



## Clinical trial results:

### Efficacy and safety of an alcohol-free formulation of 0.15% benzydamine spray in children with sore throat. Randomized, double blind, placebo-controlled study

#### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2009-014401-13  |
| Trial protocol           | IT AT SK RO ES  |
| Global end of trial date | 21 October 2011 |

#### Results information

|                                   |   |
|-----------------------------------|---|
| Result version number             | v2 (current)  |
| This version publication date     | 18 August 2018  |
| First version publication date    | 02 August 2015  |
| Version creation reason           | <ul style="list-style-type: none"><li>Changes to summary attachments</li></ul> A summary of results is uploaded replacing the CSR |
| Summary attachment (see zip file) | Synopsis (2009_014401-13.pdf)   |

#### Trial information

##### Trial identification

|                       |               |
|-----------------------|---------------|
| Sponsor protocol code | 030(B)SC09047 |
|-----------------------|---------------|

##### Additional study identifiers

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

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | ACRAF SpA   |
| Sponsor organisation address | Piazzale della stazione, s.n.c., S.Palomba- Pomezia (Rome), Italy, 00071        |
| Public contact               | Clinical Trial application Unit, ACRAF SpA, +39 0691045335, ctaunit@angelini.it |
| Scientific contact           | Clinical Trial application Unit, ACRAF SpA, +39 0691045432, ctaunit@angelini.it |

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                       | 07 March 2013   |
| Is this the analysis of the primary completion data? | No              |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 21 October 2011 |
| Was the trial ended prematurely?                     | No              |

Notes:

## General information about the trial

Main objective of the trial:

Evaluation of the analgesic activity of 0.15% benzydamine spray in single administration compared to placebo.

Protection of trial subjects:

The study was performed in accordance with the protocol (unless otherwise indicated), Good Clinical Practice (GCP) requirements, the Declaration of Helsinki (updated version), and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 01 April 2010 |
| 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 | Romania: 89  |
| Country: Number of subjects enrolled | Slovakia: 10 |
| Country: Number of subjects enrolled | Spain: 3     |
| Country: Number of subjects enrolled | Austria: 40  |
| Country: Number of subjects enrolled | Italy: 59    |
| Worldwide total number of subjects   | 201          |
| EEA total number of subjects         | 201          |

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)                     | 194 |
| Adolescents (12-17 years)                 | 7   |
| Adults (18-64 years)                      | 0   |

|                     |   |
|---------------------|---|
| From 65 to 84 years | 0 |
| 85 years and over   | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Participants were male and female outpatients 6-12 years old with objective findings that confirm the sore throat diagnosis with Tonsillo-Pharyngitis Scale > 6 points; onset of sore throat symptoms within 7 days; moderate-to-severe sore throat (Children's Sore Throat Pain Thermometer > 120mm).

### 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          |

### Arms

|                              |             |
|------------------------------|-------------|
| Are arms mutually exclusive? | Yes         |
| <b>Arm title</b>             | Benzydamine |

Arm description:

Benzydamine 0,15 % spray, a single application (4 nebulizations).

|  |                  |
|--|------------------|
| Arm type                               | Experimental     |
| Investigational medicinal product name | Benzydamine      |
| Investigational medicinal product code |                  |
| Other name                             |                  |
| Pharmaceutical forms                   | Oromucosal spray |
| Routes of administration               | Oromucosal use   |

Dosage and administration details:

A single application constituted of 4 nebulizations; each nebulization corresponds to 1.17 ml and contains about 0.25 mg of benzydamine.

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

Arm description:

Placebo spray, a single application ( 4 nebulizations).

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

Dosage and administration details:

A single application, constituted of 4 nebulizations.

| <b>Number of subjects in period 1</b> | Benzydamine | Placebo |
|---------------------------------------|-------------|---------|
| Started                               | 99          | 102     |
| Completed                             | 99          | 102     |

## Baseline characteristics

### Reporting groups

|                       |             |
|-----------------------|-------------|
| Reporting group title | Benzydamine |
|-----------------------|-------------|

Reporting group description:

Benzydamine 0,15 % spray, a single application (4 nebulizations).

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

Reporting group description:

Placebo spray, a single application ( 4 nebulizations).

| Reporting group values                                | Benzydamine | Placebo | Total |
|---|-------------|---------|-------|
| Number of subjects                                    | 99          | 102     | 201   |
| Age categorical<br>Units: Subjects                    |             |         |       |
| In utero  | 0           | 0       | 0     |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0           | 0       | 0     |
| Newborns (0-27 days)                                  | 0           | 0       | 0     |
| Infants and toddlers (28 days-23<br>months)           | 0           | 0       | 0     |
| Children (2-11 years)                                 | 95          | 99      | 194   |
| Adolescents (12-17 years)                             | 4           | 3       | 7     |
| Adults (18-64 years)                                  | 0           | 0       | 0     |
| From 65-84 years                                      | 0           | 0       | 0     |
| 85 years and over                                     | 0           | 0       | 0     |
| Age continuous<br>Units: years                        |             |         |       |
| arithmetic mean                                       | 8.8         | 8.7     | -     |
| standard deviation                                    | ± 1.8       | ± 1.7   | -     |
| Gender categorical<br>Units: Subjects                 |             |         |       |
| Female  | 47          | 57      | 104   |
| Male  | 52          | 45      | 97    |

## End points

### End points reporting groups

|   |             |
|---|-------------|
| Reporting group title   | Benzydamine |
| Reporting group description:<br>Benzydamine 0,15 % spray, a single application (4 nebulizations). |             |
| Reporting group title   | Placebo     |
| Reporting group description:<br>Placebo spray, a single application ( 4 nebulizations).           |             |

### Primary: SPID Child ITT population

|   |                           |
|---|---------------------------|
| End point title   | SPID Child ITT population |
| End point description:<br>Sum of Pain Intensity Difference Score (SPID) of the Children's Sore Throat Pain Thermometer scale by the child. CSTPT is a vertical 21 point (200 mm) VAS anchored on the bottom by the sentence "IT DOESN'T HURT AT ALL" and at the top "IT HURTS A LOT", divided at 1 cm intervals from 0 to 20. |                           |
| End point type  | Primary                   |
| End point timeframe:<br>Baseline and then after 15, 30, 45, 60 and 90 minutes from the study medications administrations.   |                           |

| End point values                     | Benzydamine        | Placebo            |  |  |
|--------------------------------------|--------------------|--------------------|--|--|
| Subject group type                   | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed          | 99                 | 102                |  |  |
| Units: mm                            |                    |                    |  |  |
| arithmetic mean (standard deviation) | -3919.1 (± 2629.7) | -4127.7 (± 2495.6) |  |  |

### Statistical analyses

|   |                                      |
|---|--------------------------------------|
| Statistical analysis title              | SPID child: Benzydamine- Placebo/ITT |
| Comparison groups                       | Benzydamine v Placebo                |
| Number of subjects included in analysis | 201                                  |
| Analysis specification                  | Pre-specified                        |
| Analysis type                           | superiority                          |
| P-value                                 | = 0.7041 <sup>[1]</sup>              |
| Method                                  | ANOVA                                |

Notes:

[1] - Not significant

### Primary: SPID Child PP population

|   |                          |
|---|--------------------------|
| End point title   | SPID Child PP population |
| End point description:<br>Sum of Pain Intensity Difference Score (SPID) of the Children's Sore Throat Pain Thermometer scale by |                          |

the child. CSTPT is a vertical 21 point (200 mm) VAS anchored on the bottom by the sentence "IT DOESN'T HURT AT ALL" and at the top "IT HURTS A LOT", divided at 1 cm intervals from 0 to 20.

|  |         |
|--|---------|
| End point type   | Primary |
| End point timeframe:   |         |
| Baseline and after 15, 30, 45, 60 and 90 minutes from the study medications administrations. |         |

| End point values                     | Benzydamine             | Placebo                 |  |  |
|--------------------------------------|-------------------------|-------------------------|--|--|
| Subject group type                   | Reporting group         | Reporting group         |  |  |
| Number of subjects analysed          | 81                      | 80                      |  |  |
| Units: mm                            |                         |                         |  |  |
| arithmetic mean (standard deviation) | -3855.9 ( $\pm$ 2696.8) | -4276.5 ( $\pm$ 2567.2) |  |  |

### Statistical analyses

|   |                                    |
|---|------------------------------------|
| Statistical analysis title              | SPID child: Benzydamine-Placebo/PP |
| Comparison groups                       | Benzydamine v Placebo              |
| Number of subjects included in analysis | 161                                |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           | superiority                        |
| P-value                                 | = 0.7277 <sup>[2]</sup>            |
| Method                                  | ANOVA                              |

Notes:

