Clinical trial results:
An exploratory study to evaluate the efficacy and safety of bilastine in reducing pruritus in patients with chronic spontaneous urticaria and other skin diseases.

Summary

EudraCT number	2016-001505-17
Trial protocol	ES HU
Global end of trial date	30 March 2017

Results information

Result version number	v1 (current)
This version publication date	26 June 2022
First version publication date	26 June 2022

Trial information

Trial identification

Sponsor protocol code	BILA-3716/PRU

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 Autonomía, 10, Leioa, Spain, 48940
Public contact	Cristina Campo, FAES FARMA S.A., +34 94 481 83 00, ccampo@faes.es
Scientific contact	Cristina Campo, FAES FARMA S.A., +34 94 481 83 00, ccampo@faes.es

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	12 December 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 March 2017
Global end of trial reached?	Yes
Global end of trial date	30 March 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The study objective will be to evaluate the efficacy of bilastine in the relief of pruritus in patients with chronic spontaneous urticaria or pruritus associated with other skin diseases.

Protection of trial subjects:

Close medical monitoring and immediate access to medical care in case of any adverse event during and after the trial, until 4 weeks after the last medication intake.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 August 2016
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	Poland: 88
Country: Number of subjects enrolled	Spain: 2
Country: Number of subjects enrolled	Hungary: 25
Worldwide total number of subjects	115
EEA total number of subjects	115

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)	108
From 65 to 84 years	7

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment was performed from August 2016 to March 2017 in 10 Clinical sites in Spain (2), Poland (3) and Hungary (5): 123 patients were screened and 115 patients were enrolled with diagnosis of chronic spontaneous urticaria (34), eczema/dermatitis (30), prurigo (25) and cutaneous pruritus (26).

Pre-assignment

Screening details:

Male and female patients between 18 and 74 years diagnosed of CSU, eczema/dermatitis, prurito or cutaneous pruritus. CSU diagnosed at least 6 weeks prior to consent, with at least 4 points (UAS Itch score sum, the last 3 days of run-in period) and 16 points (UAS7, the last 7 days before enrollment)

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Chronic spontaneous urticaria

Arm description:

Patients with pruritus due to chronic spontaneous urticaria

Arm type	Experimental
Investigational medicinal product name	Bilastine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

20 mg once daily

Arm title	Eczema/Dermatitis

Arm description:

Patients with pruritus due to dermatitis/eczema

Arm type	Experimental
Investigational medicinal product name	Bilastine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

20 mg once daily

Arm title	Prurigo

Arm description:

Patients with pruritus due to prurigo

Arm type	Experimental

Investigational medicinal product name	Bilastine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

20 mg once daily

Arm title	Cutaneous pruritus

Arm description:

Patients with pruritus due to cutaneous pruritus

Arm type	Experimental
Investigational medicinal product name	Bilastine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

20 mg once daily

Number of subjects in period 1	Chronic spontaneous urticaria	Eczema/Dermatitis	Prurigo
Started	34	30	25
Completed	31	29	24
Not completed	3	1	1
Consent withdrawn by subject	1	1	-
Protocol deviation	2	-	1

Number of subjects in period 1	Cutaneous pruritus
Started	26
Completed	26
Not completed	0
Consent withdrawn by subject	-
Protocol deviation	-

Baseline characteristics

Reporting groups

Reporting group title	Overall Trial

Reporting group description:

Pruritus patients

Reporting group values	Overall Trial	Total	
Number of subjects	115	115	
Age categorical			
Adults and elderly people			
Units: Subjects			
Adults (18-64 years)	108	108	
From 65-84 years	7	7	
Gender categorical			
Units: Subjects			
Female	86	86	
Male	29	29	

Subject analysis sets

Subject analysis set title	Safety Analysis set
Subject analysis set type	Safety analysis

Subject analysis set description:

of the 115 included patients, 34 (29.57%) patients had a diagnosis of CSU, and 81 (70.43%) had a diagnosis of eczema/dermatitis, prurigo or cutaneous pruritus group.
In the eczema/dermatitis group, which consisted of 30 patients, the following characteristics were described:
• 19 patients were diagnosed of atopic dermatitis
• 4 patients were diagnosed of chronic eczema
• 7 patients were diagnosed of contact dermatitis
In the prurigo group, which consisted of 25 patients, the following characteristics were described:
• 24 patients were diagnosed of chronic prurigo
• 1 patient was diagnosed of subacute prurigo.
Finally, in the cutaneous pruritus group, which consisted of 26 patients, the following characteristics were described:
• 24 patients were diagnosed of systemic cutaneous pruritus
• 2 patients were diagnosed of local cutaneous pruritus

Subject analysis set title	Full Analysis set
Subject analysis set type	Full analysis

Subject analysis set description:

the full analysis set (FAS) population consisted of 111 patients (96.5% of the included sample). All efficacy variables were based on the FAS population.
The FAS was defined as all patients who had taken at least one dose of study treatment and who had available a postbaseline evaluation of the primary efficacy endpoint at baseline (D0) and at week 8 (Visit 5).

Reporting group values	Safety Analysis set	Full Analysis set	
Number of subjects	115	111	
Age categorical			
Adults and elderly people			
Units: Subjects			
Adults (18-64 years)	108		

From 65-84 years	7		

Gender categorical Units: Subjects			
Female	86		
Male	29		

End points

End points reporting groups

Reporting group title	Chronic spontaneous urticaria
Reporting group description:	
Patients with pruritus due to chronic spontaneous urticaria	
Reporting group title	Eczema/Dermatitis
Reporting group description:	
Patients with pruritus due to dermatitis/eczema	
Reporting group title	Prurigo
Reporting group description:	
Patients with pruritus due to prurigo	
Reporting group title	Cutaneous pruritus
Reporting group description:	
Patients with pruritus due to cutaneous pruritus	
Subject analysis set title	Safety Analysis set
Subject analysis set type	Safety analysis

Subject analysis set description:

of the 115 included patients, 34 (29.57%) patients had a diagnosis of CSU, and 81 (70.43%) had a diagnosis of eczema/dermatitis, prurigo or cutaneous pruritus group.
In the eczema/dermatitis group, which consisted of 30 patients, the following characteristics were described:
• 19 patients were diagnosed of atopic dermatitis
• 4 patients were diagnosed of chronic eczema
• 7 patients were diagnosed of contact dermatitis
In the prurigo group, which consisted of 25 patients, the following characteristics were described:
• 24 patients were diagnosed of chronic prurigo
• 1 patient was diagnosed of subacute prurigo.
Finally, in the cutaneous pruritus group, which consisted of 26 patients, the following characteristics were described:
• 24 patients were diagnosed of systemic cutaneous pruritus
• 2 patients were diagnosed of local cutaneous pruritus

Subject analysis set title	Full Analysis set
Subject analysis set type	Full analysis

Subject analysis set description:

the full analysis set (FAS) population consisted of 111 patients (96.5% of the included sample). All efficacy variables were based on the FAS population.
The FAS was defined as all patients who had taken at least one dose of study treatment and who had available a postbaseline evaluation of the primary efficacy endpoint at baseline (D0) and at week 8 (Visit 5).

Primary: Efficacy of bilastine in the relief of pruritus

End point title	Efficacy of bilastine in the relief of pruritus

End point description:

Efficacy of bilastine in the relief of pruritus in patients with CSU or pruritus associated with other skin diseases.
The primary endpoint was the mean change in weekly pruritus severity score (mean "week 8" score – mean baseline score) and was analysed with a paired Student's t-test with 2-sided alpha=0.05, including its corresponding 95% confidence interval (CI). A non-parametric approach as the Wilcoxon test for paired data was used in case the assumptions for a parametric approach were not met

End point type	Primary

End point timeframe:

from baseline to week 8

End point values	Chronic spontaneous urticaria	Eczema/Dermatitis	Prurigo	Cutaneous pruritus
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	31	29	25	26
Units: number				
arithmetic mean (standard deviation)	-2.11 (± 0.44)	-1.36 (± 0.79)	-1.30 (± 0.92)	-1.66 (± 0.63)

Statistical analyses

Statistical analysis title	SAS® Version 9.2 or later.

Statistical analysis description:

All descriptive variables were tabulated. Quantitative variables were described showing their number of available and missing observations, mean, median, standard deviation (SD), the range (minimum and maximum) and the first and third quartiles.
Frequency and percentage described qualitative variables. Missing values were tabulated with their frequency but were not included
in the calculation of percentages

Comparison groups	Chronic spontaneous urticaria v Eczema/Dermatitis v Prurigo v Cutaneous pruritus
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Secondary: Efficacy in terms of other symptoms and signs of the disease groups

End point title	Efficacy in terms of other symptoms and signs of the disease groups

End point description:

Symptom relief was defined as the negative difference between the baseline symptom score and the corresponding symptom score.
VAS for pruritus

End point type	Secondary

End point timeframe:

From Baseline to week 8

End point values	Chronic spontaneous urticaria	Eczema/Dermatitis	Prurigo	Cutaneous pruritus
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	31	29	25	26
Units: number				
arithmetic mean (standard deviation)	-60.61 (±	-30.64 (±	-43.72 (±	-43.45 (±

16.59)	18.28)	27.41)	16.70)

Statistical analyses

No statistical analyses for this end point

Secondary: Safety and tolerability

End point title	Safety and tolerability

End point description:

Safety and tolerability of bilastine in terms of adverse events, including ECG and laboratory tests.
The safety variables included the following:
• Incidence of adverse events (AEs), serious adverse events (SAEs), and related adverse events (rAEs).
• Change of various clinical laboratory test results, ECG and vital signs

End point type	Secondary

End point timeframe:

From informed consent signature to safety follow up visit 4 weeks after final visit (week 8).

End point values	Chronic spontaneous urticaria	Eczema/Dermatitis	Prurigo	Cutaneous pruritus
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	30	25	26
Units: number	16	39	22	15

End point values	Safety Analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	115			
Units: number	92			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From informed consent signature to safety follow up visit 4 weeks after final visit (week 8).	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups	
Reporting group title	Chronic Spontaneous Urticaria
Reporting group description: -	
Reporting group title	Eczema/dermatitis
Reporting group description: -	
Reporting group title	Prurigo
Reporting group description: -	
Reporting group title	Cutaneous pruritus
Reporting group description: -	

Serious adverse events	Chronic Spontaneous Urticaria	Eczema/dermatitis	Prurigo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 34 (0.00%)	0 / 39 (0.00%)	0 / 25 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events		0	0

Serious adverse events	Cutaneous pruritus		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 26 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Chronic Spontaneous Urticaria	Eczema/dermatitis	Prurigo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 34 (29.41%)	10 / 39 (25.64%)	12 / 25 (48.00%)

Investigations			
Investigations			
subjects affected / exposed	0 / 34 (0.00%)	1 / 39 (2.56%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
Nervous system disorders			
Headache			
subjects affected / exposed[1]	1 / 31 (3.23%)	5 / 29 (17.24%)	3 / 25 (12.00%)
occurrences (all)	2	13	4
General disorders and administration site conditions			
General disorder and administration site condition			
subjects affected / exposed	1 / 34 (2.94%)	0 / 39 (0.00%)	1 / 25 (4.00%)
occurrences (all)	1	0	1
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 34 (2.94%)	0 / 39 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Toothache			
subjects affected / exposed	0 / 34 (0.00%)	2 / 39 (5.13%)	0 / 25 (0.00%)
occurrences (all)	0	2	0
Respiratory, thoracic and mediastinal disorders			
Pharyngitis			
subjects affected / exposed	3 / 34 (8.82%)	1 / 39 (2.56%)	2 / 25 (8.00%)
occurrences (all)	4	11	2
Skin and subcutaneous tissue disorders			
Prurigo			
subjects affected / exposed	0 / 34 (0.00%)	2 / 39 (5.13%)	1 / 25 (4.00%)
occurrences (all)	0	2	1
Pruritus			
subjects affected / exposed	0 / 34 (0.00%)	2 / 39 (5.13%)	2 / 25 (8.00%)
occurrences (all)	0	2	2
Urticaria			
subjects affected / exposed	2 / 34 (5.88%)	0 / 39 (0.00%)	0 / 25 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal and connective tissue disorders			
Musculoskeletal and connective tissue disorders			

subjects affected / exposed	1 / 34 (2.94%)	0 / 39 (0.00%)	3 / 25 (12.00%)
occurrences (all)	1	0	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 34 (2.94%)	0 / 39 (0.00%)	4 / 25 (16.00%)
occurrences (all)	1	0	4
Sinusitis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 39 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Cutaneous pruritus		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 26 (26.92%)		
Investigations			
Investigations			
subjects affected / exposed	0 / 26 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed[1]	1 / 26 (3.85%)		
occurrences (all)	3		
General disorders and administration site conditions			
General disorder and administration site condition			
subjects affected / exposed	0 / 26 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 26 (3.85%)		
occurrences (all)	1		
Toothache			
subjects affected / exposed	0 / 26 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Pharyngitis			
subjects affected / exposed	1 / 26 (3.85%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			

Prurigo subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all) Urticaria subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0 0 / 26 (0.00%) 0 0 / 26 (0.00%) 0		
Musculoskeletal and connective tissue disorders Musculoskeletal and connective tissue disorders subjects affected / exposed occurrences (all)	 3 / 26 (11.54%) 2		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Sinusitis subjects affected / exposed occurrences (all)	 3 / 26 (11.54%) 3 2 / 26 (7.69%) 2		

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The number of exposed patients for our undertanding refers to the total number of patient per reporting group.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 March 2017	After the closure of the database and the delivery of the first results, it was decided the convenience of perform an ad-hoc analysis for the efficacy variables in which change from baseline were reported in order to split the results of those patients who achieve a 30% improvement at Week 2 (responder patients) from those who updosed 2 x 20 mg tablets of bilastine from Week 2 to Week 8 (non-responder patients).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/30835579