



Clinical trial results:

A Multi-Center, Randomized, Double Blind, Placebo Controlled Parallel Group Study of the Safety of Levocetirizine Dihydrochloride Oral Liquid Formulation b.i.d Dosing in Children Aged 1 to < 6 Years Suffering From Allergic Rhinitis or Chronic Urticaria of Unknown Origin

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2015-000205-39 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 08 July 2008 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 28 June 2016 |
| First version publication date | 03 May 2015 |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | A00426 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00619801 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | UCB Pharma |
| Sponsor organisation address | 1950 Lake Park Drive, Smyrna, United States, 30080 |
| Public contact | Clinical Trial Registries and Results Disclosure, UCB BIOSCIENCES GmbH, 0049 2173 48 15 15, clinicaltrials@ucb.com |
| Scientific contact | Clinical Trial Registries and Results Disclosure, UCB BIOSCIENCES GmbH, 0049 2173 48 15 15, clinicaltrials@ucb.com |

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 | 27 August 2008 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 08 July 2008 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety of levocetirizine dihydrochloride in pediatric subjects aged from 1 to less than 6 years.

Protection of trial subjects:

Adequate information was provided to the subject's caregiver in both oral and written form and consent was obtained in writing prior to performance of any study specific procedure. The content and process of obtaining informed consent was in accordance with all applicable regulatory and IEC/IRB requirements. A HIPAA agreement was inserted into the final informed consent form for sites in the United States.

Background therapy:

N/A

Evidence for comparator:

N/A

| | |
|---|---------------|
| Actual start date of recruitment | 13 March 2008 |
| 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 | United States: 173 |
| Worldwide total number of subjects | 173 |
| EEA total number of subjects | 0 |

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) | 25 |
| Children (2-11 years) | 148 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |

| | |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

Subject disposition

Recruitment

Recruitment details:

A00426 began recruitment within the United States of America in March 2008. The study concluded in July 2008. A total of 173 were randomized into the study.

Pre-assignment

Screening details:

N/A

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, Carer |

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes |
| Arm title | Placebo |

Arm description:

Placebo (5 drops) dosed by mouth at breakfast time and in the evening (the evening dose should be administered approximately 12 hours later), twice a day for 2 weeks from Visit 2 (Day 0) to Visit 4 (Day 14) or the Early Discontinuation Visit (EDV).

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

Dosage and administration details:

Placebo oral drops (5 drops) dosed twice a day for 2 weeks.

| | |
|------------------|----------------|
| Arm title | Levocetirizine |
|------------------|----------------|

Arm description:

Levocetirizine dihydrochloride 1.25 mg (5 drops containing 5 mg/mL) dosed by mouth at breakfast time and in the evening (the evening dose should be administered approximately 12 hours later), twice a day for 2 weeks from Visit 2 (Day 0) to Visit 4 (Day 14) or the Early Discontinuation Visit (EDV).

| | |
|--|----------------|
| Arm type | Experimental |
| Investigational medicinal product name | Levocetirizine |
| Investigational medicinal product code | Levocetirizine |
| Other name | Xyzal |
| Pharmaceutical forms | Oral drops |
| Routes of administration | Oral use |

Dosage and administration details:

Levocetirizine dihydrochloride 1.25 mg oral drops formulation (5 drops containing 5mg/mL) dosed twice a day for 2 weeks.

| Number of subjects in period 1 | Placebo | Levocetirizine |
|---------------------------------------|---------|----------------|
| Started | 59 | 114 |
| Safety Population | 59 | 114 |
| Completed | 58 | 111 |
| Not completed | 1 | 3 |
| Consent withdrawn by subject | 1 | 1 |
| Loss of efficacy | - | 1 |
| Lack of efficacy | - | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Placebo (5 drops) dosed by mouth at breakfast time and in the evening (the evening dose should be administered approximately 12 hours later), twice a day for 2 weeks from Visit 2 (Day 0) to Visit 4 (Day 14) or the Early Discontinuation Visit (EDV).

| | |
|-----------------------|----------------|
| Reporting group title | Levocetirizine |
|-----------------------|----------------|

Reporting group description:

Levocetirizine dihydrochloride 1.25 mg (5 drops containing 5 mg/mL) dosed by mouth at breakfast time and in the evening (the evening dose should be administered approximately 12 hours later), twice a day for 2 weeks from Visit 2 (Day 0) to Visit 4 (Day 14) or the Early Discontinuation Visit (EDV).

| Reporting group values | Placebo | Levocetirizine | Total |
|---|---------|----------------|-------|
| Number of subjects | 59 | 114 | 173 |
| Age Categorical Units: Subjects | | | |
| <=18 years | 59 | 114 | 173 |
| Age Continuous Units: years | | | |
| arithmetic mean | 3.75 | 3.78 | |
| standard deviation | ± 1.45 | ± 1.38 | - |
| Gender Categorical Units: Subjects | | | |
| Female | 23 | 49 | 72 |
| Male | 36 | 65 | 101 |
| Region of Enrollment Units: Subjects | | | |
| United States | 59 | 114 | 173 |

End points

End points reporting groups

| | |
|--|----------------|
| Reporting group title | Placebo |
| Reporting group description: | |
| Placebo (5 drops) dosed by mouth at breakfast time and in the evening (the evening dose should be administered approximately 12 hours later), twice a day for 2 weeks from Visit 2 (Day 0) to Visit 4 (Day 14) or the Early Discontinuation Visit (EDV). | |
| Reporting group title | Levocetirizine |
| Reporting group description: | |
| Levocetirizine dihydrochloride 1.25 mg (5 drops containing 5 mg/mL) dosed by mouth at breakfast time and in the evening (the evening dose should be administered approximately 12 hours later), twice a day for 2 weeks from Visit 2 (Day 0) to Visit 4 (Day 14) or the Early Discontinuation Visit (EDV). | |

Primary: Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in ventricular rate (VR)

| | |
|------------------------|--|
| End point title | Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in ventricular rate (VR) ^[1] |
| End point description: | |
| End point type | Primary |
| End point timeframe: | |
| Baseline, 14 days | |

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: The primary objective of study A00426 was "to evaluate the safety of levocetirizine dihydrochloride in pediatric subjects aged from 1 to less than 6 years". So the purpose of the study was the description of the safety profile of levocetirizine dihydrochloride across several safety variables. Therefore no statistical comparisons were applied in this safety study.

| End point values | Placebo | Levocetirizine | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 56 | 110 | | |
| Units: beats per minute | | | | |
| arithmetic mean (standard deviation) | | | | |
| mean (standard deviation) | -1.5 (± 14.1) | 1.3 (± 14.2) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in RR interval

| | |
|--|--|
| End point title | Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in RR interval ^[2] |
| End point description: | |
| The RR interval refers to the respective time interval in the Electrocardiogram (ECG). | |
| End point type | Primary |

End point timeframe:

Baseline, 14 days

Notes:

[2] - 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: The primary objective of study A00426 was "to evaluate the safety of levocetirizine dihydrochloride in pediatric subjects aged from 1 to less than 6 years". So the purpose of the study was the description of the safety profile of levocetirizine dihydrochloride across several safety variables. Therefore no statistical comparisons were applied in this safety study.

| End point values | Placebo | Levocetirizine | | |
|--------------------------------------|-------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 56 ^[3] | 110 ^[4] | | |
| Units: milliseconds | | | | |
| arithmetic mean (standard deviation) | | | | |
| mean (standard deviation) | 9.2 (± 85.9) | -6.9 (± 83.4) | | |

Notes:

[3] - Safety Population; only non-missing values were analyzed.

[4] - Safety Population; only non-missing values were analyzed.

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in PR interval

| | |
|-----------------|--|
| End point title | Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in PR interval ^[5] |
|-----------------|--|

End point description:

The PR interval refers to the respective time interval in the Electrocardiogram (ECG).

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline, 14 days

Notes:

[5] - 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: The primary objective of study A00426 was "to evaluate the safety of levocetirizine dihydrochloride in pediatric subjects aged from 1 to less than 6 years". So the purpose of the study was the description of the safety profile of levocetirizine dihydrochloride across several safety variables. Therefore no statistical comparisons were applied in this safety study.

| End point values | Placebo | Levocetirizine | | |
|--------------------------------------|-------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 56 ^[6] | 110 ^[7] | | |
| Units: milliseconds | | | | |
| arithmetic mean (standard deviation) | | | | |
| mean (standard deviation) | 0.5 (± 9.6) | -0.8 (± 11) | | |

Notes:

[6] - Safety Population; only non-missing values were analyzed.

[7] - Safety Population; only non-missing values were analyzed.

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in QRS duration

| | |
|---|---|
| End point title | Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in QRS duration ^[8] |
| End point description: The QRS duration refers to the respective time duration in the Electrocardiogram (ECG). | |
| End point type | Primary |
| End point timeframe: Baseline, 14 days | |

Notes:

[8] - 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: The primary objective of study A00426 was "to evaluate the safety of levocetirizine dihydrochloride in pediatric subjects aged from 1 to less than 6 years". So the purpose of the study was the description of the safety profile of levocetirizine dihydrochloride across several safety variables. Therefore no statistical comparisons were applied in this safety study.

| End point values | Placebo | Levocetirizine | | |
|--------------------------------------|-------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 56 ^[9] | 110 ^[10] | | |
| Units: milliseconds | | | | |
| arithmetic mean (standard deviation) | | | | |
| mean (standard deviation) | 0.3 (± 6.6) | 0.9 (± 7.1) | | |

Notes:

[9] - Safety Population; only non-missing values were analyzed.

[10] - Safety Population; only non-missing values were analyzed.

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in QT interval

| | |
|--|---|
| End point title | Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in QT interval ^[11] |
| End point description: The QT interval refers to the respective time interval in the Electrocardiogram (ECG). | |
| End point type | Primary |
| End point timeframe: Baseline, 14 days | |

Notes:

[11] - 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: The primary objective of study A00426 was "to evaluate the safety of levocetirizine dihydrochloride in pediatric subjects aged from 1 to less than 6 years". So the purpose of the study was the description of the safety profile of levocetirizine dihydrochloride across several safety variables. Therefore no statistical comparisons were applied in this safety study.

| End point values | Placebo | Levocetirizine | | |
|--------------------------------------|--------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 56 ^[12] | 110 ^[13] | | |
| Units: milliseconds | | | | |
| arithmetic mean (standard deviation) | | | | |
| mean (standard deviation) | -2.8 (± 17.2) | -1.5 (± 19.2) | | |

Notes:

[12] - Safety Population; only non-missing values were analyzed.

[13] - Safety Population; only non-missing values were analyzed.

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in QT interval corrected for heart rate using Fridericia's formula (QTcF)

| | |
|-----------------|--|
| End point title | Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in QT interval corrected for heart rate using Fridericia's formula (QTcF) ^[14] |
|-----------------|--|

End point description:

The QT interval refers to the respective time interval in the Electrocardiogram (ECG).

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline, 14 days

Notes:

[14] - 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: The primary objective of study A00426 was "to evaluate the safety of levocetirizine dihydrochloride in pediatric subjects aged from 1 to less than 6 years". So the purpose of the study was the description of the safety profile of levocetirizine dihydrochloride across several safety variables. Therefore no statistical comparisons were applied in this safety study.

| End point values | Placebo | Levocetirizine | | |
|--------------------------------------|--------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 56 ^[15] | 110 ^[16] | | |
| Units: milliseconds | | | | |
| arithmetic mean (standard deviation) | | | | |
| mean (standard deviation) | -5.5 (± 14.3) | -0.3 (± 16.6) | | |

Notes:

[15] - Safety Population; only non-missing values were analyzed.

[16] - Safety Population; only non-missing values were analyzed.

Statistical analyses

No statistical analyses for this end point

Primary: Absolute value of QT interval corrected for heart rate using Fridericia's formula (QTcF) at Visit 3 (Day 7)

| | |
|-----------------|---|
| End point title | Absolute value of QT interval corrected for heart rate using Fridericia's formula (QTcF) at Visit 3 (Day 7) ^[17] |
|-----------------|---|

End point description:

The QT interval refers to the respective time interval in the Electrocardiogram (ECG).

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

7 days

Notes:

[17] - 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: The primary objective of study A00426 was "to evaluate the safety of levocetirizine dihydrochloride in pediatric subjects aged from 1 to less than 6 years". So the purpose of the study was the description of the safety profile of levocetirizine dihydrochloride across several safety variables. Therefore no statistical comparisons were applied in this safety study.

| End point values | Placebo | Levocetirizine | | |
|--------------------------------------|--------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 57 ^[18] | 112 ^[19] | | |
| Units: milliseconds | | | | |
| arithmetic mean (standard deviation) | | | | |
| mean (standard deviation) | 372.6 (± 16.5) | 368.9 (± 19.4) | | |

Notes:

[18] - Safety Population; only non-missing values were analyzed.

[19] - Safety Population; only non-missing values were analyzed.

Statistical analyses

No statistical analyses for this end point

Primary: Absolute value of QT interval corrected for heart rate using Fridericia's formula (QTcF) at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV)

| | |
|------------------------|--|
| End point title | Absolute value of QT interval corrected for heart rate using Fridericia's formula (QTcF) at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) ^[20] |
| End point description: | The QT interval refers to the respective time interval in the Electrocardiogram (ECG). |
| End point type | Primary |
| End point timeframe: | 14 days |

Notes:

[20] - 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: The primary objective of study A00426 was "to evaluate the safety of levocetirizine dihydrochloride in pediatric subjects aged from 1 to less than 6 years". So the purpose of the study was the description of the safety profile of levocetirizine dihydrochloride across several safety variables. Therefore no statistical comparisons were applied in this safety study.

| End point values | Placebo | Levocetirizine | | |
|--------------------------------------|--------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 57 ^[21] | 111 ^[22] | | |
| Units: milliseconds | | | | |
| arithmetic mean (standard deviation) | | | | |
| mean (standard deviation) | 369.8 (± 17.1) | 370.5 (± 18.5) | | |

Notes:

[21] - Safety Population; only non-missing values were analyzed.

[22] - Safety Population; only non-missing values were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline at Visit 4 (Day 14) or at Early Discontinuation

Visit (EDV) in total bilirubin

| | |
|-----------------|---|
| End point title | Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in total bilirubin |
|-----------------|---|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, 14 days

| End point values | Placebo | Levocetirizine | | |
|--|--------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 54 | 104 | | |
| Units: micromole per liter [$\mu\text{mol/L}$] | | | | |
| median (full range (min-max)) | | | | |
| median (full range) | 0 (-10.26 to 3.42) | 0 (-8.55 to 5.13) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in alanine aminotransferase (ALT)

| | |
|-----------------|--|
| End point title | Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in alanine aminotransferase (ALT) |
|-----------------|--|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, 14 days

| End point values | Placebo | Levocetirizine | | |
|-------------------------------|-------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 54 | 105 | | |
| Units: unit per liter [U/L] | | | | |
| median (full range (min-max)) | | | | |
| median (full range) | -1.5 (-12 to 167) | 1 (-21 to 138) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in aspartate aminotransferase (AST)

| | |
|-----------------|--|
| End point title | Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in aspartate aminotransferase (AST) |
|-----------------|--|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, 14 days

| End point values | Placebo | Levocetirizine | | |
|-------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 53 | 105 | | |
| Units: unit per liter [U/L] | | | | |
| median (full range (min-max)) | | | | |
| median (full range) | 1 (-15 to 52) | 1 (-16 to 58) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in blood urea nitrogen

| | |
|-----------------|---|
| End point title | Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in blood urea nitrogen |
|-----------------|---|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, 14 days

| End point values | Placebo | Levocetirizine | | |
|-------------------------------------|---------------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 54 | 105 | | |
| Units: millimole per liter [mmol/L] | | | | |
| median (full range (min-max)) | | | | |
| median (full range) | -0.1785 (-2.142 to 2.142) | 0 (-3.57 to 3.213) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in blood creatinine

| | |
|-----------------|--|
| End point title | Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in blood creatinine |
|-----------------|--|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, 14 days

| End point values | Placebo | Levocetirizine | | |
|--|--------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 54 | 105 | | |
| Units: micromole per liter [$\mu\text{mol/L}$] | | | | |
| median (full range (min-max)) | | | | |
| median (full range) | -0.884 (-17.68 to 13.26) | 1.768 (-15.912 to 16.796) | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events were collected from Visit 1 (Day -2 to -28) over randomization and On-treatment Period up to the Follow-up Visit (Day 21±2).

Adverse event reporting additional description:

Adverse Events refer to the safety population, including all subjects who were dispensed study treatment at least once.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|-----|
| Dictionary version | 9.0 |
|--------------------|-----|

Reporting groups

| | |
|-----------------------|----------------|
| Reporting group title | Levocetirizine |
|-----------------------|----------------|

Reporting group description:

Levocetirizine dihydrochloride 1.25 mg (5 drops containing 5 mg/mL) dosed by mouth at breakfast time and in the evening (the evening dose should be administered approximately 12 hours later), twice a day for 2 weeks from Visit 2 (Day 0) to Visit 4 (Day 14) or the Early Discontinuation Visit (EDV).

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Placebo (5 drops) dosed by mouth at breakfast time and in the evening (the evening dose should be administered approximately 12 hours later), twice a day for 2 weeks from Visit 2 (Day 0) to Visit 4 (Day 14) or the Early Discontinuation Visit (EDV).

| Serious adverse events | Levocetirizine | Placebo | |
|--|-----------------|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 114 (0.88%) | 0 / 59 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| alternative dictionary used: MedDRA 9.0 | | | |
| subjects affected / exposed | 1 / 114 (0.88%) | 0 / 59 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Levocetirizine | Placebo | |
|---|-------------------|------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 39 / 114 (34.21%) | 21 / 59 (35.59%) | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| alternative dictionary used: MedDRA 9.0 | | | |
| subjects affected / exposed | 5 / 114 (4.39%) | 1 / 59 (1.69%) | |
| occurrences (all) | 5 | 1 | |
| Fatigue | | | |
| alternative dictionary used: MedDRA 9.0 | | | |
| subjects affected / exposed | 1 / 114 (0.88%) | 1 / 59 (1.69%) | |
| occurrences (all) | 1 | 1 | |
| Pain | | | |
| alternative dictionary used: MedDRA 9.0 | | | |
| subjects affected / exposed | 1 / 114 (0.88%) | 0 / 59 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hunger | | | |
| alternative dictionary used: MedDRA 9.0 | | | |
| subjects affected / exposed | 0 / 114 (0.00%) | 1 / 59 (1.69%) | |
| occurrences (all) | 0 | 1 | |
| Thirst | | | |
| alternative dictionary used: MedDRA 9.0 | | | |
| subjects affected / exposed | 0 / 114 (0.00%) | 1 / 59 (1.69%) | |
| occurrences (all) | 0 | 1 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| alternative dictionary used: MedDRA 9.0 | | | |
| subjects affected / exposed | 4 / 114 (3.51%) | 5 / 59 (8.47%) | |
| occurrences (all) | 4 | 6 | |
| Asthma | | | |
| alternative dictionary used: MedDRA 9.0 | | | |
| subjects affected / exposed | 1 / 114 (0.88%) | 0 / 59 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Wheezing | | | |
| alternative dictionary used: MedDRA 9.0 | | | |

| | | | |
|--|-----------------|----------------|--|
| subjects affected / exposed | 1 / 114 (0.88%) | 1 / 59 (1.69%) | |
| occurrences (all) | 1 | 1 | |
| Epistaxis | | | |
| alternative dictionary used: MedDRA 9.0 | | | |
| subjects affected / exposed | 2 / 114 (1.75%) | 1 / 59 (1.69%) | |
| occurrences (all) | 2 | 1 | |
| Nasal discomfort | | | |
| alternative dictionary used: MedDRA 9.0 | | | |
| subjects affected / exposed | 1 / 114 (0.88%) | 0 / 59 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Rhinorrhoea | | | |
| alternative dictionary used: MedDRA 9.0 | | | |
| subjects affected / exposed | 1 / 114 (0.88%) | 0 / 59 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Respiratory tract congestion | | | |
| alternative dictionary used: MedDRA 9.0 | | | |
| subjects affected / exposed | 0 / 114 (0.00%) | 1 / 59 (1.69%) | |
| occurrences (all) | 0 | 1 | |
| Psychiatric disorders | | | |
| Sleep disorder | | | |
| alternative dictionary used: MedDRA 9.0 | | | |
| subjects affected / exposed | 2 / 114 (1.75%) | 0 / 59 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Nervousness | | | |
| alternative dictionary used: MedDRA 9.0 | | | |
| subjects affected / exposed | 1 / 114 (0.88%) | 0 / 59 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Middle insomnia | | | |
| alternative dictionary used: MedDRA 9.0 | | | |
| subjects affected / exposed | 0 / 114 (0.00%) | 1 / 59 (1.69%) | |
| occurrences (all) | 0 | 1 | |
| Restlessness | | | |
| alternative dictionary used: MedDRA 9.0 | | | |

| | | | |
|---|--|---|--|
| subjects affected / exposed occurrences (all) | 0 / 114 (0.00%) 0 | 1 / 59 (1.69%) 1 | |
| Investigations Alanine aminotransferase increased alternative dictionary used: MedDRA 9.0 subjects affected / exposed occurrences (all) | 1 / 114 (0.88%) 1 | 0 / 59 (0.00%) 0 | |
| Injury, poisoning and procedural complications Skin laceration alternative dictionary used: MedDRA 9.0 subjects affected / exposed occurrences (all) Head injury alternative dictionary used: MedDRA 9.0 subjects affected / exposed occurrences (all) | 1 / 114 (0.88%) 1 1 / 114 (0.88%) 1 | 0 / 59 (0.00%) 0 0 / 59 (0.00%) 0 | |
| Cardiac disorders Tachycardia alternative dictionary used: MedDRA 9.0 subjects affected / exposed occurrences (all) | 1 / 114 (0.88%) 1 | 0 / 59 (0.00%) 0 | |
| Nervous system disorders Somnolence alternative dictionary used: MedDRA 9.0 subjects affected / exposed occurrences (all) Headache alternative dictionary used: MedDRA 9.0 subjects affected / exposed occurrences (all) Psychomotor hyperactivity alternative dictionary used: MedDRA 9.0 subjects affected / exposed occurrences (all) | 1 / 114 (0.88%) 1 1 / 114 (0.88%) 1 0 / 114 (0.00%) 0 | 2 / 59 (3.39%) 2 1 / 59 (1.69%) 1 3 / 59 (5.08%) 3 | |
| Ear and labyrinth disorders | | | |

| | | | |
|---|----------------------|---------------------|--|
| Cerumen impaction alternative dictionary used: MedDRA 9.0 subjects affected / exposed occurrences (all) | 0 / 114 (0.00%) 0 | 1 / 59 (1.69%) 1 | |
| Eye disorders Eye swelling alternative dictionary used: MedDRA 9.0 subjects affected / exposed occurrences (all) | 1 / 114 (0.88%) 1 | 0 / 59 (0.00%) 0 | |
| Gastrointestinal disorders Diarrhoea alternative dictionary used: MedDRA 9.0 subjects affected / exposed occurrences (all) | 4 / 114 (3.51%) 4 | 2 / 59 (3.39%) 2 | |
| Vomiting alternative dictionary used: MedDRA 9.0 subjects affected / exposed occurrences (all) | 4 / 114 (3.51%) 4 | 2 / 59 (3.39%) 2 | |
| Teething alternative dictionary used: MedDRA 9.0 subjects affected / exposed occurrences (all) | 1 / 114 (0.88%) 1 | 1 / 59 (1.69%) 1 | |
| Eructation alternative dictionary used: MedDRA 9.0 subjects affected / exposed occurrences (all) | 1 / 114 (0.88%) 1 | 0 / 59 (0.00%) 0 | |
| Constipation alternative dictionary used: MedDRA 9.0 subjects affected / exposed occurrences (all) | 1 / 114 (0.88%) 1 | 0 / 59 (0.00%) 0 | |
| Abdominal pain upper alternative dictionary used: MedDRA 9.0 subjects affected / exposed occurrences (all) | 0 / 114 (0.00%) 0 | 1 / 59 (1.69%) 1 | |
| Salivary hypersecretion | | | |

| | | | |
|--|---------------------------------|--------------------------------|--|
| <p>alternative dictionary used: MedDRA 9.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 114 (0.00%)</p> <p>0</p> | <p>1 / 59 (1.69%)</p> <p>1</p> | |
| <p>Aphthous stomatitis</p> <p>alternative dictionary used: MedDRA 9.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 114 (0.00%)</p> <p>0</p> | <p>1 / 59 (1.69%)</p> <p>1</p> | |
| <p>Skin and subcutaneous tissue disorders</p> <p>Scab</p> <p>alternative dictionary used: MedDRA 9.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 114 (0.88%)</p> <p>1</p> | <p>0 / 59 (0.00%)</p> <p>0</p> | |
| <p>Dermatitis diaper</p> <p>alternative dictionary used: MedDRA 9.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 114 (0.88%)</p> <p>1</p> | <p>0 / 59 (0.00%)</p> <p>0</p> | |
| <p>Swelling face</p> <p>alternative dictionary used: MedDRA 9.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 114 (0.88%)</p> <p>1</p> | <p>0 / 59 (0.00%)</p> <p>0</p> | |
| <p>Skin irritation</p> <p>alternative dictionary used: MedDRA 9.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 114 (0.88%)</p> <p>1</p> | <p>0 / 59 (0.00%)</p> <p>0</p> | |
| <p>Rash</p> <p>alternative dictionary used: MedDRA 9.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 114 (0.88%)</p> <p>2</p> | <p>0 / 59 (0.00%)</p> <p>0</p> | |
| <p>Urticaria</p> <p>alternative dictionary used: MedDRA 9.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 114 (0.88%)</p> <p>1</p> | <p>0 / 59 (0.00%)</p> <p>0</p> | |
| <p>Rash papular</p> <p>alternative dictionary used: MedDRA 9.0</p> | | | |

| | | | |
|--|--|--|--|
| subjects affected / exposed occurrences (all) | 0 / 114 (0.00%) 0 | 1 / 59 (1.69%) 1 | |
| Musculoskeletal and connective tissue disorders Muscle spasms alternative dictionary used: MedDRA 9.0 subjects affected / exposed occurrences (all) | 0 / 114 (0.00%) 0 | 1 / 59 (1.69%) 1 | |
| Infections and infestations Upper respiratory tract infection alternative dictionary used: MedDRA 9.0 subjects affected / exposed occurrences (all) Nasopharyngitis alternative dictionary used: MedDRA 9.0 subjects affected / exposed occurrences (all) Sinusitis alternative dictionary used: MedDRA 9.0 subjects affected / exposed occurrences (all) Otitis media alternative dictionary used: MedDRA 9.0 subjects affected / exposed occurrences (all) Gastroenteritis viral alternative dictionary used: MedDRA 9.0 subjects affected / exposed occurrences (all) Viral rash alternative dictionary used: MedDRA 9.0 subjects affected / exposed occurrences (all) Viral upper respiratory tract infection alternative dictionary used: MedDRA 9.0 | 3 / 114 (2.63%) 3 1 / 114 (0.88%) 1 1 / 114 (0.88%) 1 3 / 114 (2.63%) 3 1 / 114 (0.88%) 1 1 / 114 (0.88%) 1 | 2 / 59 (3.39%) 2 0 / 59 (0.00%) 0 2 / 59 (3.39%) 2 0 / 59 (0.00%) 0 1 / 59 (1.69%) 1 0 / 59 (0.00%) 0 | |

| | | | |
|--|-----------------|----------------|--|
| subjects affected / exposed | 1 / 114 (0.88%) | 2 / 59 (3.39%) | |
| occurrences (all) | 1 | 2 | |
| Viral pharyngitis | | | |
| alternative dictionary used: MedDRA 9.0 | | | |
| subjects affected / exposed | 0 / 114 (0.00%) | 1 / 59 (1.69%) | |
| occurrences (all) | 0 | 1 | |
| Gastroenteritis | | | |
| alternative dictionary used: MedDRA 9.0 | | | |
| subjects affected / exposed | 2 / 114 (1.75%) | 0 / 59 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Folliculitis | | | |
| alternative dictionary used: MedDRA 9.0 | | | |
| subjects affected / exposed | 1 / 114 (0.88%) | 0 / 59 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hordeolum | | | |
| alternative dictionary used: MedDRA 9.0 | | | |
| subjects affected / exposed | 1 / 114 (0.88%) | 0 / 59 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Urinary tract infection | | | |
| alternative dictionary used: MedDRA 9.0 | | | |
| subjects affected / exposed | 0 / 114 (0.00%) | 1 / 59 (1.69%) | |
| occurrences (all) | 0 | 1 | |
| Metabolism and nutrition disorders | | | |
| Anorexia | | | |
| alternative dictionary used: MedDRA 9.0 | | | |
| subjects affected / exposed | 0 / 114 (0.00%) | 1 / 59 (1.69%) | |
| occurrences (all) | 0 | 1 | |
| Dehydration | | | |
| alternative dictionary used: MedDRA 9.0 | | | |
| subjects affected / exposed | 0 / 114 (0.00%) | 1 / 59 (1.69%) | |
| occurrences (all) | 0 | 1 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 20 February 2008 | <p>The protocol was amended to incorporate changes based on comments received by the Food and Drug Administration to the pre-IND file dated 14 November 2007. Efficacy assessments and serum drug concentration to assess compliance/ drug exposure were incorporated. Children aged 1 but less than 2 years were added to the inclusion criteria.</p> <p>The upper age for inclusion was clarified for children to less than 6 years of age.</p> <p>Information regarding pharmacokinetic modeling to predict dosing regimen in children less than 6 was added.</p> |
| 28 March 2008 | <p>The protocol was amended primarily to revise the exclusion criteria to require the specified washout period for subjects who are receiving exclusionary medications via breast milk during the course of the study.</p> <p>The laboratory texts exclusion criteria was amended to clarify that prior written approval from the UCB Clinical Research Physician for out of range laboratory tests is not required before enrolling a subject in the study. The decision to enroll such a subject was left up to the discretion of the Investigator.</p> <p>The prohibited concomitant medications exclusion criterion was amended to clarify that subjects taking single ingredient guaifenesin products at the time of study entry will not be required to perform the wash-out period, and that is the only cough or cold medication that subjects were allowed to take during the study period.</p> |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported