Clinical trial results:
Multi-centre, randomised, double blind, placebo-controlled, parallel, phase III study to assess the safety, tolerability and efficacy of bilastine ophthalmic solution 0.6% in adults

Summary

EudraCT number	2018-002248-95
Trial protocol	LT HU SK PL
Global end of trial date	10 December 2019

Results information

Result version number	v1 (current)
This version publication date	20 August 2021
First version publication date	20 August 2021

Trial information

Trial identification

Sponsor protocol code	BOFT-0418-SAFE

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	FAES FARMA S.A.
Sponsor organisation address	Avda. Autornomía, 10, Leioa, Spain, 48940
Public contact	R&D+i Department, Irune Temprano , FAES FARMA S.A., +34 944818300, itemprano@faes.es
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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	10 December 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 December 2019
Global end of trial reached?	Yes
Global end of trial date	10 December 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this trial is to assess the safety of bilastine ophthalmic solution 0.6% during long-term use.

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Patients, adopted by the General Assembly of the World Medical Association, Fortaleza, Brazil 2013 as well as with the valid national law(s) of the participating country/ies, with the International Conference on Harmonisation (ICH) Harmonised Tripartite Guideline for Good Clinical Practice (GCP) (E6), and with the Commission Directives 2001/20/EC and 2005/28/EC.

Additionally, the trial was conducted in compliance with the trial protocol, by trial personnel, who were qualified by education, training, and experienced in their roles. The patients were closely monitored during the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 June 2019
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	Ukraine: 76
Country: Number of subjects enrolled	Poland: 111
Country: Number of subjects enrolled	Slovakia: 47
Country: Number of subjects enrolled	Hungary: 49
Country: Number of subjects enrolled	Lithuania: 50
Worldwide total number of subjects	333
EEA total number of subjects	257

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)	321
From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

At screening, after giving informed consent, the patients were checked for elegibility. Patients were randomised to IMP only if they satisfied all the inclusion criteria and were not precluded from participation by any of the exclusion criteria.

Pre-assignment

Screening details:

In this trial, 333 adult patients with seasonal or perennial allergic conjunctivitis were included and randomised on a 2:1 ratio (stratified by indication [SAC/PAC]) to treatment with bilastine ophthalmic solution 0.6% or placebo for 56 days.

Period 1

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

Arms

Arm title	Overall population

Arm description:

Participants were randomised to receive treatment with bilastine ophthalmic solution 0.6% or placebo for 56 days.
All randomised patients received at least one dose of IMP.

Arm type	Experimental
Investigational medicinal product name	Bilastine ophtalmic solution 0,6%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops, solution
Routes of administration	Ophthalmic use

Dosage and administration details:

1 drop instilled in each eye once daily in the morning.

Investigational medicinal product name	Placebo ophtalmic solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops, solution
Routes of administration	Ophthalmic use

Dosage and administration details:

1 drop instilled in each eye once daily in the morning.

Number of subjects in period 1	Overall population
Started	333
Completed	320
Not completed	13
Adverse event, non-fatal	13

Baseline characteristics

Reporting groups

Reporting group title	Overall study (overall period)

Reporting group description:

Participants were randomised to receive treatment with bilastine ophthalmic solution 0.6% or placebo for 56 days.
All randomised patients received at least one dose of IMP.

Reporting group values	Overall study (overall period)	Total	
Number of subjects	333	333	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	321	321	
From 65-84 years	12	12	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	39		
standard deviation	± 13.66	-	
Gender categorical Units: Subjects			
Female	212	212	
Male	121	121	

Subject analysis sets

Subject analysis set title	Bilastine ophtalmic solution 0,6%
Subject analysis set type	Safety analysis

Subject analysis set description:

Safety analysis set includes all randomised patients with IMP administration (bilastine ophtalmic solution or placebo). Data from all 333 subjects were included in the safety evaluation.

Subject analysis set title	Placebo ophtalmic solution
Subject analysis set type	Safety analysis

Subject analysis set description:

Safety analysis set includes all randomised patients with IMP administration (bilastine ophtalmic solution or placebo). Data from all 333 subjects were included in the safety evaluation.

Reporting group values	Bilastine ophtalmic solution 0,6%	Placebo ophtalmic solution	
Number of subjects	218	115	

Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	210	111	
From 65-84 years	8	4	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	39.4	38.4	
standard deviation	± 14.01	± 13.01	
Gender categorical Units: Subjects			
Female	149	63	
Male	69	52	

End points

End points reporting groups

Reporting group title	Overall population
Reporting group description:	
Participants were randomised to receive treatment with bilastine ophthalmic solution 0.6% or placebo for 56 days. All randomised patients received at least one dose of IMP.	
Subject analysis set title	Bilastine ophtalmic solution 0,6%
Subject analysis set type	Safety analysis
Subject analysis set description:	
Safety analysis set includes all randomised patients with IMP administration (bilastine ophtalmic solution or placebo). Data from all 333 subjects were included in the safety evaluation.	
Subject analysis set title	Placebo ophtalmic solution
Subject analysis set type	Safety analysis
Subject analysis set description:	
Safety analysis set includes all randomised patients with IMP administration (bilastine ophtalmic solution or placebo). Data from all 333 subjects were included in the safety evaluation.	

Primary: Incidence of related treatment-emergent ocular adverse events (ocular r-TEAEs)

End point title	Incidence of related treatment-emergent ocular adverse events (ocular r-TEAEs)[1]
End point description:	
Incidence (percent of patients) of related treatment-emergent ocular adverse events (ocular r-TEAEs).	
End point type	Primary
End point timeframe:	
The period for evaluating ocular r-TEAEs started when the study drug was administered and ended with last follow-up.	

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 analyses were performed for the comparison of ocular r-TEAE incidences between the two treatment groups due to the low numbers of TEAEs in relation to the sample size.

End point values	Overall population	Bilastine ophtalmic solution 0,6%	Placebo ophtalmic solution	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	333	218	115	
Units: Percent of patients				
number (not applicable)				
Dry eye	1.2	0.9	1.7	
Eye discharge	0.6	0.9	0	
Eye irritation	0.6	0.5	0.9	
Conjunctivitis allergic	0.3	0	0.9	
Eye pruritus	0.3	0	0.9	
Lacrimation increased	0.3	0.5	0	
Ocular discomfort	0.3	0.5	0	
Patients with at least one ocular r-TEAE	3.3	2.8	4.3	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The period for evaluating adverse events started when the study drug was administered and ended with last follow-up.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	Bilastine ophtalmic solution 0.6%

Reporting group description:

Adverse events occured during Bilastine ophtalmic solution 0.6% administration

Reporting group title	Placebo ophtalmic solution

Reporting group description:

Adverse events occured during Placebo ophtalmic solution administration

Reporting group title	Overall population

Reporting group description: -

Serious adverse events	Bilastine ophtalmic solution 0.6%	Placebo ophtalmic solution	Overall population
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 218 (0.00%)	0 / 115 (0.00%)	0 / 333 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	Bilastine ophtalmic solution 0.6%	Placebo ophtalmic solution	Overall population
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 218 (12.84%)	18 / 115 (15.65%)	46 / 333 (13.81%)
Vascular disorders			
Vascular disorders			
subjects affected / exposed	1 / 218 (0.46%)	1 / 115 (0.87%)	2 / 333 (0.60%)
occurrences (all)	1	1	2
General disorders and administration site conditions			
General disorders and administration site conditions			

subjects affected / exposed	1 / 218 (0.46%)	0 / 115 (0.00%)	1 / 333 (0.30%)
occurrences (all)	1	0	1
Respiratory, thoracic and mediastinal disorders			
Respiratory, thoracic and mediastinal disorders			
subjects affected / exposed	1 / 218 (0.46%)	2 / 115 (1.74%)	3 / 333 (0.90%)
occurrences (all)	1	2	3
Investigations			
Investigations			
subjects affected / exposed	1 / 218 (0.46%)	0 / 115 (0.00%)	1 / 333 (0.30%)
occurrences (all)	1	0	1
Injury, poisoning and procedural complications			
Injury, poisoning and procedural complications			
subjects affected / exposed	2 / 218 (0.92%)	1 / 115 (0.87%)	3 / 333 (0.90%)
occurrences (all)	2	1	3
Cardiac disorders			
Cardiac disorders			
subjects affected / exposed	0 / 218 (0.00%)	1 / 115 (0.87%)	1 / 333 (0.30%)
occurrences (all)	0	1	1
Nervous system disorders			
Nervous system disorders			
subjects affected / exposed	4 / 218 (1.83%)	0 / 115 (0.00%)	4 / 333 (1.20%)
occurrences (all)	5	0	5
Ear and labyrinth disorders			
Ear and labyrinth disorders			
subjects affected / exposed	1 / 218 (0.46%)	0 / 115 (0.00%)	1 / 333 (0.30%)
occurrences (all)	1	0	1
Eye disorders			
Eye disorders			
subjects affected / exposed	12 / 218 (5.50%)	6 / 115 (5.22%)	18 / 333 (5.41%)
occurrences (all)	15	6	21
Gastrointestinal disorders			
Gastrointestinal disorders			
subjects affected / exposed	2 / 218 (0.92%)	1 / 115 (0.87%)	3 / 333 (0.90%)
occurrences (all)	3	1	4
Skin and subcutaneous tissue disorders			

Skin and subcutaneous tissue disorders			
subjects affected / exposed	1 / 218 (0.46%)	2 / 115 (1.74%)	3 / 333 (0.90%)
occurrences (all)	2	2	4
Musculoskeletal and connective tissue disorders			
Musculoskeletal and connective tissue disorders			
subjects affected / exposed	1 / 218 (0.46%)	0 / 115 (0.00%)	1 / 333 (0.30%)
occurrences (all)	1	0	1
Infections and infestations			
Infections and infestations			
subjects affected / exposed	7 / 218 (3.21%)	6 / 115 (5.22%)	13 / 333 (3.90%)
occurrences (all)	7	7	14
Metabolism and nutrition disorders			
Metabolism and nutrition disorders			
subjects affected / exposed	0 / 218 (0.00%)	1 / 115 (0.87%)	1 / 333 (0.30%)
occurrences (all)	0	1	1

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