Clinical trial results:
A 2-year, Multicenter, Double-masked, Randomized, Parallel Study of the Safety of LUMIGAN® 0.1 mg/mL Compared with LUMIGAN® 0.3 mg/mL in Patients with Glaucoma or Ocular Hypertension

Summary

EudraCT number	2010-023917-68
Trial protocol	DE HU GB ES CZ BE IT
Global end of trial date	06 December 2016

Results information

Result version number	v1 (current)
This version publication date	20 January 2018
First version publication date	20 January 2018

Trial information

Trial identification

Sponsor protocol code	192024-054

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01298700
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Allergan, Inc
Sponsor organisation address	Marlow International, The Parkway, Marlow, Buckinghamshire, United Kingdom, SL7 1YL
Public contact	Therapeutic Area Head, Allergan, Inc, +1 7142464500,
Scientific contact	Therapeutic Area Head, Allergan, Inc, +1 7142464500, clinicaltrials@allergan.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	06 December 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 December 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study will evaluate the long-term safety of bimatoprost 0.01% ophthalmic solution compared with bimatoprost 0.03% ophthalmic solution in patients with glaucoma or ocular hypertension.

Protection of trial subjects:

All participants were required to read and sign an informed consent form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 May 2011
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	Belgium: 153
Country: Number of subjects enrolled	Czech Republic: 51
Country: Number of subjects enrolled	Germany: 57
Country: Number of subjects enrolled	Spain: 193
Country: Number of subjects enrolled	France: 15
Country: Number of subjects enrolled	United Kingdom: 117
Country: Number of subjects enrolled	Hungary: 33
Country: Number of subjects enrolled	Israel: 60
Country: Number of subjects enrolled	Italy: 57
Country: Number of subjects enrolled	Poland: 70
Worldwide total number of subjects	806
EEA total number of subjects	746

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	441
From 65 to 84 years	359
85 years and over	6

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	806
Number of subjects completed	798

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Did not Receive Treatment: 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	Investigator, Monitor, Subject, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Bimatoprost 0.01% Ophthalmic Solution

Arm description:

One drop of bimatoprost 0.01% ophthalmic solution instilled to each eye, once daily in the evening for 2 years.

Arm type	Experimental
Investigational medicinal product name	Bimatoprost 0.01% Ophthalmic Solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops, solution
Routes of administration	Ophthalmic use

Dosage and administration details:

1 drop in each eye once daily in the evening.

Arm title	Bimatoprost 0.03% Ophthalmic Solution

Arm description:

One drop of bimatoprost 0.03% ophthalmic solution instilled to each eye, once daily in the evening for 2 years.

Arm type	Active comparator
Investigational medicinal product name	Bimatoprost 0.03% Ophthalmic Solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops, solution
Routes of administration	Ophthalmic use

Dosage and administration details:

1 drop in each eye once daily in the evening.

Number of subjects in period 1[1]	Bimatoprost 0.01% Ophthalmic Solution	Bimatoprost 0.03% Ophthalmic Solution
Started	400	398
Completed	302	303
Not completed	98	95
Consent withdrawn by subject	12	9
Adverse event, non-fatal	50	51
Lost to follow-up	5	2
Other Miscellaneous Reasons	16	15
Lack of efficacy	9	14
Protocol deviation	6	4

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: Baseline Period is based on the Safety Population that included all participants who received at least one dose of study drug.

Baseline characteristics

Reporting groups	
Reporting group title	Bimatoprost 0.01% Ophthalmic Solution
Reporting group description:	
One drop of bimatoprost 0.01% ophthalmic solution instilled to each eye, once daily in the evening for 2 years.	
Reporting group title	Bimatoprost 0.03% Ophthalmic Solution
Reporting group description:	
One drop of bimatoprost 0.03% ophthalmic solution instilled to each eye, once daily in the evening for 2 years.	

Reporting group values	Bimatoprost 0.01% Ophthalmic Solution	Bimatoprost 0.03% Ophthalmic Solution	Total
Number of subjects	400	398	798
Age Categorical Units: Subjects			
< 45 years	22	26	48
≥ 45 years to ≤ 65 years	216	211	427
> 65 years	162	161	323
Age Continuous Units: years			
arithmetic mean	62.7	62.2	
standard deviation	± 11.0	± 11.5	-
Gender, Male/Female Units: Subjects			
Female	197	187	384
Male	203	211	414

End points

End points reporting groups

Reporting group title	Bimatoprost 0.01% Ophthalmic Solution
Reporting group description:	
One drop of bimatoprost 0.01% ophthalmic solution instilled to each eye, once daily in the evening for 2 years.	
Reporting group title	Bimatoprost 0.03% Ophthalmic Solution
Reporting group description:	
One drop of bimatoprost 0.03% ophthalmic solution instilled to each eye, once daily in the evening for 2 years.	

Primary: Percentage of Participants Reporting One or More Treatment-Related Ocular Surface Adverse Events

End point title	Percentage of Participants Reporting One or More Treatment-Related Ocular Surface Adverse Events
End point description:	
An adverse event (AE) was defined as any untoward medical occurrence in a patient or clinical investigation participant administered a pharmaceutical product and that did not necessarily have a causal relationship with this treatment. An AE could therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product. The percentage of participants with ocular (eye) surface AEs deemed related to treatment by the investigator are reported.	
End point type	Primary
End point timeframe:	
24 Months	

End point values	Bimatoprost 0.01% Ophthalmic Solution	Bimatoprost 0.03% Ophthalmic Solution		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	400	398		
Units: percentage of participants				
number (not applicable)	33.3	37.7		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Bimatoprost 0.01% Ophthalmic Solution v Bimatoprost 0.03% Ophthalmic Solution

Number of subjects included in analysis	798
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.148 [1]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Mean difference (final values)
Point estimate	-4.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11
upper limit	1.9

Notes:

[1] - P-value was stratified by baseline prostaglandin analogue (PGA) treatment(yes/no) and by baseline active ocular surface finding (present/absent).

Secondary: Percentage of Participants Reporting One or More Treatment-Related Ocular Surface Adverse Events excluding "Conjunctival Hyperemia"

End point title	Percentage of Participants Reporting One or More Treatment-Related Ocular Surface Adverse Events excluding "Conjunctival Hyperemia"

End point description:

An adverse event (AE) was defined as any untoward medical occurrence in a patient or clinical investigation participant administered a pharmaceutical product and that did not necessarily have a causal relationship with this treatment. An AE could therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product. The percentage of participants with ocular (eye) surface AEs deemed related to treatment by the investigator excluding AEs with the preferred term Conjunctival hyperemia are reported.

End point type	Secondary

End point timeframe:

24 Months

End point values	Bimatoprost 0.01% Ophthalmic Solution	Bimatoprost 0.03% Ophthalmic Solution		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	400	398		
Units: percentage of participants				
number (not applicable)	26.0	29.6		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

24 Months

Adverse event reporting additional description:

Safety Population, all participants who received at least one dose of study drug, was used to determine the number of participants at risk for Serious and Non-serious Adverse Events.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Bimatoprost 0.01% Ophthalmic Solution

Reporting group description:

One drop of bimatoprost 0.01% ophthalmic solution instilled to each eye, once daily in the evening for 2 years.

Reporting group title	Bimatoprost 0.03% Ophthalmic Solution

Reporting group description:

One drop of bimatoprost 0.03% ophthalmic solution instilled to each eye, once daily in the evening for 2 years.

Serious adverse events	Bimatoprost 0.01% Ophthalmic Solution	Bimatoprost 0.03% Ophthalmic Solution	
Total subjects affected by serious adverse events			
subjects affected / exposed	45 / 400 (11.25%)	40 / 398 (10.05%)	
number of deaths (all causes)	4	2	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung neoplasm malignant			
subjects affected / exposed	1 / 400 (0.25%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hodgkin’s disease			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Laryngeal squamous cell carcinoma			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Lip squamous cell carcinoma			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningioma benign			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cancer			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tubular breast carcinoma			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			
subjects affected / exposed	0 / 400 (0.00%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer metastatic			
subjects affected / exposed	0 / 400 (0.00%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric cancer			

subjects affected / exposed	0 / 400 (0.00%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to central nervous system			
subjects affected / exposed	0 / 400 (0.00%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to lung			
subjects affected / exposed	0 / 400 (0.00%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal carcinoma			
subjects affected / exposed	0 / 400 (0.00%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Arteriosclerosis			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Inguinal hernia repair			
subjects affected / exposed	0 / 400 (0.00%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			

subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Catheter site inflammation			
subjects affected / exposed	0 / 400 (0.00%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 400 (0.00%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Vaginal prolapse			
subjects affected / exposed[1]	1 / 197 (0.51%)	0 / 187 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign prostatic hyperplasia			
subjects affected / exposed[2]	0 / 203 (0.00%)	1 / 211 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pneumothorax			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute pulmonary oedema			
subjects affected / exposed	0 / 400 (0.00%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sleep apnoea syndrome			

subjects affected / exposed	0 / 400 (0.00%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Completed suicide			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Investigations			
Intraocular pressure fluctuation			
subjects affected / exposed	4 / 400 (1.00%)	2 / 398 (0.50%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intraocular pressure increased			
subjects affected / exposed	1 / 400 (0.25%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clavicle fracture			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Limb crushing injury			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary contusion			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Upper limb fracture			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture			
subjects affected / exposed	0 / 400 (0.00%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			

subjects affected / exposed	0 / 400 (0.00%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	0 / 400 (0.00%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	0 / 400 (0.00%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urostomy complication			
subjects affected / exposed	0 / 400 (0.00%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture			
subjects affected / exposed	0 / 400 (0.00%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	2 / 400 (0.50%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	2 / 400 (0.50%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute coronary syndrome			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery thrombosis			

subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	0 / 400 (0.00%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	2 / 400 (0.50%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cervical radiculopathy			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocephalus			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	0 / 400 (0.00%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Headache			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 400 (0.00%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Partial seizures			
subjects affected / exposed	0 / 400 (0.00%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 400 (0.25%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	0 / 400 (0.00%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	2 / 400 (0.50%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angle closure glaucoma			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cataract cortical			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macular hole			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal detachment			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Vitreous adhesions			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glaucoma			
subjects affected / exposed	0 / 400 (0.00%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Optic neuropathy			
subjects affected / exposed	0 / 400 (0.00%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Anal haemorrhage			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal haematoma			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	0 / 400 (0.00%)	2 / 398 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Barrett’s oesophagus			
subjects affected / exposed	0 / 400 (0.00%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal perforation			

subjects affected / exposed	0 / 400 (0.00%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			
subjects affected / exposed	0 / 400 (0.00%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis relapsing			
subjects affected / exposed	0 / 400 (0.00%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritoneal haematoma			
subjects affected / exposed	0 / 400 (0.00%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cirrhosis			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis acute			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	0 / 400 (0.00%)	2 / 398 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			

subjects affected / exposed	0 / 400 (0.00%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrotic syndrome			
subjects affected / exposed	0 / 400 (0.00%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	0 / 400 (0.00%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder prolapse			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	1 / 400 (0.25%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar spinal stenosis			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal disorder			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthropathy			
subjects affected / exposed	0 / 400 (0.00%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infections and infestations			
Anal abscess			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonsillar abscess			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 400 (0.00%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Echinococciasis			
subjects affected / exposed	0 / 400 (0.00%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 400 (0.00%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vestibular neuronitis			
subjects affected / exposed	0 / 400 (0.00%)	1 / 398 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			

Hypocalcaemia			
subjects affected / exposed	1 / 400 (0.25%)	0 / 398 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Adverse Event is gender specific and includes only female participants.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Adverse Event is gender specific and includes only male participants.

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

Non-serious adverse events	Bimatoprost 0.01% Ophthalmic Solution	Bimatoprost 0.03% Ophthalmic Solution	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	167 / 400 (41.75%)	186 / 398 (46.73%)	
Eye disorders			
Blepharitis			
subjects affected / exposed	14 / 400 (3.50%)	23 / 398 (5.78%)	
occurrences (all)	30	44	
Cataract			
subjects affected / exposed	20 / 400 (5.00%)	24 / 398 (6.03%)	
occurrences (all)	33	37	
Conjunctival hyperaemia			
subjects affected / exposed	80 / 400 (20.00%)	90 / 398 (22.61%)	
occurrences (all)	153	195	
Dry eye			
subjects affected / exposed	36 / 400 (9.00%)	42 / 398 (10.55%)	
occurrences (all)	68	81	
Eye pain			
subjects affected / exposed	21 / 400 (5.25%)	20 / 398 (5.03%)	
occurrences (all)	40	37	
Foreign body sensation in eyes			
subjects affected / exposed	11 / 400 (2.75%)	21 / 398 (5.28%)	
occurrences (all)	18	37	
Punctate keratitis			
subjects affected / exposed	22 / 400 (5.50%)	30 / 398 (7.54%)	
occurrences (all)	44	51	
Infections and infestations			

Influenza subjects affected / exposed occurrences (all)	26 / 400 (6.50%) 30	21 / 398 (5.28%) 21	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 November 2010	Amendment 1: The protocol was amended to change the procedure for measuring Tear Breakup Time (TBUT) due to the lack of wide availability of the originally planned test material, and to allow the use of an additional method for corneal pachymetry. Other changes were made to enhance consistency and clarity throughout the document, and to provide additional details about procedures. The amendment was implemented prior to enrollment of any patients into the study.
11 March 2013	Amendment 2: The protocol was amended to provide clarity for treatment randomization and stratification by using a flow diagram rather than the text description. Other changes were made to enhance consistency and clarity throughout the document, and to provide additional details about VF examination. In addition, the estimated number of sites was updated from 20-25 to 50 to reflect the current plans for study enrollment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported