exclusion criteria (86) and Withdrawal of consent (5).

Baseline characteristics

Reporting groups	
Reporting group title	0.375% Bamosiran
Reporting group description:	
Bamosiran, a 21-nucleotide siRNA for ocular administration (eye drops) once daily in each eye over a period of 28 days at a dose of 0.375%	
Reporting group title	0.75% Bamosiran
Reporting group description:	
Bamosiran, a 21-nucleotide siRNA for ocular administration (eye drops) once daily in each eye over a period of 28 days at a dose of 0.75%	
Reporting group title	1.125% Bamosiran
Reporting group description:	
Bamosiran, a 21-nucleotide siRNA for ocular administration (eye drops) once daily in each eye over a period of 28 days at a dose of 1.125%	
Reporting group title	1.5% Bamosiran
Reporting group description:	
Bamosiran, a 21-nucleotide siRNA for ocular administration (eye drops) once daily in each eye over a period of 28 days at a dose of 1.5%	
Reporting group title	0.5% Timolol
Reporting group description:	
Timolol maleate for ocular administration (eye drops) bid in each eye over a period of 28 days at a dose of 0.5%.	

Reporting group values	0.375% Bamosiran	0.75% Bamosiran	1.125% Bamosiran
Number of subjects	37	40	37
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	60.7	59.4	61.5
standard deviation	± 10.4	± 12.9	± 10.1
Gender categorical Units: Subjects			
Female	25	24	22
Male	12	16	15
Race Units: Subjects			
Asian	0	0	0
Black	4	4	2
White	33	36	35
Ethnicity Units: Subjects			
Hispanic or Latino	3	7	5
Non-Hispanic or Latino	34	33	32
Height Units: cm			
arithmetic mean	166	167	166
standard deviation	± 9	± 10	± 13

Weight			
Units: Kg			
arithmetic mean	81.7	77.8	78
standard deviation	± 18.7	± 18.2	± 19.6
BMI			
BMI=Body mass index			
Units: Kg/m2			
arithmetic mean	29.5	28.1	27.9
standard deviation	± 6.1	± 6.4	± 4.6
Body temperature			
Units: celsius temperature			
arithmetic mean	36.4	36.4	36.5
standard deviation	± 0.4	± 0.4	± 0.4
Gonioscopy test results			
Units: quadrants			
arithmetic mean	3.5	3.7	3.4
standard deviation	± 0.5	± 0.5	± 0.5

Reporting group values	1.5% Bamosiran	0.5% Timolol	Total
Number of subjects	33	37	184
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	62.4	60.2	
standard deviation	± 11.1	± 11.5	-
Gender categorical			
Units: Subjects			
Female	24	24	119
Male	9	13	65
Race			
Units: Subjects			
Asian	0	1	1
Black	5	3	18
White	28	33	165
Ethnicity			
Units: Subjects			
Hispanic or Latino	3	2	20
Non-Hispanic or Latino	30	35	164
Height			
Units: cm			
arithmetic mean	165	167	
standard deviation	± 11	± 10	-
Weight			
Units: Kg			
arithmetic mean	76.5	85.1	
standard deviation	± 17.4	± 19.1	-
BMI			
BMI=Body mass index			
Units: Kg/m2			

arithmetic mean	28.2	30.6	
standard deviation	± 5.9	± 7.2	-
Body temperature Units: celsius temperature			
arithmetic mean	36.4	36.5	
standard deviation	± 0.5	± 0.3	-
Gonioscopy test results Units: quadrants			
arithmetic mean	3.5	3.6	
standard deviation	± 0.5	± 0.5	-

End points

End points reporting groups	
Reporting group title	0.375% Bamosiran
Reporting group description:	
Bamosiran, a 21-nucleotide siRNA for ocular administration (eye drops) once daily in each eye over a period of 28 days at a dose of 0.375%	
Reporting group title	0.75% Bamosiran
Reporting group description:	
Bamosiran, a 21-nucleotide siRNA for ocular administration (eye drops) once daily in each eye over a period of 28 days at a dose of 0.75%	
Reporting group title	1.125% Bamosiran
Reporting group description:	
Bamosiran, a 21-nucleotide siRNA for ocular administration (eye drops) once daily in each eye over a period of 28 days at a dose of 1.125%	
Reporting group title	1.5% Bamosiran
Reporting group description:	
Bamosiran, a 21-nucleotide siRNA for ocular administration (eye drops) once daily in each eye over a period of 28 days at a dose of 1.5%	
Reporting group title	0.5% Timolol
Reporting group description:	
Timolol maleate for ocular administration (eye drops) bid in each eye over a period of 28 days at a dose of 0.5%.	

Primary: Changes in diurnal IOP after 28 days of treatment	
End point title	Changes in diurnal IOP after 28 days of treatment
End point description:	
End point type	Primary
End point timeframe:	
The absolute change in mean diurnal IOP after 28 days of treatment vs day 0. The mean diurnal IOP was assessed as the mean value of the assessments at 9h, 12h and 15h, both baseline and after 28 days of treatment comparing the four levels of concentration	

End point values	0.375% Bamosiran	0.75% Bamosiran	1.125% Bamosiran	1.5% Bamosiran
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	38	35	33
Units: mmHg				
arithmetic mean (standard deviation)	-2.4 (± 2.6)	-3.2 (± 2.9)	-3.1 (± 2.5)	-3.1 (± 3.2)

End point values	0.5% Timolol			
Subject group type	Reporting group			
Number of subjects analysed	35			
Units: mmHg				

arithmetic mean (standard deviation)	-6.1 (± 2.2)			

Attachments (see zip file)	Change IOP/Change IOP.bmp

Statistical analyses

Statistical analysis title	Differences between groups

Statistical analysis description:

All groups showed a reduction in the mean IOP at the end of the study, without reaching statistical significance when concentrations of bamosiran were compared. However, the concentration of bamosiran 0.75% showed the highest reduction at Day 28, followed close by the higher concentrations.

Comparison groups	1.125% Bamosiran v 0.375% Bamosiran v 1.5% Bamosiran v 0.5% Timolol v 0.75% Bamosiran
Number of subjects included in analysis	177
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 1 [2]
Method	ANCOVA

Notes:

[1] - Timolol 0.5% was statistically significant different when compared to the concentrations of bamosiran after 28 days of treatment (ANCOVA;p<0.001).
Timolol 0.5% vs Bamosiran 1.5% -2.967 95%CI(-4.235;-1.698) p=<0.001
Timolol 0.5% vs Bamosiran 1.125% -3.056 95%CI(-4.302;-1.810) p=<0.001
Timolol 0.5% vs Bamosiran 0.75% -2.910 95%CI(-4.134;-1.685) p=<0.001
Timolol 0.5% vs Bamosiran 0.375% -3.793 95%CI(-5.050;-2.536) p=<0.001
[2] - 1.5%-1.125%: -0.059 (-1.38;1.26) p=0.930
1.5%-0.75%: 0.065 (-1.23;1.36) p=0.921
1.5%-0.375%: -0.821 (-2.15;0.51) p=0.225
1.125%-0.75%: 0.124 (-1.15;1.40) p=0.847
1.125%-0.375%: -0.762 (-0.72;0.55) p=0.252
0.75%-0.375%: -0.886 (-2.17;0.40) p=0.17

Secondary: Changes in diurnal IOP after 14 days of treatment

End point title	Changes in diurnal IOP after 14 days of treatment

End point description:

End point type	Secondary

End point timeframe:

after 14 days of treatment (D14) versus baseline, assessed as the mean value of the assessments performed at 09:00, 12:00 and 15:00, both at baseline and after 14 days

End point values	0.375% Bamosiran	0.75% Bamosiran	1.125% Bamosiran	1.5% Bamosiran
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	38	35	33
Units: mmHg				
arithmetic mean (standard deviation)	-2.4 (± 2.6)	-2.9 (± 2.4)	-2.5 (± 2.1)	-2.4 (± 3.1)

End point values	0.5% Timolol			
Subject group type	Reporting group			
Number of subjects analysed	35			
Units: mmHg				
arithmetic mean (standard deviation)	-5.8 (± 1.9)			

Statistical analyses

Statistical analysis title	Differences between groups

Statistical analysis description:

No statistically significant differences were found among the concentrations of bamosiran with respect to the mean diurnal IOP after 14 days. Although no statistically significant differences were found, the concentration of 0.75% of bamosiran seems to show the highest percentage of decrease (12%) with respect to the other concentrations.

Comparison groups	0.375% Bamosiran v 0.75% Bamosiran v 1.125% Bamosiran v 1.5% Bamosiran v 0.5% Timolol
Number of subjects included in analysis	177
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 1 [4]
Method	ANCOVA

Notes:

[3] - Timolol 0.5% was statistically significant different when compared to the concentrations of bamosiran both after 14 days of treatment (ANCOVA; p<0.001).
Timolol 0.5% vs Bamosiran 1.5%: -3.394 95%CI(-4.557; -2.232) p=<0.001
Timolol 0.5% vs Bamosiran 1.125%: -3.363 95%CI(-4.505; -2.221) p=<0.001
Timolol 0.5% vs Bamosiran 0.75%: -2.865 95%CI(-3.987; -1.742) p=<0.001
Timolol 0.5% vs Bamosiran 0.375%: -3.513 95%CI(-4.665; -2.360) p=<0.001
[4] - 1.5%-1.125%: 0.043 (-1.17;1.26) p=0.944
1.5%-0.75%: 0.532 (-0.66;1.73) p=0.381
1.5%-0.375%: -0.122 (-1.35;1.11) p=0.845
1.125%-0.75%: 0.488 (-0.69;1.66) p=0.412
1.125%-0.375%: -0.165 (-1.37;1.04) p=0.788
0.75%-0.375%: -0.653 (-1.84;0.53) p=0.279

Secondary: GQL-15 Questionnaire at Day 29

End point title	GQL-15 Questionnaire at Day 29

End point description:

The GQL-15 is a 15-item, 4-domain tool. The instrument is based on the premise that perceived visual disability (dark adaptation, disability glare, outdoor mobility tasks and activities using peripheral vision) is significantly associated with binocular visual field loss.

End point type	Secondary

End point timeframe:

Patients were asked to rate their quality of life by means of the GQL-15 questionnaire at Day 29

End point values	0.375% Bamosiran	0.75% Bamosiran	1.125% Bamosiran	1.5% Bamosiran
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	38	35	33
Units: points				
arithmetic mean (standard deviation)				
GQL-15 Total Score	20 (± 8.28)	20.7 (± 7.68)	19.4 (± 6.34)	22 (± 9.65)
Central and near vision - Recognizing faces	1.3 (± 0.61)	1.2 (± 0.63)	1.3 (± 0.63)	1.4 (± 0.8)
Central and near vision - Reading newspapers	1.3 (± 0.78)	1.3 (± 0.67)	1.4 (± 0.88)	1.3 (± 0.54)
Peripheral vision - Seeing objects	1.2 (± 0.58)	1.2 (± 0.51)	1.1 (± 0.43)	1.2 (± 0.61)
Peripheral vision - Walking	1.4 (± 0.77)	1.4 (± 0.72)	1.4 (± 0.98)	1.6 (± 0.84)
Peripheral vision - Tripping	1.2 (± 0.47)	1.2 (± 0.43)	1.1 (± 0.37)	1.4 (± 0.79)
Peripheral vision - Judging distance	1.3 (± 0.55)	1.3 (± 0.71)	1.2 (± 0.38)	1.4 (± 0.74)
Peripheral vision - steps/stairs	1.3 (± 0.68)	1.4 (± 0.79)	1.1 (± 0.37)	1.4 (± 0.83)
Peripheral vision - Bumping	1.2 (± 0.52)	1.2 (± 0.47)	1.1 (± 0.42)	1.3 (± 0.68)
Dark adaptation - Walking	1.3 (± 0.83)	1.4 (± 0.76)	1.4 (± 0.69)	1.5 (± 1)
Dark adaptation - Seeing at night	1.4 (± 0.88)	1.7 (± 0.93)	1.4 (± 0.73)	1.8 (± 0.93)
Dark adaptation - Adjusting	1.4 (± 0.8)	1.5 (± 0.73)	1.5 (± 0.82)	1.5 (± 0.87)
Dark adaptation - Change dark/light	1.5 (± 0.7)	1.6 (± 0.75)	1.5 (± 0.7)	1.8 (± 0.83)
Dark adaptation - Finding	1.3 (± 0.62)	1.3 (± 0.69)	1.1 (± 0.36)	1.3 (± 0.69)
Outdoor mobility - Crossing the road	1.3 (± 0.81)	1.2 (± 0.58)	1.1 (± 0.24)	1.3 (± 0.76)

End point values	0.5% Timolol			
Subject group type	Reporting group			
Number of subjects analysed	35			
Units: points				
arithmetic mean (standard deviation)				
GQL-15 Total Score	18.7 (± 6.21)			
Central and near vision - Recognizing faces	1.2 (± 0.58)			
Central and near vision - Reading newspapers	1.4 (± 0.84)			
Peripheral vision - Seeing objects	1.1 (± 0.6)			
Peripheral vision - Walking	1.4 (± 0.77)			
Peripheral vision - Tripping	1.1 (± 0.4)			
Peripheral vision - Judging distance	1.2 (± 0.38)			
Peripheral vision - steps/stairs	1.1 (± 0.43)			
Peripheral vision - Bumping	1.1 (± 0.24)			
Dark adaptation - Walking	1.3 (± 0.61)			
Dark adaptation - Seeing at night	1.5 (± 0.74)			
Dark adaptation - Adjusting	1.4 (± 0.94)			
Dark adaptation - Change dark/light	1.4 (± 0.69)			
Dark adaptation - Finding	1.1 (± 0.28)			
Outdoor mobility - Crossing the road	1.1 (± 0.24)			

Statistical analyses

Statistical analysis title	Differences between groups
Comparison groups	0.375% Bamosiran v 0.75% Bamosiran v 1.125% Bamosiran v 1.5% Bamosiran v 0.5% Timolol
Number of subjects included in analysis	177
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	= 0.038 [6]
Method	ANCOVA

Notes:

[5] - No statistically significant differences between Timolol 0.5% group and all the bamosiran concentration groups in any of the domains throughout the study. However, statistically significant differences were found in favour of the bamosiran 1.5% group when compared to bamosiran 1.125% group in the peripheral vision score.
[6] - bamosiran 1.5% group compared to bamosiran 1.125% group

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Overall period	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups	
Reporting group title	0.375% Bamosiran
Reporting group description:	
Bamosiran, a 21-nucleotide siRNA for ocular administration (eye drops) once daily in each eye over a period of 28 days at doses of 0.375%	
Reporting group title	0.75% Bamosiran
Reporting group description:	
Bamosiran, a 21-nucleotide siRNA for ocular administration (eye drops) once daily in each eye over a period of 28 days at doses of 0.75%	
Reporting group title	1.125% Bamosiran
Reporting group description:	
Bamosiran, a 21-nucleotide siRNA for ocular administration (eye drops) once daily in each eye over a period of 28 days at doses of 1.125%	
Reporting group title	1.5% Bamosiran
Reporting group description:	
Bamosiran, a 21-nucleotide siRNA for ocular administration (eye drops) once daily in each eye over a period of 28 days at doses of 1.5%	
Reporting group title	0.5% Timolol
Reporting group description:	
Timolol maleate for ocular administration (eye drops) bid in each eye over a period of 28 days at a dose of 0.5%.	

Serious adverse events	0.375% Bamosiran	0.75% Bamosiran	1.125% Bamosiran
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 37 (0.00%)	0 / 40 (0.00%)	0 / 37 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	1.5% Bamosiran	0.5% Timolol	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 33 (0.00%)	0 / 37 (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: 5 %

Non-serious adverse events	0.375% Bamosiran	0.75% Bamosiran	1.125% Bamosiran
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 37 (43.24%)	18 / 40 (45.00%)	15 / 37 (40.54%)
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 37 (2.70%)	1 / 40 (2.50%)	3 / 37 (8.11%)
occurrences (all)	1	5	3
Eye disorders			
Conjunctival hyperaemia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 40 (0.00%)	3 / 37 (8.11%)
occurrences (all)	2	0	3
Eye pruritus			
subjects affected / exposed	2 / 37 (5.41%)	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	2	1	0
Lacrimation increased			
subjects affected / exposed	0 / 37 (0.00%)	2 / 40 (5.00%)	0 / 37 (0.00%)
occurrences (all)	0	2	0
Ocular discomfort			
subjects affected / exposed	0 / 37 (0.00%)	3 / 40 (7.50%)	0 / 37 (0.00%)
occurrences (all)	0	3	0
Vision blurred			
subjects affected / exposed	0 / 37 (0.00%)	2 / 40 (5.00%)	0 / 37 (0.00%)
occurrences (all)	0	2	0
Gastrointestinal disorders			
Toothache			
subjects affected / exposed	0 / 37 (0.00%)	2 / 40 (5.00%)	0 / 37 (0.00%)
occurrences (all)	0	2	0
Instillation site pain			
subjects affected / exposed	0 / 37 (0.00%)	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 37 (5.41%)	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	2	0	1

Non-serious adverse events	1.5% Bamosiran	0.5% Timolol	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 33 (30.30%)	9 / 37 (24.32%)	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 33 (3.03%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Conjunctival hyperaemia			
subjects affected / exposed	2 / 33 (6.06%)	1 / 37 (2.70%)	
occurrences (all)	2	1	
Eye pruritus			
subjects affected / exposed	0 / 33 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Lacrimation increased			
subjects affected / exposed	0 / 33 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Ocular discomfort			
subjects affected / exposed	1 / 33 (3.03%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Vision blurred			
subjects affected / exposed	0 / 33 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Toothache			
subjects affected / exposed	0 / 33 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Instillation site pain			
subjects affected / exposed	0 / 33 (0.00%)	2 / 37 (5.41%)	
occurrences (all)	0	2	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 33 (3.03%)	0 / 37 (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