[2] - Not significant

### Secondary: SPID Parent ITT population

|   |                            |
|---|----------------------------|
| End point title   | SPID Parent ITT population |
| End point description:  |                            |
| Sum of Pain Intensity Difference Score (SPID) of the Children's Sore Throat Pain Intensity scale by the parent. This scale is a horizontal VAS presented as a line (100 mm in length) anchored by word descriptors at each end: on the left by the sentence "NO PAIN", and on the right "VERY SEVERE PAIN". |                            |
| End point type  | Secondary                  |
| End point timeframe:  |                            |
| Baseline and then after 15, 30, 45, 60 and 90 minutes from the study medications administrations.   |                            |



| End point values                     | Benzydamine             | Placebo                 |  |  |
|--------------------------------------|-------------------------|-------------------------|--|--|
| Subject group type                   | Reporting group         | Reporting group         |  |  |
| Number of subjects analysed          | 99                      | 102                     |  |  |
| Units: mm                            |                         |                         |  |  |
| arithmetic mean (standard deviation) | -1830.7 ( $\pm$ 1202.5) | -1922.9 ( $\pm$ 1387.1) |  |  |

## Statistical analyses

| Statistical analysis title              | SPID parent : Benzydamine- Placebo/ITT |
|---|--|
| Comparison groups                       | Benzydamine v Placebo                  |
| Number of subjects included in analysis | 201                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | superiority                            |
| P-value                                 | = 0.7041 <sup>[3]</sup>                |
| Method                                  | ANOVA                                  |

Notes:

[3] - Not significant

## Secondary: SPID Investigator ITT population

|                 |                                  |
|-----------------|----------------------------------|
| End point title | SPID Investigator ITT population |
|-----------------|----------------------------------|

End point description:

Sum of Pain Intensity Difference Score (SPID) of the Children's Sore Throat Pain Intensity scale by the investigator. This scale is a horizontal VAS presented as a line (100 mm in length) anchored by word descriptors at each end: on the left by the sentence "NO PAIN", and on the right "VERY SEVERE PAIN".

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

End point timeframe:

Baseline and then after 15, 30, 45, 60 and 90 minutes from the study medications administrations.

| End point values                     | Benzydamine             | Placebo                 |  |  |
|--------------------------------------|-------------------------|-------------------------|--|--|
| Subject group type                   | Reporting group         | Reporting group         |  |  |
| Number of subjects analysed          | 99                      | 102                     |  |  |
| Units: mm                            |                         |                         |  |  |
| arithmetic mean (standard deviation) | -1902.5 ( $\pm$ 1012.1) | -1895.7 ( $\pm$ 1176.8) |  |  |

## Statistical analyses

| Statistical analysis title | SPID investigator: Benzydamine- Placebo/ITT |
|----------------------------|---|
| Comparison groups          | Benzydamine v Placebo                       |

|   |                         |
|---|-------------------------|
| Number of subjects included in analysis | 201                     |
| Analysis specification                  | Pre-specified           |
| Analysis type                           | superiority             |
| P-value                                 | = 0.7303 <sup>[4]</sup> |
| Method                                  | ANOVA                   |

Notes:

[4] - Not significant

### Secondary: TOTPAR Child ITT population

|                 |                             |
|-----------------|-----------------------------|
| End point title | TOTPAR Child ITT population |
|-----------------|-----------------------------|

End point description:

Children's Sore Throat Relief was estimated as the area under the pain relief versus time curve (TOTPAR). At all fixed times, the child was also asked to indicate pain intensity using the horizontal scale to rate the sore throat relief, consisting of 5 cartoon faces ranging from a tearful face for "NO RELIEF " on the left to a smiling face for "COMPLETE RELIEF " on the right.

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

End point timeframe:

After 15, 30, 45, 60 and 90 minutes from the study medications administrations.

| End point values                     | Benzydamine     | Placebo         |  |  |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type                   | Reporting group | Reporting group |  |  |
| Number of subjects analysed          | 99              | 102             |  |  |
| Units: score on a scale              |                 |                 |  |  |
| arithmetic mean (standard deviation) | 214.1 (± 65.1)  | 217.3 (± 65.6)  |  |  |

### Statistical analyses

|   |                                 |
|---|---------------------------------|
| <b>Statistical analysis title</b>       | TOTPAR: Benzydamine-Placebo/ITT |
| Comparison groups                       | Benzydamine v Placebo           |
| Number of subjects included in analysis | 201                             |
| Analysis specification                  | Pre-specified                   |
| Analysis type                           | superiority                     |
| P-value                                 | = 0.9082 <sup>[5]</sup>         |
| Method                                  | ANOVA                           |

Notes:

[5] - Not significant

### Secondary: SPID Parent PP population

|                 |                           |
|-----------------|---------------------------|
| End point title | SPID Parent PP population |
|-----------------|---------------------------|

End point description:

Sum of Pain Intensity Difference Score (SPID) of the Children's Sore Throat Pain Intensity Scale by the parent. This scale is a horizontal VAS presented as a line (100 mm in length) anchored by word descriptors at each end: on the left by the sentence "NO PAIN", and on the right "VERY SEVERE PAIN".

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

End point timeframe:

Baseline and after 15, 30, 45, 60 and 90 minutes from the study medications administrations.

| End point values                     | Benzydamine             | Placebo                 |  |  |
|--------------------------------------|-------------------------|-------------------------|--|--|
| Subject group type                   | Reporting group         | Reporting group         |  |  |
| Number of subjects analysed          | 81                      | 80                      |  |  |
| Units: mm                            |                         |                         |  |  |
| arithmetic mean (standard deviation) | -1738.5 ( $\pm$ 1254.5) | -1984.6 ( $\pm$ 1460.5) |  |  |

## Statistical analyses

|   |                                       |
|---|---------------------------------------|
| Statistical analysis title              | SPID parent : Benzydamine- Placebo/PP |
| Comparison groups                       | Benzydamine v Placebo                 |
| Number of subjects included in analysis | 161                                   |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | superiority                           |
| P-value                                 | = 0.7708 <sup>[6]</sup>               |
| Method                                  | ANOVA                                 |

Notes:

[6] - Not significant

## Secondary: SPID Investigator PP population

|   |                                 |
|---|---------------------------------|
| End point title   | SPID Investigator PP population |
| End point description:  |                                 |
| Sum of Pain Intensity Difference Score (SPID) of the Children's Sore Throat Pain Intensity scale by the investigator. This scale is a horizontal VAS presented as a line (100 mm in length) anchored by word descriptors at each end: on the left by the sentence "NO PAIN", and on the right "VERY SEVERE PAIN". |                                 |
| End point type  | Secondary                       |

End point timeframe:

Baseline and after 15, 30, 45, 60 and 90 minutes from the study medications administrations.

| End point values                     | Benzydamine             | Placebo                 |  |  |
|--------------------------------------|-------------------------|-------------------------|--|--|
| Subject group type                   | Reporting group         | Reporting group         |  |  |
| Number of subjects analysed          | 81                      | 80                      |  |  |
| Units: mm                            |                         |                         |  |  |
| arithmetic mean (standard deviation) | -1894.2 ( $\pm$ 1055.7) | -1963.8 ( $\pm$ 1248.2) |  |  |

## Statistical analyses

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | SPID investigator : Benzydamine- Placebo/PP |
| Comparison groups                       | Benzydamine v Placebo                       |
| Number of subjects included in analysis | 161   |
| Analysis specification                  | Pre-specified                               |
| Analysis type                           | superiority                                 |
| P-value                                 | = 0.5945 <sup>[7]</sup>                     |
| Method                                  | ANOVA                                       |

Notes:

[7] - Not significant

### Secondary: TOTPAR Child PP population

|  |                            |
|--|----------------------------|
| End point title  | TOTPAR Child PP population |
| End point description:   |                            |
| Children's Sore Throat Relief was estimated as the area under the pain relief versus time curve (TOTPAR). At all fixed times, the child was also asked to indicate pain intensity using the horizontal scale to rate the sore throat relief, consisting of 5 cartoon faces ranging from a tearful face for "NO RELIEF " on the left to a smiling face for "COMPLETE RELIEF " on the right. |                            |
| End point type   | Secondary                  |
| End point timeframe:   |                            |
| After 15, 30, 45, 60 and 90 minutes from the study medications administrations.  |                            |

|                                      |                 |                 |  |  |
|--------------------------------------|-----------------|-----------------|--|--|
| <b>End point values</b>              | Benzydamine     | Placebo         |  |  |
| Subject group type                   | Reporting group | Reporting group |  |  |
| Number of subjects analysed          | 81              | 79              |  |  |
| Units: score on a scale              |                 |                 |  |  |
| arithmetic mean (standard deviation) | 214.1 (± 69.5)  | 220.5 (± 68.5)  |  |  |

### Statistical analyses

|   |                                |
|---|--------------------------------|
| <b>Statistical analysis title</b>       | TOTPAR: Benzydamine-Placebo/PP |
| Comparison groups                       | Benzydamine v Placebo          |
| Number of subjects included in analysis | 160                            |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           | superiority                    |
| P-value                                 | = 0.8113 <sup>[8]</sup>        |
| Method                                  | ANOVA                          |

