



## Clinical trial results:

**A multicenter, randomized, double blind, parallel group, vehicle controlled, study of the safety and efficacy of calcitriol 3 mcg/g ointment applied twice daily for 8 weeks in pediatric subjects (2 to 12 years of age) with mild to moderate plaque psoriasis**

### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2014-001744-38  |
| Trial protocol           | DE BE ES HU IT  |
| Global end of trial date | 18 January 2016 |

### Results information

|                                |               |
|--------------------------------|---------------|
| Result version number          | v1 (current)  |
| This version publication date  | 26 March 2017 |
| First version publication date | 26 March 2017 |

### Trial information

#### Trial identification

|                       |                  |
|-----------------------|------------------|
| Sponsor protocol code | 2RD.06.SPR.18132 |
|-----------------------|------------------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02186665 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | GALDERMA R&D, LLC   |
| Sponsor organisation address | 5 Cedar Brook Drive Suite 1, Cranburry, United States,                                |
| Public contact               | CTA Coordinator, GALDERMA R&D, SNC, +33 (0)493-95-70-85, cta.coordinator@galderma.com |
| Scientific contact           | CTA Coordinator, GALDERMA R&D, SNC, +33 (0)493-95-70-85, cta.coordinator@galderma.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? | Yes |

Notes:

## Results analysis stage

|  |                  |
|--|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 05 December 2016 |
| Is this the analysis of the primary completion data? | No               |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 18 January 2016  |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

To compare the safety of up to 8 weeks of treatment with calcitriol 3 mcg/g ointment versus its vehicle, when used twice daily, without occlusion, to treat children aged 2 to 12 years, with plaque psoriasis (excluding the face and scalp).

To evaluate the effect of twice daily use of calcitriol 3 mcg/g ointment versus vehicle on calcium metabolism in children aged 2 to 12 years with plaque psoriasis (excluding face and scalp).

To compare the efficacy of up to 8 weeks of treatment with calcitriol 3 mcg/g ointment versus its vehicle, when used twice daily, without occlusion, to treat children aged 2 to 12 years, with plaque psoriasis (excluding face and scalp).

Protection of trial subjects:

All study participants were required to read and sign an informed consent.

Background therapy: -

Evidence for comparator: -

|   |              |
|---|--------------|
| Actual start date of recruitment                          | 15 July 2014 |
| Long term follow-up planned                               | No           |
| Independent data monitoring committee (IDMC) involvement? | Yes          |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                  |
|--------------------------------------|------------------|
| Country: Number of subjects enrolled | Canada: 1        |
| Country: Number of subjects enrolled | United States: 9 |
| Country: Number of subjects enrolled | Spain: 2         |
| Country: Number of subjects enrolled | Belgium: 3       |
| Country: Number of subjects enrolled | Hungary: 3       |
| Country: Number of subjects enrolled | Italy: 1         |
| Worldwide total number of subjects   | 19               |
| EEA total number of subjects         | 9                |

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)                    | 16 |
| Adolescents (12-17 years)                | 3  |
| Adults (18-64 years)                     | 0  |
| From 65 to 84 years                      | 0  |
| 85 years and over                        | 0  |

## Subject disposition

### Recruitment

Recruitment details:

A total of 29 subjects were screened and 19 were randomized in 13 sites in US, Canada and Europe.

### Pre-assignment

Screening details:

A total of 29 subjects were screened and 19 were randomized. All subjects were treated with either calcitriol ointment or its vehicle.

### Period 1

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

### Arms

|                              |     |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

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

Arm description:

calcitriol 3mcg/g ointment

|  |                            |
|--|----------------------------|
| Arm type                               | Experimental               |
| Investigational medicinal product name | calcitriol 3mcg/g ointment |
| Investigational medicinal product code | CD2027                     |
| Other name                             |                            |
| Pharmaceutical forms                   | Ointment                   |
| Routes of administration               | Cutaneous use              |

Dosage and administration details:

Twice daily application (morning and evening) on psoriatic skin during 8 weeks

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

Arm description: -

|  |                  |
|--|------------------|
| Arm type                               | Placebo          |
| Investigational medicinal product name | vehicle ointment |
| Investigational medicinal product code |                  |
| Other name                             |                  |
| Pharmaceutical forms                   | Ointment         |
| Routes of administration               | Cutaneous use    |

Dosage and administration details:

Twice daily application (morning and evening) on psoriatic skin during 8 weeks

| Number of subjects in period 1 | Calcitriol ointment | placebo |
|--------------------------------|---------------------|---------|
| Started                        | 8                   | 11      |
| Completed                      | 8                   | 10      |
| Not completed                  | 0                   | 1       |
| Consent withdrawn by subject   | -                   | 1       |



## Baseline characteristics

### Reporting groups

|  |                     |
|--|---------------------|
| Reporting group title                                      | Calcitriol ointment |
| Reporting group description:<br>calcitriol 3mcg/g ointment |                     |
| Reporting group title                                      | placebo             |
| Reporting group description: -                             |                     |

| Reporting group values                                | Calcitriol ointment | placebo | Total |
|---|---------------------|---------|-------|
| Number of subjects                                    | 8                   | 11      | 19    |
| 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)                                 | 7                   | 9       | 16    |
| Adolescents (12-17 years)                             | 1                   | 2       | 3     |
| 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                                       | 9.6                 | 9.8     |       |
| standard deviation                                    | ± 1.8               | ± 1.8   | -     |
| Gender categorical<br>Units: Subjects                 |                     |         |       |
| Female  | 5                   | 7       | 12    |
| Male  | 3                   | 4       | 7     |

## End points

### End points reporting groups

|                                |                     |
|--------------------------------|---------------------|
| Reporting group title          | Calcitriol ointment |
| Reporting group description:   |                     |
| calcitriol 3mcg/g ointment     |                     |
| Reporting group title          | placebo             |
| Reporting group description: - |                     |

### Primary: Success of Investigator's Global Assessment ( IGA)

|  |  |
|--|--|
| End point title  | Success of Investigator's Global Assessment ( IGA) |
| End point description:   |  |
| The number of subjects with a minimum improvement of 2 grades from baseline in the IGA score and a severity rating of 0 (clear) or 1 (almost clear) at Week 8 (LOCF) |  |
| End point type   | Primary  |
| End point timeframe:   |  |
| Baseline to week 8   |  |

| End point values            | Calcitriol ointment | placebo         |  |  |
|-----------------------------|---------------------|-----------------|--|--|
| Subject group type          | Reporting group     | Reporting group |  |  |
| Number of subjects analysed | 8                   | 11              |  |  |
| Units: participants         | 3                   | 7               |  |  |

### Statistical analyses

|   |                               |
|---|-------------------------------|
| Statistical analysis title  | Intent to treat-Week 8-LOCF   |
| Statistical analysis description:   |                               |
| Success rate at Week 8 (ITT, LOCF) was analyzed as primary analysis.  |                               |
| Success rate= % of subjects with an IGA of 0 (clear) or 1 (almost clear), and at least a 2 grade improvement from baseline. |                               |
| ITT population: All randomized subjects to whom study medication is dispensed   |                               |
| Comparison groups   | Calcitriol ointment v placebo |
| Number of subjects included in analysis   | 19                            |
| Analysis specification  | Pre-specified                 |
| Analysis type   | superiority                   |
| P-value   | = 0.37 <sup>[1]</sup>         |
| Method  | Fisher exact                  |

Notes:

[1] - P-value is based on Fisher's exact test.

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

16 weeks

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

### Dictionary used

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

|                    |    |
|--------------------|----|
| Dictionary version | 15 |
|--------------------|----|

### Reporting groups

|                       |                     |
|-----------------------|---------------------|
| Reporting group title | Calcitriol ointment |
|-----------------------|---------------------|

Reporting group description:

calcitriol 3mcg/g ointment

|                       |         |
|-----------------------|---------|
| Reporting group title | placebo |
|-----------------------|---------|

Reporting group description: -

| Serious adverse events                            | Calcitriol ointment | placebo        |  |
|---|---------------------|----------------|--|
| Total subjects affected by serious adverse events |                     |                |  |
| subjects affected / exposed                       | 0 / 8 (0.00%)       | 0 / 11 (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: 0 %

| Non-serious adverse events                            | Calcitriol ointment | placebo         |  |
|---|---------------------|-----------------|--|
| Total subjects affected by non-serious adverse events |                     |                 |  |
| subjects affected / exposed                           | 6 / 8 (75.00%)      | 8 / 11 (72.73%) |  |
| Investigations  |                     |                 |  |
| Blood pressure increased                              |                     |                 |  |
| subjects affected / exposed                           | 0 / 8 (0.00%)       | 1 / 11 (9.09%)  |  |
| occurrences (all)                                     | 0                   | 2               |  |
| Urine calcium/creatinine ratio increased              |                     |                 |  |
| subjects affected / exposed                           | 0 / 8 (0.00%)       | 1 / 11 (9.09%)  |  |
| occurrences (all)                                     | 0                   | 1               |  |
| Injury, poisoning and procedural complications        |                     |                 |  |
| Arthropod bite  |                     |                 |  |



