Clinical trial results:
Bimatoprost in the Treatment of Eyelash Hypotrichosis

Summary

EudraCT number	2012-003007-35
Trial protocol	GB SE
Global end of trial date	17 March 2014

Results information

Result version number	v1 (current)
This version publication date	26 March 2016
First version publication date	26 March 2016

Trial information

Trial identification

Sponsor protocol code	192024-046

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01698554
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Allergan Limited
Sponsor organisation address	Allergan Limited Marlow International the Parkway, Marlow, United Kingdom, SL7 1YL
Public contact	Allergan Limited EU Regulatory Dept, Allergan Limited, +44 1628 494444, ml-eu_reg_affairs@allergan.com
Scientific contact	Allergan Limited EU Regulatory Dept, Allergan Limited, +44 1628 494444, ml-eu_reg_affairs@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	20 August 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 March 2014
Global end of trial reached?	Yes
Global end of trial date	17 March 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study evaluated the safety and efficacy of bimatoprost solution formulation A compared with bimatoprost solution 0.03% (LATISSE®) and vehicle in the treatment of eyelash hypotrichosis (inadequate eyelashes).

Protection of trial subjects:

All study participants were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 November 2012
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	Russian Federation: 20
Country: Number of subjects enrolled	Sweden: 20
Country: Number of subjects enrolled	United Kingdom: 31
Country: Number of subjects enrolled	United States: 393
Worldwide total number of subjects	464
EEA total number of subjects	51

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)	393
From 65 to 84 years	71

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study took place at 26 centers in the United States (US), United Kingdom and Sweden (members of the European Union [EU]) and the Russia Federation from 15 November 2012 to 17 March 2014.

Pre-assignment

Screening details:

Participants with eyelash hypotrichosis were enrolled in one of 4 treatment groups (2:2:1:1): bimatoprost formulation A solution, bimatoprost solution 0.03 %, vehicle of bimatoprost formulation A solution or vehicle of bimatoprost solution 0.03 %

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, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	bimatoprost formulation A solution

Arm description:

Bimatoprost formulation A solution single-dose vial applied to the upper eyelid of both eyes once daily for 4 months using the supplied applicator.

Arm type	Experimental
Investigational medicinal product name	bimatoprost formulation A solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Cutaneous use

Dosage and administration details:

Solution applied to the upper eyelid of both eyes.

Arm title	bimatoprost solution 0.03 %

Arm description:

Bimatoprost solution 0.03 % (LATISSE®) multi-dose vial applied to the upper eyelid of both eyes once daily for 4 months using the supplied applicator.

Arm type	Active comparator
Investigational medicinal product name	bimatoprost solution 0.03 %
Investigational medicinal product code	
Other name	LATISSE®
Pharmaceutical forms	Cutaneous solution
Routes of administration	Cutaneous use

Dosage and administration details:

Solution applied to the upper eyelid of each eye.

Arm title	vehicle of bimatoprost formulation A solution

Arm description:

Vehicle of bimatoprost formulation A solution single-dose vial applied to the upper eyelid of both eyes once daily for 4 months using the supplied applicator.

Arm type	Placebo

Investigational medicinal product name	vehicle of bimatoprost formulation A solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Cutaneous use

Dosage and administration details:

Solution applied to the upper eyelid of both eyes.

Arm title	vehicle of bimatoprost solution 0.03 %

Arm description:

Vehicle of bimatoprost solution 0.03 % multi-dose vial applied to the upper eyelid of both eyes once daily for 4 months using the supplied applicator.

Arm type	Placebo
Investigational medicinal product name	vehicle of bimatoprost solution 0.03 %
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Cutaneous use

Dosage and administration details:

Solution applied to the upper eyelid of both eyes.

Number of subjects in period 1	bimatoprost formulation A solution	bimatoprost solution 0.03 %	vehicle of bimatoprost formulation A solution
Started	153	157	75
Completed	147	147	73
Not completed	6	10	2
Adverse event, non-fatal	2	5	-
Personal Reasons	-	5	1
Lost to follow-up	1	-	-
Other Miscellaneous Reasons	1	-	-
Protocol deviation	2	-	1

Number of subjects in period 1	vehicle of bimatoprost solution 0.03 %
Started	79
Completed	77
Not completed	2
Adverse event, non-fatal	1
Personal Reasons	1
Lost to follow-up	-
Other Miscellaneous Reasons	-
Protocol deviation	-

Baseline characteristics

Reporting groups	
Reporting group title	bimatoprost formulation A solution
Reporting group description:	
Bimatoprost formulation A solution single-dose vial applied to the upper eyelid of both eyes once daily for 4 months using the supplied applicator.	
Reporting group title	bimatoprost solution 0.03 %
Reporting group description:	
Bimatoprost solution 0.03 % (LATISSE®) multi-dose vial applied to the upper eyelid of both eyes once daily for 4 months using the supplied applicator.	
Reporting group title	vehicle of bimatoprost formulation A solution
Reporting group description:	
Vehicle of bimatoprost formulation A solution single-dose vial applied to the upper eyelid of both eyes once daily for 4 months using the supplied applicator.	
Reporting group title	vehicle of bimatoprost solution 0.03 %
Reporting group description:	
Vehicle of bimatoprost solution 0.03 % multi-dose vial applied to the upper eyelid of both eyes once daily for 4 months using the supplied applicator.	

Reporting group values	bimatoprost formulation A solution	bimatoprost solution 0.03 %	vehicle of bimatoprost formulation A solution
Number of subjects	153	157	75
Age categorical			
Units: Subjects			
<45 years	27	34	16
45 to 65 years	104	106	47
>65 years	22	17	12
Age continuous			
Units: years			
arithmetic mean	53.9	52.5	54.1
standard deviation	± 11.8	± 11.01	± 12.86
Gender, Male/Female			
Units: Participants			
Female	150	153	75
Male	3	4	0

Reporting group values	vehicle of bimatoprost solution 0.03 %	Total	
Number of subjects	79	464	
Age categorical			
Units: Subjects			
<45 years	15	92	
45 to 65 years	55	312	
>65 years	9	60	
Age continuous			
Units: years			
arithmetic mean	52.6		
standard deviation	± 12.22	-	

Gender, Male/Female Units: Participants			
Female	79	457	
Male	0	7	

End points

End points reporting groups

Reporting group title	bimatoprost formulation A solution
Reporting group description:	
Bimatoprost formulation A solution single-dose vial applied to the upper eyelid of both eyes once daily for 4 months using the supplied applicator.	
Reporting group title	bimatoprost solution 0.03 %
Reporting group description:	
Bimatoprost solution 0.03 % (LATISSE®) multi-dose vial applied to the upper eyelid of both eyes once daily for 4 months using the supplied applicator.	
Reporting group title	vehicle of bimatoprost formulation A solution
Reporting group description:	
Vehicle of bimatoprost formulation A solution single-dose vial applied to the upper eyelid of both eyes once daily for 4 months using the supplied applicator.	
Reporting group title	vehicle of bimatoprost solution 0.03 %
Reporting group description:	
Vehicle of bimatoprost solution 0.03 % multi-dose vial applied to the upper eyelid of both eyes once daily for 4 months using the supplied applicator.	

Primary: Percentage of Participants with at Least a 1-Grade Increase (Improvement) from Baseline in the Investigator's Assessment of Overall Eyelash Prominence (GEA)

End point title	Percentage of Participants with at Least a 1-Grade Increase (Improvement) from Baseline in the Investigator's Assessment of Overall Eyelash Prominence (GEA)[1]
End point description:	
The investigator evaluated the overall eyelash prominence in both eyes using the GEA 4-point scale: 1= minimal, 2= moderate, 3= marked and 4= very marked. A 1-grade improvement in the GEA score from Baseline indicated improvement.	
End point type	Primary
End point timeframe:	
Baseline, Month 4	

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: No Statistical Analysis is reported for this outcome measure

End point values	bimatoprost formulation A solution	bimatoprost solution 0.03 %	vehicle of bimatoprost formulation A solution	vehicle of bimatoprost solution 0.03 %
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	153	157	75	79
Units: percentage of participants				
number (not applicable)	82.4	83.4	24	20.3

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Upper Eyelash Length as Measured Using Digital Image Analysis (DIA)

End point title	Change from Baseline in Upper Eyelash Length as Measured Using Digital Image Analysis (DIA)

End point description:

Photographs were taken of the eyelashes and assessed using DIA. Length was measured in millimeters (mm). Data from both eyes were averaged for each participant for analysis. A positive change from Baseline indicated longer length (improvement)

End point type	Secondary

End point timeframe:

Baseline, Month 4

End point values	bimatoprost formulation A solution	bimatoprost solution 0.03 %	vehicle of bimatoprost formulation A solution	vehicle of bimatoprost solution 0.03 %
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	152	157	75	79
Units: mm				
arithmetic mean (standard deviation)				
Baseline	6.09 (± 0.856)	5.97 (± 0.789)	5.9 (± 0.812)	6.03 (± 0.852)
Change from Baseline at Month 4	1.61 (± 0.888)	1.62 (± 0.955)	0.08 (± 0.442)	0.05 (± 0.482)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Upper Eyelash Thickness/Fullness as Measured Using DIA

End point title	Change from Baseline in Upper Eyelash Thickness/Fullness as Measured Using DIA

End point description:

Photographs were taken of the eyelashes and assessed using DIA. Eyelash thickness (fullness) was measured in millimeters squared (mm^2). Data from both eyes were averaged for each participant for analysis. A positive change from Baseline indicated fuller eyelashes (improvement).

End point type	Secondary

End point timeframe:

Baseline, Month 4

End point values	bimatoprost formulation A solution	bimatoprost solution 0.03 %	vehicle of bimatoprost formulation A solution	vehicle of bimatoprost solution 0.03 %
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	151	156	74	78
Units: mm^2				
arithmetic mean (standard deviation)				
Baseline	0.85 (± 0.4)	0.82 (± 0.404)	0.76 (± 0.333)	0.81 (± 0.38)
Change from Baseline At Month 4	0.58 (± 0.359)	0.64 (± 0.392)	0.02 (± 0.196)	0.03 (± 0.237)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Upper Eyelash Intensity (Darkness) as Measured Using DIA

End point title	Change from Baseline in Upper Eyelash Intensity (Darkness) as Measured Using DIA

End point description:

Photographs were taken of the eyelashes and assessed using DIA. Eyelash darkness (intensity) was measured in both eyes and averaged for analysis using a scale where 0=black and 255=white. A negative change from Baseline indicated darker eyelashes (improvement).

End point type	Secondary

End point timeframe:

Baseline, Month 4

End point values	bimatoprost formulation A solution	bimatoprost solution 0.03 %	vehicle of bimatoprost formulation A solution	vehicle of bimatoprost solution 0.03 %
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	151	156	74	78
Units: intensity units				
arithmetic mean (standard deviation)				
Baseline	145.33 (± 24.024)	147.39 (± 24.934)	147.44 (± 22.323)	145.79 (± 26.67)
Change from Baseline at Month 4	-23.98 (± 15.719)	-24.78 (± 16.417)	-2.78 (± 10.443)	0.17 (± 10.065)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Satisfied or Very Satisfied in the Patient's Assessment of Overall Eyelash Satisfaction as Measured by the Eyelash Satisfaction Questionnaire (ESQ-9)

End point title	Percentage of Participants Satisfied or Very Satisfied in the

	Patient's Assessment of Overall Eyelash Satisfaction as Measured by the Eyelash Satisfaction Questionnaire (ESQ-9)

End point description:

Participants rated their overall eyelash satisfaction by answering Eyelash Satisfaction Questionnaire (ESQ-9) question #3: "Overall, how satisfied are you with your eyelashes?" using a 5-point scale: 1= very unsatisfied (worst), 2= unsatisfied, 3= neutral, 4= satisfied or 5= very satisfied (best). The percentage of participants who rated their satisfaction as satisfied or very satisfied at Month 4 is reported.

End point type	Secondary

End point timeframe:

Month 4

End point values	bimatoprost formulation A solution	bimatoprost solution 0.03 %	vehicle of bimatoprost formulation A solution	vehicle of bimatoprost solution 0.03 %
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	153	157	75	79
Units: percentage of participants				
number (not applicable)	71.2	65	28	20.3

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to 157 Days	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups	
Reporting group title	bimatoprost formulation A solution
Reporting group description:	
Bimatoprost formulation A solution single-dose vial applied to the upper eyelid of both eyes once daily for 4 months using the supplied applicator.	
Reporting group title	vehicle of bimatoprost formulation A solution
Reporting group description:	
Vehicle of bimatoprost formulation A solution single-dose vial applied to the upper eyelid of both eyes once daily for 4 months using the supplied applicator.	
Reporting group title	vehicle of bimatoprost solution 0.03 %
Reporting group description:	
Vehicle of bimatoprost solution 0.03 % multi-dose vial applied to the upper eyelid of both eyes once daily for 4 months using the supplied applicator.	
Reporting group title	bimatoprost solution 0.03 %
Reporting group description:	
Bimatoprost solution 0.03 % (LATISSE®) multi-dose vial applied to the upper eyelid of both eyes once daily for 4 months using the supplied applicator.	

Serious adverse events	bimatoprost formulation A solution	vehicle of bimatoprost formulation A solution	vehicle of bimatoprost solution 0.03 %
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 153 (0.00%)	1 / 75 (1.33%)	1 / 79 (1.27%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 153 (0.00%)	0 / 75 (0.00%)	0 / 79 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Hiatus hernia			

subjects affected / exposed	0 / 153 (0.00%)	0 / 75 (0.00%)	0 / 79 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Menorrhagia	Additional description: female population		
subjects affected / exposed	0 / 153 (0.00%)	0 / 75 (0.00%)	1 / 79 (1.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 153 (0.00%)	1 / 75 (1.33%)	0 / 79 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 153 (0.00%)	0 / 75 (0.00%)	0 / 79 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis viral			
subjects affected / exposed	0 / 153 (0.00%)	0 / 75 (0.00%)	0 / 79 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 153 (0.00%)	0 / 75 (0.00%)	0 / 79 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	bimatoprost solution 0.03 %		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 157 (3.18%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			

subjects affected / exposed	1 / 157 (0.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Hiatus hernia			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Menorrhagia	Additional description: female population		
subjects affected / exposed	0 / 157 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 157 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Meningitis viral			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 157 (0.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	bimatoprost formulation A solution	vehicle of bimatoprost formulation A solution	vehicle of bimatoprost solution 0.03 %
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 153 (4.58%)	3 / 75 (4.00%)	3 / 79 (3.80%)
Investigations			
Intraocular pressure decreased			
subjects affected / exposed	7 / 153 (4.58%)	3 / 75 (4.00%)	3 / 79 (3.80%)
occurrences (all)	9	3	3

Non-serious adverse events	bimatoprost solution 0.03 %		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 157 (5.10%)		
Investigations			
Intraocular pressure decreased			
subjects affected / exposed	8 / 157 (5.10%)		
occurrences (all)	10		

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