



## Clinical trial results:

**An open label, 52 week, multicenter study, of long term management to evaluate effectiveness, tolerability and safety of pimecrolimus cream 1%, Elidel® in pediatric patients with mild to moderate atopic dermatitis in a daily practice**

### Summary

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2017-001766-25    |
| Trial protocol           | Outside EU/EEA    |
| Global end of trial date | 18 September 2007 |

### Results information

|                                |               |
|--------------------------------|---------------|
| Result version number          | v1 (current)  |
| This version publication date  | 25 March 2018 |
| First version publication date | 25 March 2018 |

### Trial information

#### Trial identification

|                       |              |
|-----------------------|--------------|
| Sponsor protocol code | CASM981CVE01 |
|-----------------------|--------------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT00509990 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Novartis Pharma AG   |
| Sponsor organisation address | CH-4002, Basel, Switzerland,                                   |
| Public contact               | Clinical Disclosure Office, Novartis Pharma AG, +41 613241111, |
| Scientific contact           | Clinical Disclosure Office, Novartis Pharma AG, +41 613241111, |

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                       | 18 September 2007 |
| Is this the analysis of the primary completion data? | No                |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 18 September 2007 |
| Was the trial ended prematurely?                     | No                |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the use of corticosteroid from day 1 to week 52 in patients using Elidel® cream 1% for the long term management in mild to moderate atopic dermatitis (AD) in pediatric patients in a daily practice.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 26 April 2005 |
| 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 | Mexico: 90                            |
| Country: Number of subjects enrolled | Venezuela, Bolivarian Republic of: 89 |
| Worldwide total number of subjects   | 179                                   |
| 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)  | 62  |
| Children (2-11 years)                     | 117 |
| 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: -

### Pre-assignment

Screening details:

A total of 179 children between 3 months and 12 year old, from a total of 10 centers located in Mexico and Venezuela, were enrolled.

### Period 1

|                              |                                 |
|------------------------------|---------------------------------|
| Period 1 title               | Overall Period (overall period) |
| Is this the baseline period? | Yes                             |
| Allocation method            | Non-randomised - controlled     |
| Blinding used                | Not blinded                     |

### Arms

|  |                        |
|--|------------------------|
| Arm title                              | Pimecrolimus cream 1 % |
| Arm description: -                     |                        |
| Arm type                               | Experimental           |
| Investigational medicinal product name | Pimecrolimus cream 1 % |
| Investigational medicinal product code |                        |
| Other name                             | Elidel                 |
| Pharmaceutical forms                   | Cream                  |
| Routes of administration               | Topical use            |

Dosage and administration details:

Elidel® b.i.d. on "as needed" basis to all affected areas.

| Number of subjects in period 1    | Pimecrolimus cream 1 % |
|-----------------------------------|------------------------|
| Started                           | 179                    |
| Completed                         | 157                    |
| Not completed                     | 22                     |
| Consent withdrawn by subject      | 7                      |
| Protocol violation                | 1                      |
| Unsatisfactory therapeutic effect | 1                      |
| Lost to follow-up                 | 12                     |
| Enrollment failure                | 1                      |

## Baseline characteristics

### Reporting groups

|                       |                |
|-----------------------|----------------|
| Reporting group title | Overall Period |
|-----------------------|----------------|

Reporting group description: -

| Reporting group values                                | Overall Period | Total |  |
|---|----------------|-------|--|
| Number of subjects                                    | 179            | 179   |  |
| Age categorical                                       |                |       |  |
| Units: Subjects                                       |                |       |  |
| In utero  | 0              | 0     |  |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0              | 0     |  |
| Newborns (0-27 days)                                  | 0              | 0     |  |
| Infants and toddlers (28 days-23<br>months)           | 62             | 62    |  |
| Children (2-11 years)                                 | 117            | 117   |  |
| Adolescents (12-17 years)                             | 0              | 0     |  |
| Adults (18-64 years)                                  | 0              | 0     |  |
| From 65-84 years                                      | 0              | 0     |  |
| 85 years and over                                     | 0              | 0     |  |
| Age continuous  |                |       |  |
| Units: years  |                |       |  |
| arithmetic mean                                       | 4.13           |       |  |
| standard deviation                                    | ± 3.28         | -     |  |
| Gender categorical                                    |                |       |  |
| Units: Subjects                                       |                |       |  |
| Female  | 96             | 96    |  |
| Male  | 83             | 83    |  |

## End points

### End points reporting groups

|                                |                        |
|--------------------------------|------------------------|
| Reporting group title          | Pimecrolimus cream 1 % |
| Reporting group description: - |                        |

### Primary: Total and relative number of patients distribution based on Corticosteroid use

|   |   |
|---|---|
| End point title   | Total and relative number of patients distribution based on Corticosteroid use <sup>[1]</sup> |
| End point description:<br>Corticosteroids use by patients during the course of the study. |   |
| End point type  | Primary   |
| End point timeframe:<br>up to week 52   |   |

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: No statistical analyses have been reported for this primary end point.

| End point values            | Pimecrolimus cream 1 % |  |  |  |
|-----------------------------|------------------------|--|--|--|
| Subject group type          | Reporting group        |  |  |  |
| Number of subjects analysed | 130 <sup>[2]</sup>     |  |  |  |
| Units: patients             |                        |  |  |  |
| number (not applicable)     |                        |  |  |  |
| No                          | 84                     |  |  |  |
| Yes                         | 46                     |  |  |  |

Notes:

[2] - Primary Endpoint population (per protocol)

### Statistical analyses

No statistical analyses for this end point

### Primary: Total and relative number of patients based on number of disease flares that required Corticosteroids treatment

|                                       |  |
|---------------------------------------|--|
| End point title                       | Total and relative number of patients based on number of disease flares that required Corticosteroids treatment <sup>[3]</sup> |
| End point description:                |  |
| End point type                        | Primary  |
| End point timeframe:<br>up to week 52 |  |

Notes:

[3] - 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: No statistical analyses have been reported for this primary end point.

|                             |                        |  |  |  |
|-----------------------------|------------------------|--|--|--|
| <b>End point values</b>     | Pimecrolimus cream 1 % |  |  |  |
| Subject group type          | Reporting group        |  |  |  |
| Number of subjects analysed | 130 <sup>[4]</sup>     |  |  |  |
| Units: patients             |                        |  |  |  |
| number (not applicable)     |                        |  |  |  |
| 01                          | 23                     |  |  |  |
| 02                          | 10                     |  |  |  |
| 03                          | 2                      |  |  |  |
| 04                          | 3                      |  |  |  |
| 05                          | 2                      |  |  |  |
| More than 5                 | 3                      |  |  |  |
| Total                       | 46                     |  |  |  |

Notes:

[4] - Primary Endpoint population (per protocol)

### Statistical analyses

No statistical analyses for this end point

### Primary: Duration of use of corticosteroids (non-continuous), within those patients that did use corticosteroids

|   |  |
|---|--|
| End point title   | Duration of use of corticosteroids (non-continuous), within those patients that did use corticosteroids <sup>[5]</sup> |
| End point description:<br>The average number of days Corticosteroids were used in the 52 week observation period. |  |
| End point type  | Primary  |
| End point timeframe:<br>up to week 52   |  |

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: No statistical analyses have been reported for this primary end point.

|                             |                        |  |  |  |
|-----------------------------|------------------------|--|--|--|
| <b>End point values</b>     | Pimecrolimus cream 1 % |  |  |  |
| Subject group type          | Reporting group        |  |  |  |
| Number of subjects analysed | 179 <sup>[6]</sup>     |  |  |  |
| Units: days                 |                        |  |  |  |
| number (not applicable)     |                        |  |  |  |
| Less than a week            | 15                     |  |  |  |
| 1-2 weeks                   | 12                     |  |  |  |
| 2-4 weeks                   | 12                     |  |  |  |
| More than a month           | 7                      |  |  |  |
| Total                       | 46                     |  |  |  |

Notes:

[6] - Primary Endpoint population (per protocol)

### Statistical analyses

No statistical analyses for this end point

## Secondary: Relative Patient distribution based on Investigator Global Assessment (IGA) per Visit

|   |   |
|---|---|
| End point title   | Relative Patient distribution based on Investigator Global Assessment (IGA) per Visit |
| End point description:<br>The evaluation of IGA indicates that the percentage of patients "without disease" and "almost without disease". |   |
| End point type  | Secondary   |
| End point timeframe:<br>up to week 52   |   |

| End point values                         | Pimecrolimus cream 1 % |  |  |  |
|--|------------------------|--|--|--|
| Subject group type                       | Reporting group        |  |  |  |
| Number of subjects analysed              | 179 <sup>[7]</sup>     |  |  |  |
| Units: percent                           |                        |  |  |  |
| number (not applicable)                  |                        |  |  |  |
| Visit 1 - No disease - Almost no disease | 17.9                   |  |  |  |
| Visit 1 - Mild disease - Severe Disease  | 82.1                   |  |  |  |
| Visit 1 - Unknown                        | 0                      |  |  |  |
| Visit 1 - Total                          | 100                    |  |  |  |
| Visit 1 - Base                           | 179                    |  |  |  |
| Visit 2 - No disease - Almost no disease | 69.5                   |  |  |  |
| Visit 2 - Mild disease - Severe Disease  | 29.9                   |  |  |  |
| Visit 2 - Unknown                        | 0.6                    |  |  |  |
| Visit 2 - Total                          | 100                    |  |  |  |
| Visit 2 - Base                           | 174                    |  |  |  |
| Visit 3 - No disease - Almost no disease | 78.8                   |  |  |  |
| Visit 3 - Mild disease - Severe Disease  | 21.12                  |  |  |  |
| Visit 3 - Unknown                        | 0                      |  |  |  |
| Visit 3 - Total                          | 100                    |  |  |  |
| Visit 3 - Base                           | 170                    |  |  |  |
| Visit 4 - No disease - Almost no disease | 82.9                   |  |  |  |
| Visit 4 - Mild disease - Severe Disease  | 16.5                   |  |  |  |
| Visit 4 - Unknown                        | 0.6                    |  |  |  |
| Visit 4 - Total                          | 100                    |  |  |  |
| Visit 4 - Base                           | 164                    |  |  |  |
| Visit 5 - No disease - Almost no disease | 78.6                   |  |  |  |
| Visit 5 - Mild disease - Severe Disease  | 21.4                   |  |  |  |
| Visit 5 - Unknown                        | 0                      |  |  |  |
| Visit 5 - Total                          | 100                    |  |  |  |
| Visit 5 - Base                           | 159                    |  |  |  |
| Visit 6 - No disease - Almost no disease | 80.9                   |  |  |  |
| Visit 6 - Mild disease - Severe Disease  | 19.1                   |  |  |  |
| Visit 6 - Unknown                        | 0                      |  |  |  |
| Visit 6 - Total                          | 100                    |  |  |  |
| Visit 6 - Base                           | 157                    |  |  |  |



Notes:

[7] - per protocol population

## Statistical analyses

No statistical analyses for this end point

### Secondary: Relative Patient distribution based on Investigator Facial Global Assessment per Visit

|                 |  |
|-----------------|--|
| End point title | Relative Patient distribution based on Investigator Facial Global Assessment per Visit |
|-----------------|--|

End point description:

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

End point timeframe:

up to week 52

| End point values                         | Pimecrolimus cream 1 % |  |  |  |
|--|------------------------|--|--|--|
| Subject group type                       | Reporting group        |  |  |  |
| Number of subjects analysed              | 179 <sup>[8]</sup>     |  |  |  |
| Units: percent                           |                        |  |  |  |
| number (not applicable)                  |                        |  |  |  |
| Visit 1 - No disease - Almost no disease | 63.1                   |  |  |  |
| Visit 1 - Mild disease - Severe Disease  | 3639                   |  |  |  |
| Visit 1 - Unknown                        | 0                      |  |  |  |
| Visit 1 - Total                          | 100                    |  |  |  |
| Visit 1 - Base                           | 179                    |  |  |  |
| Visit 2 - No disease - Almost no disease | 90.8                   |  |  |  |
| Visit 2 - Mild disease - Severe Disease  | 8.6                    |  |  |  |
| Visit 2 - Unknown                        | 0.6                    |  |  |  |
| Visit 2 - Total                          | 100                    |  |  |  |
| Visit 2 - Base                           | 174                    |  |  |  |
| Visit 3 - No disease - Almost no disease | 95.3                   |  |  |  |
| Visit 3 - Mild disease - Severe Disease  | 4.7                    |  |  |  |
| Visit 3 - Unknown                        | 0                      |  |  |  |
| Visit 3 - Total                          | 100                    |  |  |  |
| Visit 3 - Base                           | 170                    |  |  |  |
| Visit 4 - No disease - Almost no disease | 93.9                   |  |  |  |
| Visit 4 - Mild disease - Severe Disease  | 6.1                    |  |  |  |
| Visit 4 - Unknown                        | 0.6                    |  |  |  |
| Visit 4 - Total                          | 100                    |  |  |  |
| Visit 4 - Base                           | 164                    |  |  |  |
| Visit 5 - No disease - Almost no disease | 93.1                   |  |  |  |
| Visit 5 - Mild disease - Severe Disease  | 6.3                    |  |  |  |
| Visit 5 - Unknown                        | 0.6                    |  |  |  |

|  |      |  |  |  |
|--|------|--|--|--|
| Visit 5 - Total                          | 100  |  |  |  |
| Visit 5 - Base                           | 159  |  |  |  |
| Visit 6 - No disease - Almost no disease | 96.2 |  |  |  |
| Visit 6 - Mild disease - Severe Disease  | 3.8  |  |  |  |
| Visit 6 - Unknown                        | 0    |  |  |  |
| Visit 6 - Total                          | 100  |  |  |  |
| Visit 6 - Base                           | 157  |  |  |  |

Notes:

[8] - per protocol population

### Statistical analyses

No statistical analyses for this end point

### Secondary: Average Scores for Parent Index Quality of Life questionnaire per Visit

|                        |   |
|------------------------|---|
| End point title        | Average Scores for Parent Index Quality of Life questionnaire per Visit |
| End point description: |   |
| End point type         | Secondary   |
| End point timeframe:   |   |
| up to week 52          |   |

| End point values            | Pimecrolimus cream 1 % |  |  |  |
|-----------------------------|------------------------|--|--|--|
| Subject group type          | Reporting group        |  |  |  |
| Number of subjects analysed | 179 <sup>[9]</sup>     |  |  |  |
| Units: scores on a scale    |                        |  |  |  |
| number (not applicable)     |                        |  |  |  |
| Visit 1                     | 12.32                  |  |  |  |
| Visit 4                     | 8.82                   |  |  |  |
| Visit 6                     | 7.22                   |  |  |  |

Notes:

[9] - per protocol population

n = 148, 156, 140

### Statistical analyses

No statistical analyses for this end point

### Secondary: Average Scores for Child Index Quality of Life questionnaire per Visit

|                        |  |
|------------------------|--|
| End point title        | Average Scores for Child Index Quality of Life questionnaire per Visit |
| End point description: |  |
| End point type         | Secondary  |
| End point timeframe:   |  |
| up to week 52          |  |

|                             |                        |  |  |  |
|-----------------------------|------------------------|--|--|--|
| <b>End point values</b>     | Pimecrolimus cream 1 % |  |  |  |
| Subject group type          | Reporting group        |  |  |  |
| Number of subjects analysed | 179 <sup>[10]</sup>    |  |  |  |
| Units: scores on a scale    |                        |  |  |  |
| number (not applicable)     |                        |  |  |  |
| Visit 1                     | 7.9                    |  |  |  |
| Visit 2                     | 4.4                    |  |  |  |
| Visit 3                     | 3.9                    |  |  |  |
| Visit 4                     | 2.7                    |  |  |  |
| Visit 5                     | 2.4                    |  |  |  |
| Visit 6                     | 2.2                    |  |  |  |

Notes:

[10] - per protocol population

n= 53, 54, 59, 62, 52, 53

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All adverse events reported in this record are from date of First Patient First Treatment until Last Patient Last Visit.

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

### Dictionary used

|                    |             |
|--------------------|-------------|
| Dictionary name    | Unspecified |
| Dictionary version | unk         |

### Reporting groups

|                       |                        |
|-----------------------|------------------------|
| Reporting group title | Pimecrolimus cream 1 % |
|-----------------------|------------------------|

Reporting group description: -

| Serious adverse events                                     | Pimecrolimus cream<br>1 % |  |  |
|--|---------------------------|--|--|
| Total subjects affected by serious adverse events          |                           |  |  |
| subjects affected / exposed                                | 3 / 179 (1.68%)           |  |  |
| number of deaths (all causes)                              | 0                         |  |  |
| number of deaths resulting from adverse events             | 0                         |  |  |
| Gastrointestinal disorders                                 |                           |  |  |
| Diarrhea and gastroenteritis of presumed infectious origin |                           |  |  |
| subjects affected / exposed                                | 1 / 179 (0.56%)           |  |  |
| occurrences causally related to treatment / all            | 0 / 1                     |  |  |
| deaths causally related to treatment / all                 | 0 / 0                     |  |  |
| Infections and infestations                                |                           |  |  |
| Cellulitis, unspecified                                    |                           |  |  |
| subjects affected / exposed                                | 1 / 179 (0.56%)           |  |  |
| occurrences causally related to treatment / all            | 0 / 1                     |  |  |
| deaths causally related to treatment / all                 | 0 / 0                     |  |  |
| Pneumonia, unspecified                                     |                           |  |  |
| subjects affected / exposed                                | 1 / 179 (0.56%)           |  |  |
| occurrences causally related to treatment / all            | 0 / 1                     |  |  |
| deaths causally related to treatment / all                 | 0 / 0                     |  |  |

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

|  |   |  |  |
|--|---|--|--|
| <b>Non-serious adverse events</b>  | Pimecrolimus cream<br>1 %   |  |  |
| Total subjects affected by non-serious adverse events<br>subjects affected / exposed   | 135 / 179 (75.42%)  |  |  |
| Gastrointestinal disorders<br>Diarrhoea infectious<br>subjects affected / exposed<br>occurrences (all)   | 44 / 179 (24.58%)<br><br>44   |  |  |
| Respiratory, thoracic and mediastinal disorders<br>Acute Upper Respiratory Tract Infection<br>subjects affected / exposed<br>occurrences (all)<br><br>Allergic Rhinitis<br>subjects affected / exposed<br>occurrences (all)<br><br>Cough<br>subjects affected / exposed<br>occurrences (all) | 134 / 179 (74.86%)<br><br>134<br><br>71 / 179 (39.66%)<br><br>71<br><br>59 / 179 (32.96%)<br><br>59 |  |  |

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported