Clinical trial results:
Treatment of functional EPIFORA with Botulinum Toxin A (BoNTA) versus lateral tarsal strip (LTS) surgery.

Summary

EudraCT number	2016-000740-34
Trial protocol	ES
Global end of trial date	05 February 2019

Results information

Result version number	v1 (current)
This version publication date	30 June 2022
First version publication date	30 June 2022

Trial information

Trial identification

Sponsor protocol code	EPITBA12

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Hospital Universitario de Fuenlabrada
Sponsor organisation address	Camino del Molino nº 2, Fuenlabrada, Madrid, Spain, 28942
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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	25 February 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 February 2019
Global end of trial reached?	Yes
Global end of trial date	05 February 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Compare through the Munk Scale the efficacy of Botulinum Toxin A (IncobotulinuntoxinA) versus lateral tarsal strip, which is the usual surgery technique to treat the functional epifora, after 6 weeks of treatment.

Protection of trial subjects:

The study was conducted in accordance with the tenets of Declaration of the Helsinki and following the legal regulation on clinical trials in Spain. Ethics approval was obtained from the Fuenlabrada University Hospital (Madrid) Institutional Review Board and the study was registered with the clinical trial registration number EudraCT 2016-000740-34.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 May 2017
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: 30
Worldwide total number of subjects	30
EEA total number of subjects	30

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)	15
From 65 to 84 years	15
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

30 patients were recruited between November 2017 and July 2018. 15 were randomized to Botulinum Toxin A (BoNTA) and 15 to lateral tarsal strip (LTS). After randomization, 5 patients withdrew their consent. Therefore, 12 patients were treated with BoNTA and 13 with a LTS. One BoNTA-treated patient dropped out of the study due to a lost to follow-up.

Pre-assignment

Screening details:

Inclusion criteria
- Patients older than 18 years.
- Epiphora with patent tear duct with a minimum value of grade 3 on the Munk scale.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Botulinum Toxin A (BoNTA)

Arm description:

Patients assigned to the BoNTA treatment group received a transconjunctival injection of BoNTA (XEOMIN®, Merz) into the palpebral lobe of the lacrimal gland of the affected eye. BoNTA was reconstituted with sterile saline at a concentration of 50 U in 0.5 ml. The injections were always performed by the same doctor. BoNTA treatment was not repeated in any patient during the study.

Arm type	Experimental
Investigational medicinal product name	Botulinum toxin A injection (XEOMIN®, Merz)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Conjunctival use

Dosage and administration details:

Injection of botulinum toxin A (XEOMIN®, Merz) in the palpebral lobe of the lacrimal gland of the affected eye. BoNTA was reconstituted with sterile saline at a concentration of 50 U in 0.5 ml. The injections were always performed by the same doctor after administering topical anesthesia to the patient. To deliver BoNTA treatment, the lateral upper eyelid will be manually everted while the patient looks down and away from the lacrimal gland. This maneuver will expose the palpebral lobe of the lacrimal gland where the BoNTA treatment will be injected. This treatment was not repeated in any patient during the study.

Arm title	Lateral tarsal strip (LTS)

Arm description:

Lateral tarsal strip (LTS) surgery. It will always be performed by the same surgeon. Steps to follow:
- Lateral canthotomy with Westcott scissors. Dissection of the orbicularis over the lateral orbital rim to visualize the periosteum.
- Cantholysis: cutting of the lower branch of the lateral canthal tendon, separating it from the orbital rim.
- Formation of the strip.
- Shortening of the strip.
- Reinsertion of the strip to the inner face of the lateral orbital rim.

Arm type	Surgery

No investigational medicinal product assigned in this arm

Number of subjects in period 1[1]	Botulinum Toxin A (BoNTA)	Lateral tarsal strip (LTS)
Started	12	13
Completed	11	13
Not completed	1	0
Lost to follow-up	1	-

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: After randomization, 5 patients withdrew their consent.

Baseline characteristics

Reporting groups	
Reporting group title	Botulinum Toxin A (BoNTA)
Reporting group description:	
Patients assigned to the BoNTA treatment group received a transconjunctival injection of BoNTA (XEOMIN®, Merz) into the palpebral lobe of the lacrimal gland of the affected eye. BoNTA was reconstituted with sterile saline at a concentration of 50 U in 0.5 ml. The injections were always performed by the same doctor. BoNTA treatment was not repeated in any patient during the study.	
Reporting group title	Lateral tarsal strip (LTS)
Reporting group description:	
Lateral tarsal strip (LTS) surgery. It will always be performed by the same surgeon. Steps to follow: - Lateral canthotomy with Westcott scissors. Dissection of the orbicularis over the lateral orbital rim to visualize the periosteum. - Cantholysis: cutting of the lower branch of the lateral canthal tendon, separating it from the orbital rim. - Formation of the strip. - Shortening of the strip. - Reinsertion of the strip to the inner face of the lateral orbital rim.	

Reporting group values	Botulinum Toxin A (BoNTA)	Lateral tarsal strip (LTS)	Total
Number of subjects	12	13	25
Age categorical Units: Subjects			
Adults (18-64 years)	7	6	13
From 65-84 years	5	7	12
Age continuous Units: years			
arithmetic mean	61.50	62.23	
standard deviation	± 9.68	± 13.02	-
Gender categorical Units: Subjects			
Female	12	10	22
Male	0	3	3
Functional epiphora eye Units: Subjects			
Right	1	3	4
Left	2	3	5
Both	9	7	16
Munk scale			
Subjective evaluation of epiphora was graded using the Munk scale according to the number of times a day the patient reported dabbing away tears: 0 = no epiphora; 1 = occasional epiphora requiring dabbing less than twice a day; 2 = epiphora requiring dabbing 2-4 times a day; 3 = epiphora requiring dabbing 5-10 times a day; 4 = epiphora requiring dabbing more than 10 times a day.			
Units: point			
arithmetic mean	3.90	3.90	
standard deviation	± 0.30	± 0.31	-
Schirmer test			
Test that has the purpose of measuring the amount of tears in the eye by humidifying some strips of filter paper placed in the conjunctival fornix.			
Units: mm			
arithmetic mean	15.24	12.40	

standard deviation	± 6.83	± 7.01	-
Visual acuity			
Test to measure the best corrected visual acuity (BCVA) on a decimal scale (0-1).			
Units: scale			
arithmetic mean	0.77	0.88	
standard deviation	± 0.22	± 0.14	-
Eyelid traction			
Millimeters of separation between the lower eyelid and the eyeball in the horizontal traction of the lower eyelid.			
Units: milimeter			
arithmetic mean	7.10	7.60	
standard deviation	± 1.34	± 0.99	-
Eyelid spring			
Number of blinks for the lower eyelid to return to its normal position after downward traction of the lower eyelid.			
Units: Frequency			
arithmetic mean	0.48	0.70	
standard deviation	± 0.60	± 0.57	-
Subjective evaluation of epiphora with the quality questionnaire			
Subjective evaluation of epiphora with the quality questionnaire. This is a quality questionnaire that evaluates how often you have discomfort due to your tearing in various activities of daily living using a scale of 0 to 4: Grade 0: It never bothers you. Grade 1: Sometimes. Grade 2: Frequently. Grade 3: Almost always. Grade 4: Always.			
Units: point			
arithmetic mean	2.71	2.90	
standard deviation	± 0.72	± 0.92	-

End points

End points reporting groups

Reporting group title	Botulinum Toxin A (BoNTA)

Reporting group description:

Patients assigned to the BoNTA treatment group received a transconjunctival injection of BoNTA (XEOMIN®, Merz) into the palpebral lobe of the lacrimal gland of the affected eye. BoNTA was reconstituted with sterile saline at a concentration of 50 U in 0.5 ml. The injections were always performed by the same doctor. BoNTA treatment was not repeated in any patient during the study.

Reporting group title	Lateral tarsal strip (LTS)

Reporting group description:

Lateral tarsal strip (LTS) surgery. It will always be performed by the same surgeon. Steps to follow:
- Lateral canthotomy with Westcott scissors. Dissection of the orbicularis over the lateral orbital rim to visualize the periosteum.
- Cantholysis: cutting of the lower branch of the lateral canthal tendon, separating it from the orbital rim.
- Formation of the strip.
- Shortening of the strip.
- Reinsertion of the strip to the inner face of the lateral orbital rim.

Primary: Munk scale at 6 weeks of treatment

End point title	Munk scale at 6 weeks of treatment

End point description:

Munk scale is a score according to the number of times a day the patient reported dabbing away tears: 0 = no epiphora; 1 = occasional epiphora requiring dabbing less than twice a day; 2 = epiphora requiring dabbing 2-4 times a day; 3 = epiphora requiring dabbing 5-10 times a day; 4 = epiphora requiring dabbing more than 10 times a day.

End point type	Primary

End point timeframe:

January 2018- January 2019

End point values	Botulinum Toxin A (BoNTA)	Lateral tarsal strip (LTS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	10		
Units: point				
arithmetic mean (confidence interval 95%)	1.43 (0.90 to 2.00)	2.35 (1.70 to 3.00)		

Statistical analyses

Statistical analysis title	Change at 6 weeks in the Munk scale (BoNTA)

Statistical analysis description:

Change at 6 weeks of treatment in the Munk scale from baseline in the BoNTA treatment group using a paired samples t-student test.

Comparison groups	Botulinum Toxin A (BoNTA) v Lateral tarsal strip (LTS)

Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-2.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	-1.9

Statistical analysis title	Change at 6 weeks in the Munk scale (LTS)
Statistical analysis description:	
Change at 6 weeks of treatment in the Munk scale from baseline in the LTS treatment group using a paired samples t-student test.	
Comparison groups	Botulinum Toxin A (BoNTA) v Lateral tarsal strip (LTS)
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-1.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	-0.9

Statistical analysis title	Change at 6 weeks in the Munk scale
Statistical analysis description:	
Change at 6 weeks of treatment in the Munk scale from baseline using a paired samples t-student test.	
Comparison groups	Botulinum Toxin A (BoNTA) v Lateral tarsal strip (LTS)
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.015
Method	t-test, 2-sided

Secondary: Test schirmer at 6 week of treatment	
End point title	Test schirmer at 6 week of treatment

End point description:

Schirmer strip was placed on the lower conjunctival sac between the lateral area and the external third of the sac for 5 min to measure the production of tears in millimeters from 0 to 15 mm.

End point type	Secondary

End point timeframe:

January 2018-January 2019

End point values	Botulinum Toxin A (BoNTA)	Lateral tarsal strip (LTS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	10		
Units: milimeter				
arithmetic mean (confidence interval 95%)	13.80 (9.70 to 17.90)	11.75 (8.80 to 14.70)		

Statistical analyses

Statistical analysis title	Change at 6 weeks in the Schirmer test (BoNTA)

Statistical analysis description:

Change at 6 weeks of treatment in the Schirmer test from baseline in the BoNTA treatment group using an paired samples t-student test.

Comparison groups	Lateral tarsal strip (LTS) v Botulinum Toxin A (BoNTA)
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.366
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-1.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.7
upper limit	1.8

Statistical analysis title	Change at 6 weeks in the Schirmer test (LTS)

Statistical analysis description:

Change at 6 weeks of treatment in the Munk scale from baseline in the BoNTA treatment group using a paired samples t-student test.

Comparison groups	Botulinum Toxin A (BoNTA) v Lateral tarsal strip (LTS)

Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.742
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-0.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.7
upper limit	3.4

Statistical analysis title	Change at 6 weeks in the Schirmer test
Statistical analysis description:	
Change at 6 weeks of treatment in the Munk scale from baseline using a paired samples t-student test.	
Comparison groups	Botulinum Toxin A (BoNTA) v Lateral tarsal strip (LTS)
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.766
Method	t-test, 2-sided

Secondary: Visual acuity at 6 week of treatment	
End point title	Visual acuity at 6 week of treatment
End point description:	
Test to measure the best corrected visual acuity (BCVA) on a decimal scale (0-1).	
End point type	Secondary
End point timeframe:	
January 2018-January 2019	

End point values	Botulinum Toxin A (BoNTA)	Lateral tarsal strip (LTS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	10		
Units: scale				
arithmetic mean (confidence interval 95%)	0.70 (0.60 to 0.80)	0.86 (0.80 to 0.90)		

Statistical analyses

Statistical analysis title	Change at 6 weeks in visual acuity (BoNTA)
Statistical analysis description:	
Change at 6 weeks of treatment in the visual acuity from baseline in the BoNTA treatment group using a paired samples t-student test.	
Comparison groups	Botulinum Toxin A (BoNTA) v Lateral tarsal strip (LTS)
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.135
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0

Statistical analysis title	Change at 6 weeks in the visual acuity (LTS)
Statistical analysis description:	
Change at 6 weeks of treatment in the visual acuity from baseline in the LTS treatment group using a paired samples t-student test.	
Comparison groups	Botulinum Toxin A (BoNTA) v Lateral tarsal strip (LTS)
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.125
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0

Statistical analysis title	Change at 6 weeks in the visual acuity
Statistical analysis description:	
Change at 6 weeks of treatment in the Munk scale from baseline using a paired samples t-student test.	
Comparison groups	Botulinum Toxin A (BoNTA) v Lateral tarsal strip (LTS)
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.682
Method	t-test, 2-sided

Secondary: Eyelid traction at 6 week of treatment

End point title	Eyelid traction at 6 week of treatment
End point description:	
Millimeters of separation between the lower eyelid and the eyeball in the horizontal traction of the lower eyelid.	
End point type	Secondary
End point timeframe:	
January 2018-January 2019	

End point values	Botulinum Toxin A (BoNTA)	Lateral tarsal strip (LTS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	10		
Units: milimeter				
arithmetic mean (confidence interval 95%)	6.67 (6.20 to 7.10)	5.60 (5.00 to 6.20)		

Statistical analyses

Statistical analysis title	Change at 6 weeks in eyelid traction (BoNTA)
Statistical analysis description:	
Change at 6 weeks of treatment in eyelid traction from baseline in the BoNTA treatment group using a paired samples t-student test.	
Comparison groups	Botulinum Toxin A (BoNTA) v Lateral tarsal strip (LTS)
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.107
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.1

Statistical analysis title	Change at 6 weeks in eyelid traction (LTS)
Statistical analysis description:	
Change at 6 weeks of treatment in eyelid traction from baseline in the LTS treatment group using a paired samples t-student test.	

Comparison groups	Botulinum Toxin A (BoNTA) v Lateral tarsal strip (LTS)
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.6
upper limit	-1.4

Statistical analysis title	Change at 6 weeks in eyelid traction
Statistical analysis description:	
Change at 6 weeks of treatment in the Munk scale from baseline using a paired samples t-student test.	
Comparison groups	Botulinum Toxin A (BoNTA) v Lateral tarsal strip (LTS)
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0006
Method	t-test, 2-sided

Secondary: Eyelid spring at 6 week of treatment

End point title	Eyelid spring at 6 week of treatment
End point description:	
Number of blinks for the lower eyelid to return to its normal position after downward traction of the lower eyelid.	
End point type	Secondary
End point timeframe:	
January 2018-January 2019	

End point values	Botulinum Toxin A (BoNTA)	Lateral tarsal strip (LTS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	10		
Units: Frequency				
arithmetic mean (confidence interval 95%)	0.38 (0.10 to 0.60)	0.05 (-0.10 to 0.20)		

Statistical analyses

Statistical analysis title	Change at 6 weeks in eyelid spring (BoNTA)

Statistical analysis description:

Change at 6 weeks of treatment in eyelid spring from baseline in the BoNTA treatment group using a paired samples t-student test.

Comparison groups	Botulinum Toxin A (BoNTA) v Lateral tarsal strip (LTS)
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.625
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.1

Statistical analysis title	Change at 6 weeks in eyelid spring (LTS)

Statistical analysis description:

Change at 6 weeks of treatment in eyelid spring from baseline in the LTS treatment group using a paired samples t-student test.

Comparison groups	Botulinum Toxin A (BoNTA) v Lateral tarsal strip (LTS)
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0005
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-0.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	-0.4

Statistical analysis title	Change at 6 weeks in eyelid spring

Statistical analysis description:

Change at 6 weeks of treatment in eyelid spring from baseline using a paired samples t-student test.