|  |                    |                     |  |
|--|--------------------|---------------------|--|
| subjects affected / exposed<br>occurrences (all) | 0 / 8 (0.00%)<br>0 | 1 / 11 (9.09%)<br>1 |  |
| Gastrointestinal disorders                       |                    |                     |  |
| Abdominal pain                                   |                    |                     |  |
| subjects affected / exposed                      | 1 / 8 (12.50%)     | 0 / 11 (0.00%)      |  |
| occurrences (all)                                | 1                  | 0                   |  |
| Diarrhoea  |                    |                     |  |
| subjects affected / exposed                      | 1 / 8 (12.50%)     | 0 / 11 (0.00%)      |  |
| occurrences (all)                                | 2                  | 0                   |  |
| Respiratory, thoracic and mediastinal disorders  |                    |                     |  |
| Cough  |                    |                     |  |
| subjects affected / exposed                      | 0 / 8 (0.00%)      | 2 / 11 (18.18%)     |  |
| occurrences (all)                                | 0                  | 2                   |  |
| Oropharyngeal pain                               |                    |                     |  |
| subjects affected / exposed                      | 1 / 8 (12.50%)     | 0 / 11 (0.00%)      |  |
| occurrences (all)                                | 1                  | 0                   |  |
| Skin and subcutaneous tissue disorders           |                    |                     |  |
| Pruritus   |                    |                     |  |
| subjects affected / exposed                      | 0 / 8 (0.00%)      | 1 / 11 (9.09%)      |  |
| occurrences (all)                                | 0                  | 1                   |  |
| Psoriasis  |                    |                     |  |
| subjects affected / exposed                      | 0 / 8 (0.00%)      | 1 / 11 (9.09%)      |  |
| occurrences (all)                                | 0                  | 1                   |  |
| Skin irritation                                  |                    |                     |  |
| subjects affected / exposed                      | 2 / 8 (25.00%)     | 0 / 11 (0.00%)      |  |
| occurrences (all)                                | 2                  | 0                   |  |
| Renal and urinary disorders                      |                    |                     |  |
| Hypercalciuria                                   |                    |                     |  |
| subjects affected / exposed                      | 0 / 8 (0.00%)      | 1 / 11 (9.09%)      |  |
| occurrences (all)                                | 0                  | 1                   |  |
| Musculoskeletal and connective tissue disorders  |                    |                     |  |
| Myalgia  |                    |                     |  |
| subjects affected / exposed                      | 0 / 8 (0.00%)      | 1 / 11 (9.09%)      |  |
| occurrences (all)                                | 0                  | 1                   |  |
| Infections and infestations                      |                    |                     |  |

|                                   |                |                 |  |
|-----------------------------------|----------------|-----------------|--|
| Conjunctivitis bacterial          |                |                 |  |
| subjects affected / exposed       | 1 / 8 (12.50%) | 0 / 11 (0.00%)  |  |
| occurrences (all)                 | 1              | 0               |  |
| Gastroenteritis                   |                |                 |  |
| subjects affected / exposed       | 1 / 8 (12.50%) | 0 / 11 (0.00%)  |  |
| occurrences (all)                 | 1              | 0               |  |
| Laryngitis                        |                |                 |  |
| subjects affected / exposed       | 0 / 8 (0.00%)  | 1 / 11 (9.09%)  |  |
| occurrences (all)                 | 0              | 1               |  |
| Lice infestation                  |                |                 |  |
| subjects affected / exposed       | 1 / 8 (12.50%) | 0 / 11 (0.00%)  |  |
| occurrences (all)                 | 1              | 0               |  |
| Molluscum contagiosum             |                |                 |  |
| subjects affected / exposed       | 1 / 8 (12.50%) | 0 / 11 (0.00%)  |  |
| occurrences (all)                 | 1              | 0               |  |
| Nasopharyngitis                   |                |                 |  |
| subjects affected / exposed       | 0 / 8 (0.00%)  | 2 / 11 (18.18%) |  |
| occurrences (all)                 | 0              | 4               |  |
| Upper respiratory tract infection |                |                 |  |
| subjects affected / exposed       | 0 / 8 (0.00%)  | 1 / 11 (9.09%)  |  |
| occurrences (all)                 | 0              | 1               |  |
| Urinary tract infection           |                |                 |  |
| subjects affected / exposed       | 0 / 8 (0.00%)  | 1 / 11 (9.09%)  |  |
| occurrences (all)                 | 0              | 1               |  |
| Viral infection                   |                |                 |  |
| subjects affected / exposed       | 0 / 8 (0.00%)  | 1 / 11 (9.09%)  |  |
| occurrences (all)                 | 0              | 1               |  |

## 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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

|   |
|---|
| Study was closed early due to slow enrollment |
|---|

Notes: