



## 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        |
| <b>Arm title</b>             | 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

|                  |               |
|------------------|---------------|
| <b>Arm title</b> | 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

|                  |            |
|------------------|------------|
| <b>Arm title</b> | 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

|                  |         |
|------------------|---------|
| <b>Arm title</b> | 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

| <b>Number of subjects in period 1</b> | Bilastine | Desloratadine | Rupatadine |
|---------------------------------------|-----------|---------------|------------|
| Started                               | 24        | 24            | 24         |
| Completed                             | 24        | 24            | 24         |

| <b>Number of subjects in period 1</b> | 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<br>Units: Subjects    |               |       |  |
| Adults (18-64 years)                  | 24            | 24    |  |
| Gender categorical<br>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:<br>Subjects who completed the clinical study |                         |

| Reporting group values                | Pharmacodynamic profile |  |  |
|---------------------------------------|-------------------------|--|--|
| Number of subjects                    | 24                      |  |  |
| Age categorical<br>Units: Subjects    |                         |  |  |
| Adults (18-64 years)                  | 24                      |  |  |
| Gender categorical<br>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.



| <b>End point values</b>              | 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

| <b>Statistical analysis title</b>  | 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

| <b>End point title</b>   | 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. |                         |

| <b>End point values</b>         | 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



## 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 | 1 / 24 (4.17%) |  |  |
| occurrences (all)           | 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>