Comparison groups	Botulinum Toxin A (BoNTA) v Lateral tarsal strip (LTS)

Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0026
Method	t-test, 2-sided

Secondary: Subjective evaluation of epiphora with the quality questionnaire at 6 weeks to treatment

End point title	Subjective evaluation of epiphora with the quality questionnaire at 6 weeks to treatment

End point description:

Subjective evaluation of epiphora with the quality questionnaire. This is a quality questionnaire that evaluates how often you have discomfort due to your tearing in various activities of daily living using a scale of 0 to 4:
Grade 0: It never bothers you.
Grade 1: Sometimes.
Grade 2: Frequently.
Grade 3: Almost always.
Grade 4: Always.

End point type	Secondary

End point timeframe:

January 2018-January 2019

End point values	Botulinum Toxin A (BoNTA)	Lateral tarsal strip (LTS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	7		
Units: points				
arithmetic mean (confidence interval 95%)	1.35 (0.60 to 2.10)	1.34 (0.70 to 2.00)		

Statistical analyses

Statistical analysis title	Change at 6 weeks in quality questionnaire (BoNTA)

Statistical analysis description:

Change at 6 weeks of treatment in quality questionnaire from baseline in the BoNTA treatment group using a paired samples t-student test.

Comparison groups	Botulinum Toxin A (BoNTA) v Lateral tarsal strip (LTS)
Number of subjects included in analysis	13
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.007
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)

Confidence interval	
level	95 %

Statistical analysis title	Change at 6 weeks in quality questionnaire (LTS)

Statistical analysis description:

Change at 6 weeks of treatment in quality questionnaire from baseline in the LTS treatment group using a paired samples t-student test.

Comparison groups	Botulinum Toxin A (BoNTA) v Lateral tarsal strip (LTS)
Number of subjects included in analysis	13
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0003
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-1.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	-0.9

Statistical analysis title	Change at 6 weeks in quality questionnaire

Statistical analysis description:

Change at 6 weeks of treatment in quality questionnaire from baseline using a paired samples t-student test.

Comparison groups	Botulinum Toxin A (BoNTA) v Lateral tarsal strip (LTS)
Number of subjects included in analysis	13
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.918
Method	t-test, 2-sided

Secondary: Treatment duration

End point title	Treatment duration

End point description:

End point type	Secondary

End point timeframe:

January 2018-January 2019

End point values	Botulinum Toxin A (BoNTA)	Lateral tarsal strip (LTS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	13		
Units: week				
arithmetic mean (standard deviation)	26.14 (± 9.48)	23.61 (± 11.79)		

Statistical analyses

Statistical analysis title	Differences between the duration of the treatments
Comparison groups	Botulinum Toxin A (BoNTA) v Lateral tarsal strip (LTS)
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.937
Method	t-test, 2-sided

Adverse events

Adverse events information

Timeframe for reporting adverse events:

January 2018-January 2019

Adverse event reporting additional description:

There were 9 adverse events in 9 patients (36.0%), of which 5 occurred in 5 patients treated with BoNTA (41.7%) and 4 in 4 patients treated with LST (30.8%). In patients treated with BoNTA, 3 palpebral ptosis, 1 metamorphopsia and 1 conjunctivitis occurred. In those treated with LST, 3 scar discomfort and 1 wound infection occurred.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	BoNTA

Reporting group description:

In patients treated with Botulinum Toxin A (BoNTA), 3 palpebral ptosis, 1 metamorphopsia and 1 conjunctivitis occurred

Reporting group title	Lateral tarsal strip (LTS)

Reporting group description:

In those treated with lateral tarsal strip (LTS), 3 scar discomfort and 1 wound infection occurred.

Serious adverse events	BoNTA	Lateral tarsal strip (LTS)	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (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: 0 %

Non-serious adverse events	BoNTA	Lateral tarsal strip (LTS)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 12 (41.67%)	4 / 13 (30.77%)	
Eye disorders			
Eyelid ptosis			
subjects affected / exposed	3 / 12 (25.00%)	0 / 13 (0.00%)	
occurrences (all)	3	0	
Metamorphopsia			

subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 13 (0.00%) 0	
Skin and subcutaneous tissue disorders Wound infection subjects affected / exposed occurrences (all) Scar discomfort subjects affected / exposed occurrences (all)	 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0	 1 / 13 (7.69%) 1 3 / 13 (23.08%) 3	
Infections and infestations Conjunctivitis subjects affected / exposed occurrences (all)	 1 / 12 (8.33%) 0	 0 / 13 (0.00%) 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