Notes:

[8] - Not significant

### Secondary: Tolerability evaluation Investigator/ good 90 minutes

|   |   |
|---|---|
| End point title   | Tolerability evaluation Investigator/ good 90 minutes |
| End point description:  |   |
| A global tolerability rating was expressed by the Investigator through a 5-point categorical scale (very good, good, fair, poor and very poor). |   |
| End point type  | Secondary   |

End point timeframe:  
after 90 minutes and 4 days post-treatment

| End point values            | Benzydamine     | Placebo         |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 99              | 102             |  |  |
| Units: percent              |                 |                 |  |  |
| number (not applicable)     | 1               | 0               |  |  |

### Statistical analyses

| Statistical analysis title              | Tolerability evaluation investigator |
|---|--------------------------------------|
| Comparison groups                       | Benzydamine v Placebo                |
| Number of subjects included in analysis | 201                                  |
| Analysis specification                  | Pre-specified                        |
| Analysis type                           | superiority                          |
| P-value                                 | = 0.3173 <sup>[9]</sup>              |
| Method                                  | Cochran-Mantel-Haenszel              |

Notes:

[9] - Not significant

### Secondary: Tolerability evaluation Investigator/very good 90 minutes

|   |   |
|---|---|
| End point title   | Tolerability evaluation Investigator/very good 90 minutes |
| End point description:<br>A global tolerability rating was expressed by the Investigator through a 5-point categorical scale (very good, good, fair, poor and very poor). |   |
| End point type  | Secondary   |
| End point timeframe:<br>after 90 minutes and 4 days post-treatment  |   |

| End point values            | Benzydamine     | Placebo         |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 99              | 102             |  |  |
| Units: percent              |                 |                 |  |  |
| number (not applicable)     | 99              | 100             |  |  |

### Statistical analyses

| Statistical analysis title | Tolerability evaluation investigator |
|----------------------------|--------------------------------------|
| Comparison groups          | Benzydamine v Placebo                |

|   |                          |
|---|--------------------------|
| Number of subjects included in analysis | 201                      |
| Analysis specification                  | Pre-specified            |
| Analysis type                           | superiority              |
| P-value                                 | = 0.3173 <sup>[10]</sup> |
| Method                                  | Cochran-Mantel-Haenszel  |

Notes:

[10] - Not significant

#### Secondary: Tolerability evaluation Investigator/ good Day 4

|                 |  |
|-----------------|--|
| End point title | Tolerability evaluation Investigator/ good Day 4 |
|-----------------|--|

End point description:

A global tolerability rating was expressed by the Investigator through a 5-point categorical scale (very good, good, fair, poor and very poor).

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

End point timeframe:

after 90 minutes and 4 days post-treatment

| End point values            | Benzydamine     | Placebo         |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 99              | 102             |  |  |
| Units: percent              |                 |                 |  |  |
| number (not applicable)     | 0               | 1               |  |  |

#### Statistical analyses

|   |                                      |
|---|--------------------------------------|
| Statistical analysis title              | Tolerability evaluation investigator |
| Comparison groups                       | Benzydamine v Placebo                |
| Number of subjects included in analysis | 201                                  |
| Analysis specification                  | Pre-specified                        |
| Analysis type                           | superiority                          |
| P-value                                 | = 0.3173 <sup>[11]</sup>             |
| Method                                  | Cochran-Mantel-Haenszel              |

Notes:

[11] - Not significant

#### Secondary: Tolerability evaluation Investigator/ very good Day 4

|                 |   |
|-----------------|---|
| End point title | Tolerability evaluation Investigator/ very good Day 4 |
|-----------------|---|

End point description:

A global tolerability rating was expressed by the Investigator through a 5-point categorical scale (very good, good, fair, poor and very poor).

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

End point timeframe:

after 90 minutes and 4 days post-treatment

| End point values            | Benzydamine     | Placebo         |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 99              | 102             |  |  |
| Units: percent              |                 |                 |  |  |
| number (not applicable)     | 100             | 99              |  |  |

### Statistical analyses

| Statistical analysis title              | Tolerability evaluation investigator |
|---|--------------------------------------|
| Comparison groups                       | Benzydamine v Placebo                |
| Number of subjects included in analysis | 201                                  |
| Analysis specification                  | Pre-specified                        |
| Analysis type                           | superiority                          |
| P-value                                 | = 0.3173 <sup>[12]</sup>             |
| Method                                  | Cochran-Mantel-Haenszel              |

Notes:

[12] - Not significant

### Secondary: Taste evaluation Child- Fresh

| End point title | Taste evaluation Child- Fresh |
|-----------------|-------------------------------|
|-----------------|-------------------------------|

End point description:

The Investigator asked the children the taste of the administered formulation, in terms of fresh (yes/no), sweet (yes/no), bitter (yes/no), and a global assessment in terms of good or bad. Only positive answers are reported.

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

End point timeframe:

After the first administration and before the first efficacy assessment.

| End point values            | Benzydamine     | Placebo         |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 99              | 102             |  |  |
| Units: percent              |                 |                 |  |  |
| number (not applicable)     | 88.9            | 88.2            |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Taste evaluation Child- Sweet

|  |                               |
|--|-------------------------------|
| End point title  | Taste evaluation Child- Sweet |
| End point description:<br>The Investigator asked the children the taste of the administered formulation, in terms of fresh (yes/no), sweet (yes/no), bitter (yes/no), and a global assessment in terms of good or bad. Only positive answers are reported. |                               |
| End point type   | Secondary                     |
| End point timeframe:<br>After the first administration and before the first efficacy assessment.   |                               |

| End point values            | Benzydamine     | Placebo         |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 99              | 102             |  |  |
| Units: percent              |                 |                 |  |  |
| number (not applicable)     | 67.7            | 66.7            |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Taste evaluation Child- Bitter

|  |                                |
|--|--------------------------------|
| End point title  | Taste evaluation Child- Bitter |
| End point description:<br>The Investigator asked the children the taste of the administered formulation, in terms of fresh (yes/no), sweet (yes/no), bitter (yes/no), and a global assessment in terms of good or bad. Only positive answers are reported. |                                |
| End point type   | Secondary                      |
| End point timeframe:<br>After the first administration and before the first efficacy assessment.   |                                |

| End point values            | Benzydamine     | Placebo         |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 99              | 102             |  |  |
| Units: percent              |                 |                 |  |  |
| number (not applicable)     | 12.1            | 14.7            |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Taste evaluation Child- Global assessment- Good

|                 |   |
|-----------------|---|
| End point title | Taste evaluation Child- Global assessment- Good |
|-----------------|---|



End point description:

The Investigator asked the children the taste of the administered formulation, in terms of global assessment in terms of good or bad.

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

End point timeframe:

After the first administration and before the first efficacy assessment.

| End point values            | Benzydamine     | Placebo         |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 99              | 102             |  |  |
| Units: percent              |                 |                 |  |  |
| number (not applicable)     | 90.9            | 93.1            |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Taste evaluation Child- Global assessment- Bad

|                 |  |
|-----------------|--|
| End point title | Taste evaluation Child- Global assessment- Bad |
|-----------------|--|

End point description:

The Investigator asked the children the taste of the administered formulation, in terms of global assessment in terms of good or bad.

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

End point timeframe:

After the first administration and before the first efficacy assessment.

| End point values            | Benzydamine     | Placebo         |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 99              | 102             |  |  |
| Units: percent              |                 |                 |  |  |
| number (not applicable)     | 9.1             | 6.9             |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Baseline up to the final visit (day 4)

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 14.1 |
|--------------------|------|

### Reporting groups

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

Reporting group description: -

|                       |             |
|-----------------------|-------------|
| Reporting group title | Benzydamine |
|-----------------------|-------------|

Reporting group description: -

| Serious adverse events                            | Placebo         | Benzydamine    |  |
|---|-----------------|----------------|--|
| Total subjects affected by serious adverse events |                 |                |  |
| subjects affected / exposed                       | 0 / 102 (0.00%) | 0 / 99 (0.00%) |  |
| number of deaths (all causes)                     | 0               | 0              |  |
| number of deaths resulting from adverse events    | 0               | 0              |  |

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

| Non-serious adverse events                            | Placebo           | Benzydamine      |  |
|---|-------------------|------------------|--|
| Total subjects affected by non-serious adverse events |                   |                  |  |
| subjects affected / exposed                           | 13 / 102 (12.75%) | 12 / 99 (12.12%) |  |
| General disorders and administration site conditions  |                   |                  |  |
| Pyrexia   |                   |                  |  |
| subjects affected / exposed                           | 7 / 102 (6.86%)   | 7 / 99 (7.07%)   |  |
| occurrences (all)                                     | 7                 | 7                |  |

## **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