Clinical trial results:
A single-centre, randomized, double-blind, crossover, single-dose clinical trial to compare bilastine, desloratadine, rupatadine and placebo in the suppression of wheal and flare induced by intradermal histamine in healthy volunteers.

Summary

EudraCT number	2015-000790-13
Trial protocol	ES
Global end of trial date	31 July 2015

Results information

Result version number	v1 (current)
This version publication date	07 July 2022
First version publication date	07 July 2022

Trial information

Trial identification

Sponsor protocol code	BIL-0115-MED

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	Avenida Autonomía, 10, Leioa, Spain, 48940
Public contact	Clinical Research Director, FAES FARMA, S.A., +34 944818300, ccampo@faes.es
Scientific contact	Clinical Research Director, FAES FARMA, S.A., +34 944818300, 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	24 February 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 July 2015
Global end of trial reached?	Yes
Global end of trial date	31 July 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

TO COMPARE THE EFFICACY OF BILASTINE 20 MG, DESLORATADINE 5 MG AND RUPATADINE 10 MG IN THE REDUCTION OF HISTAMINE-INDUCED SKIN REACTIVITY IN HEALTHY VOLUNTEERS.

Protection of trial subjects:

Participating subjects were healthy volunteers, fully informed before entering the trial. Study subjects received only one dose of each of the study drugs to minimize risks and inconvenience for them, and they were provided with the contact of the medical team in case of any adverse event happened.

Background therapy:

Not applicable, the participant subjects were healthy volunteers

Evidence for comparator:

The three active drugs (bilastine, rupatadine and desloratadine) are the most recent second-generation H1-receptor antagonists introduced in clinical practice. The main purpose of this study was to compare their activity through the wheal and flare response model. This is a validated model, induced by an intradermal histamine injection, able to evaluate the peripheric antihistamine activity.

Actual start date of recruitment	06 July 2015
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: 24
Worldwide total number of subjects	24
EEA total number of subjects	24

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)	24

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participating healthy volunteers (n=24) were recruited between July 6th and 31st, 2015, in Hospital Santa Creu i Sant Pau in Barcelona, Spain.

Pre-assignment

Screening details:

32 subjects were included in the study, 5 were excluded and 3 were left as reserves. 24 volunteers were randomized.
When the screening examinations showed any disqualifying abnormality, the subject was excluded from the study.
24 patients received and were exposed to the active treatments and placebo. Thus, 96 observations were analysed.

Period 1

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

Blinding implementation details:

To guarantee double-blind conditions, all the drugs were presented in identical capsules consisting of special opaque material for clinical studies. The sample labels had no information that would allow identification of the treatment administered. During the experimental phase of the study, closed individual randomization envelopes were filed in a zone at the CIM-Sant Pau only accessible to the investigator team. The 24 patients were also exposed to placebo treatment.

Arms

Are arms mutually exclusive?	No
Arm title	Bilastine

Arm description:

This study (phase IV clinical trial in healthy volunteers) was conducted according to a crossover, randomized, double-blind and placebo-controlled design comprising one inclusion phase and one experimental phase which include four treatment periods. A minimum 7 days wash-out period between treatment periods was established. To guarantee double-blind conditions, all the drugs were presented in identical capsules consisting of special opaque material for clinical studies. The sample labels had no information that would allow identification of the treatment administered. In every treatment period, study drug was administered as one single oral dose in fasting conditions.
24 volunteers were exposed to all study arms/treatments (bilastine, desloratadine, rupatadine and placebo), thus, 96 observations were analysed.

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	Desloratadine

Arm description:

This study (phase IV clinical trial in healthy volunteers) was conducted according to a crossover, randomized, double-blind and placebo-controlled design comprising one inclusion phase and one experimental phase which include four treatment periods. A minimum 7 days wash-out period between treatment periods was established. In every treatment period, study drug was administered as one

single oral dose in fasting conditions. 24 volunteers were exposed to all study arms/treatments (bilastine, desloratadine, rupatadine and placebo), thus, 96 observations were analysed.

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

Dosage and administration details:

5 mg once daily

Arm title	Rupatadine

Arm description:

This study (phase IV clinical trial in healthy volunteers) was conducted according to a crossover, randomized, double-blind and placebo-controlled design comprising one inclusion phase and one experimental phase which include four treatment periods. A minimum 7 days wash-out period between treatment periods was established. In every treatment period, study drug was administered as one single oral dose in fasting conditions. 24 volunteers were exposed to all study arms/treatments (bilastine, desloratadine, rupatadine and placebo), thus, 96 observations were analysed.

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

Dosage and administration details:

10 mg once daily

Arm title	Placebo

Arm description:

This study (phase IV clinical trial in healthy volunteers) was conducted according to a crossover, randomized, double-blind and placebo-controlled design comprising one inclusion phase and one experimental phase which include four treatment periods. A minimum 7 days wash-out period between treatment periods was established. In every treatment period, study drug was administered as one single oral dose in fasting conditions. 24 volunteers were exposed to all study arms/treatments (bilastine, desloratadine, rupatadine and placebo), thus, 96 observations were analysed.

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

Dosage and administration details:

once daily

Number of subjects in period 1	Bilastine	Desloratadine	Rupatadine
Started	24	24	24
Completed	24	24	24

Number of subjects in period 1	Placebo
Started	24
Completed	24

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	24	24	
Age categorical Units: Subjects			
Adults (18-64 years)	24	24	
Gender categorical Units: Subjects			
Female	12	12	
Male	12	12	

Subject analysis sets

Subject analysis set title	Pharmacodynamic profile
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects who completed the clinical study

Reporting group values	Pharmacodynamic profile		
Number of subjects	24		
Age categorical Units: Subjects			
Adults (18-64 years)	24		
Gender categorical Units: Subjects			
Female	12		
Male	12		

End points

End points reporting groups

Reporting group title	Bilastine

Reporting group description:

This study (phase IV clinical trial in healthy volunteers) was conducted according to a crossover, randomized, double-blind and placebo-controlled design comprising one inclusion phase and one experimental phase which include four treatment periods. A minimum 7 days wash-out period between treatment periods was established. To guarantee double-blind conditions, all the drugs were presented in identical capsules consisting of special opaque material for clinical studies. The sample labels had no information that would allow identification of the treatment administered. In every treatment period, study drug was administered as one single oral dose in fasting conditions.
24 volunteers were exposed to all study arms/treatments (bilastine, desloratadine, rupatadine and placebo), thus, 96 observations were analysed.

Reporting group title	Desloratadine

Reporting group description:

This study (phase IV clinical trial in healthy volunteers) was conducted according to a crossover, randomized, double-blind and placebo-controlled design comprising one inclusion phase and one experimental phase which include four treatment periods. A minimum 7 days wash-out period between treatment periods was established. In every treatment period, study drug was administered as one single oral dose in fasting conditions. 24 volunteers were exposed to all study arms/treatments (bilastine, desloratadine, rupatadine and placebo), thus, 96 observations were analysed.

Reporting group title	Rupatadine

Reporting group description:

This study (phase IV clinical trial in healthy volunteers) was conducted according to a crossover, randomized, double-blind and placebo-controlled design comprising one inclusion phase and one experimental phase which include four treatment periods. A minimum 7 days wash-out period between treatment periods was established. In every treatment period, study drug was administered as one single oral dose in fasting conditions. 24 volunteers were exposed to all study arms/treatments (bilastine, desloratadine, rupatadine and placebo), thus, 96 observations were analysed.

Reporting group title	Placebo

Reporting group description:

This study (phase IV clinical trial in healthy volunteers) was conducted according to a crossover, randomized, double-blind and placebo-controlled design comprising one inclusion phase and one experimental phase which include four treatment periods. A minimum 7 days wash-out period between treatment periods was established. In every treatment period, study drug was administered as one single oral dose in fasting conditions. 24 volunteers were exposed to all study arms/treatments (bilastine, desloratadine, rupatadine and placebo), thus, 96 observations were analysed.

Subject analysis set title	Pharmacodynamic profile
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects who completed the clinical study

Primary: Efficacy of Bilastine in the reduction of wheal size

End point title	Efficacy of Bilastine in the reduction of wheal size

End point description:

Compare the efficacy of Bilastine 20 mg, Desloratadine 5 mg and Rupatadine 10 mg in the reduction of histamine-induced skin reactivity in healthy volunteers

End point type	Primary

End point timeframe:

The study comprised four treatment periods in which the corresponding treatments were administered as single oral doses. A minimum 7 days wash-out period between treatment periods was established.

End point values	Bilastine	Desloratadine	Rupatadine	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24	24	24	24
Units: mm2				
arithmetic mean (standard deviation)	83.098 (± 12.07)	38.046 (± 20.97)	37.302 (± 22.55)	-0.234 (± 36.55)

Statistical analyses

Statistical analysis title	IBM-SPSS (v22.0)

Statistical analysis description:

All the statistical analyses a $p<0.05$ was considered the criterion for rejecting the null hypothesis (H0). Baseline conditions were analysed by means of one-way ANOVA (treatment factor), expressing the data as direct values.
The analysis of maximum inhibition time and onset of action were descriptive.

Comparison groups	Bilastine v Desloratadine v Rupatadine v Placebo
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	ANOVA

Secondary: Safety and tolerability

End point title	Safety and tolerability

End point description:

24 healthy volunteers received all treatments and all were exposed to the study arms (Bilastine, Desloratadine, Rupatadine and Placebo), therefore, 96 observations were analysed.

End point type	Secondary

End point timeframe:

The study comprised four treatment periods in which the corresponding treatments were administered as single oral doses. A minimum 7 days wash-out period between treatment periods was established.

End point values	Bilastine	Desloratadine	Rupatadine	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24	24	24	24
Units: number of adverse events	2	2	1	1

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The study comprised four treatment periods in which the corresponding treatments were administered as single oral doses. A minimum 7 days wash-out period between treatment periods was established.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Total population

Reporting group description:

24 volunteers.
1 subject was affected by 3 adverse events, and 3 subjects were affected by 1 adverse event each.

Serious adverse events	Total population		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 24 (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	Total population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 24 (16.67%)		
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 24 (12.50%)		
occurrences (all)	3		
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		
Gastrointestinal disorders			
Vomiting			

subjects affected / exposed occurrences (all)	1 / 24 (4.17%) 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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/27659218