



## Clinical trial results:

### STUDY OF THE EFFICACY AND SAFETY OF A PAD™ CALCIPOTRIOL CREAM IN THE PSORIASIS PLAQUE TEST

#### Summary

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2015-003893-34    |
| Trial protocol           | FR                |
| Global end of trial date | 27 September 2016 |

#### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 28 June 2020 |
| First version publication date | 28 June 2020 |

#### Trial information

##### Trial identification

|                       |           |
|-----------------------|-----------|
| Sponsor protocol code | MC2-16-C1 |
|-----------------------|-----------|

##### Additional study identifiers

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

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | MC2 Therapeutics Ltd.  |
| Sponsor organisation address | C/O Agern Allé 24-26, Hørsholm, Denmark, 2970  |
| Public contact               | Senior Project Manager, Clinical Operations, MC2 Therapeutics Ltd., 45 20157033, isa@mc2therapeutics.com |
| Scientific contact           | Senior Project Manager, Clinical Operations, MC2 Therapeutics Ltd., 45 20157033, isa@mc2therapeutics.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 September 2016 |
| Is this the analysis of the primary completion data? | Yes               |
| Primary completion date                              | 27 September 2016 |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 27 September 2016 |
| Was the trial ended prematurely?                     | No                |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective is to evaluate the efficacy of a PAD Calcipotriol cream MC2-01 (calcipotriol) compared to two calcipotriol reference formulations (Daivonex® cream and Daivonex® ointment) in patients with plaque psoriasis

Protection of trial subjects:

The Risk/benefit ratio assessment was based on a 4-week psoriasis study on 33 patients with psoriasis plaque. This study showed that the three MC1-01 formulations were safe and well tolerated.

The patient were treated with once daily application of the investigational medical products, six days a week (every day except Sunday) for 4 weeks. Each application site was of approximately 3 cm<sup>2</sup> on one or more psoriatic plaques of identical severity (similar baseline Total Plaque Score (TPS) ≥ 5.

Monitoring of Adverse Events and local tolerance assessment was done twice weekly. During and following a patient's participation in the trial, the investigator was to ensure adequate medical care to patients for any adverse events, as applicable.

Background therapy: -

Evidence for comparator:

The 3 comparator products were all approved topical cream or ointments containing either calcipotriol or calcipotriol/betamethasone.

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 19 April 2016 |
| 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 | France: 24 |
| Worldwide total number of subjects   | 24         |
| EEA total number of subjects         | 24         |

Notes:

### Subjects enrolled per age group

|   |   |
|---|---|
| In utero                                  | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days)                      | 0 |
| Infants and toddlers (28 days-23          | 0 |

|                           |    |
|---------------------------|----|
| months)                   |    |
| Children (2-11 years)     | 0  |
| Adolescents (12-17 years) | 0  |
| Adults (18-64 years)      | 24 |
| From 65 to 84 years       | 0  |
| 85 years and over         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

All subjects in the study was selected from an internal database of potential candidates at the clinic. All subject has had previously accepted to be contacted in case of potential participation in a study.

### Pre-assignment

Screening details:

A signed informed consent form was obtained prior to performing any study related activities. Prior to the baseline a washout period up to 21 days had to be completed if the subject was treated or has recently been treated with anti-psoriatic treatments or other relevant medications.

### Period 1

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

Blinding implementation details:

All 6 products were provided to an unblinded person in charge of product application. The products were labelled from A - F. The same person was also provided with a randomization list, indicated the allocation of the 6 products to each of the 6 test sites.

The subject, Investigator, monitor and assessor were all kept blinded to the product allocation.

### Arms

|           |            |
|-----------|------------|
| Arm title | Test sites |
|-----------|------------|

Arm description:

Each patient received repeatedly applications with 6 products:

- MC2-01 (calcipotriol) cream
- MC2-01 (vehicle)
- MC2-01 (Calcipotriol/betamethasone dipropionate) cream
- Daivobet (Calcipotriol/betamethasone dipropionate) ointment
- Daivonex® (calcipotriol) cream
- Daivonex® (calcipotriol) ointment

The 6 products was randomly applied by a qualified person, under non-occlusive conditions, using a sticker to define the areas of products application, once daily, except Sundays, for a total of 24 applications.

|  |                             |
|--|-----------------------------|
| Arm type                               | Experimental                |
| Investigational medicinal product name | MC2-01 (calcipotriol) cream |
| Investigational medicinal product code |                             |
| Other name                             |                             |
| Pharmaceutical forms                   | Cream                       |
| Routes of administration               | Topical use                 |

Dosage and administration details:

MC2-01 cream contains calcipotriol (50µg/g). The dose regimen was 50 µl repeatedly topical (cutaneous to the skin) applications to a predefined test site with an area of 2 cm in diameter, once daily, except Sundays, for a total of 24 applications. The application was covered with a non-occlusive gaze dressing.

|  |                |
|--|----------------|
| Investigational medicinal product name | MC2-01 vehicle |
| Investigational medicinal product code |                |
| Other name                             |                |
| Pharmaceutical forms                   | Cream          |
| Routes of administration               | Topical use    |

Dosage and administration details:

MC2-01 cream does not contain any active ingredient. The dose regimen was 50 µl repeatedly topical

(cutaneous to the skin) applications to a predefined test site with an area of 2 cm in diameter, once daily, except Sundays, for a total of 24 applications. The application was covered with a non-occlusive gaze dressing.

|  |  |
|--|--|
| Investigational medicinal product name | MC2-01 (Calcipotriol/betamethasone dipropionate) cream |
| Investigational medicinal product code |  |
| Other name                             |  |
| Pharmaceutical forms                   | Cream  |
| Routes of administration               | Topical use  |

Dosage and administration details:

MC2-01 cream contains calcipotriol / betamethasone dipropionate (50µg/g / 0.5mg/g). The dose regimen was 50 µl repeatedly topical (cutaneous to the skin) applications to a predefined test site with an area of 2 cm in diameter, once daily, except Sundays, for a total of 24 applications. The application was covered with a non-occlusive gaze dressing.

|  |                    |
|--|--------------------|
| Investigational medicinal product name | Daivobet® ointment |
| Investigational medicinal product code |                    |
| Other name                             |                    |
| Pharmaceutical forms                   | Cream              |
| Routes of administration               | Topical use        |

Dosage and administration details:

Daivobet® ointment contains calcipotriol / betamethasone dipropionate (50µg/g / 0.5mg/g). The dose regimen was 50 µl repeatedly topical (cutaneous to the skin) applications to a predefined test site with an area of 2 cm in diameter, once daily, except Sundays, for a total of 24 applications. The application was covered with a non-occlusive gaze dressing.

|  |                 |
|--|-----------------|
| Investigational medicinal product name | Daivonex® cream |
| Investigational medicinal product code |                 |
| Other name                             |                 |
| Pharmaceutical forms                   | Cream           |
| Routes of administration               | Topical use     |

Dosage and administration details:

Daivonex® cream contains calcipotriol (50µg/g). The dose regimen was 50 µl repeatedly topical (cutaneous to the skin) applications to a predefined test site with an area of 2 cm in diameter, once daily, except Sundays, for a total of 24 applications. The application was covered with a non-occlusive gaze dressing.

|  |                    |
|--|--------------------|
| Investigational medicinal product name | Daivonex® ointment |
| Investigational medicinal product code |                    |
| Other name                             |                    |
| Pharmaceutical forms                   | Cream              |
| Routes of administration               | Topical use        |

Dosage and administration details:

Daivonex® ointment contains calcipotriol (50µg/g). The dose regimen was 50 µl repeatedly topical (cutaneous to the skin) applications to a predefined test site with an area of 2 cm in diameter, once daily, except Sundays, for a total of 24 applications. The application was covered with a non-occlusive gaze dressing.

| Number of subjects in period 1 | Test sites |
|--------------------------------|------------|
| Started                        | 24         |
| Completed                      | 24         |



## Baseline characteristics

### Reporting groups

|                       |            |
|-----------------------|------------|
| Reporting group title | Test phase |
|-----------------------|------------|

Reporting group description: -

| Reporting group values | Test phase | Total |  |
|------------------------|------------|-------|--|
| Number of subjects     | 24         | 24    |  |
| Age categorical        |            |       |  |
| Units: Subjects        |            |       |  |
| Adults (18-64 years)   | 24         | 24    |  |
| Gender categorical     |            |       |  |
| Units: Subjects        |            |       |  |
| Female                 | 9          | 9     |  |
| Male                   | 15         | 15    |  |
| FitzPatrick Skin Type  |            |       |  |
| Units: Subjects        |            |       |  |
| Skintype I             | 0          | 0     |  |
| Skintype II            | 2          | 2     |  |
| Skintype III           | 22         | 22    |  |
| Skintype IV            | 0          | 0     |  |

## End points

### End points reporting groups

|                       |            |
|-----------------------|------------|
| Reporting group title | Test sites |
|-----------------------|------------|

Reporting group description:

Each patient received repeatedly applications with 6 products:

- MC2-01 (calcipotriol) cream
- MC2-01 (vehicle)
- MC2-01 (Calcipotriol/betamethasone dipropionate) cream
- Daivobet (Calcipotriol/betamethasone dipropionate) ointment
- Daivonex® (calcipotriol) cream
- Daivonex® (calcipotriol) ointment

The 6 products was randomly applied by a qualified person, under non-occlusive conditions, using a sticker to define the areas of products application, once daily, except Sundays, for a total of 24 applications.

|                            |                             |
|----------------------------|-----------------------------|
| Subject analysis set title | MC2-01 (calcipotriol) cream |
|----------------------------|-----------------------------|

|                           |               |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

All 24 randomized subjects were included in the Full Analysis Set and analyzed for absolute change in Total Clinical score (TCS) from baseline of End of Trial.

|                            |                |
|----------------------------|----------------|
| Subject analysis set title | MC2-01 vehicle |
|----------------------------|----------------|

|                           |               |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

All 24 randomized subjects were included in the Full Analysis Set and analyzed for absolute change in Total Clinical score (TCS) from baseline of End of Trial.

|                            |  |
|----------------------------|--|
| Subject analysis set title | MC2-01 (Calcipotriol/betamethasone dipropionate) cream |
|----------------------------|--|

|                           |               |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

All 24 randomized subjects were included in the Full Analysis Set and analyzed for absolute change in Total Clinical score (TCS) from baseline of End of Trial.

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | Daivobet® ointment |
|----------------------------|--------------------|

|                           |               |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

All 24 randomized subjects were included in the Full Analysis Set and analyzed for absolute change in Total Clinical score (TCS) from baseline of End of Trial.

|                            |                 |
|----------------------------|-----------------|
| Subject analysis set title | Daivonex® cream |
|----------------------------|-----------------|

|                           |               |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

All 24 randomized subjects were included in the Full Analysis Set and analyzed for absolute change in Total Clinical score (TCS) from baseline of End of Trial.

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | Daivonex® ointment |
|----------------------------|--------------------|

|                           |               |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

All 24 randomized subjects were included in the Full Analysis Set and analyzed for absolute change in Total Clinical score (TCS) from baseline of End of Trial.



**Primary: TCS score**

|  |           |
|--|-----------|
| End point title  | TCS score |
| End point description:<br>Absolute change in Trial Clinical Score (TCS). |           |
| End point type   | Primary   |
| End point timeframe:<br>Absolute change from baseline to end of trial.   |           |

| End point values                     | MC2-01<br>(calcipotriol)<br>cream | MC2-01 vehicle       | MC2-01<br>(Calcipotriol/be<br>tamethasone<br>dipropionate)<br>cream | Daivobet®<br>ointment |
|--------------------------------------|-----------------------------------|----------------------|---|-----------------------|
| Subject group type                   | Subject analysis set              | Subject analysis set | Subject analysis set  | Subject analysis set  |
| Number of subjects analysed          | 24                                | 24                   | 24  | 24                    |
| Units: Score                         |                                   |                      |   |                       |
| arithmetic mean (standard deviation) | -2.5 (± 1.3)                      | -1.2 (± 1.0)         | -5.1 (± 1.2)  | -5.5 (± 1.1)          |

| End point values                     | Daivonex®<br>cream   | Daivonex®<br>ointment |  |  |
|--------------------------------------|----------------------|-----------------------|--|--|
| Subject group type                   | Subject analysis set | Subject analysis set  |  |  |
| Number of subjects analysed          | 24                   | 24                    |  |  |
| Units: Score                         |                      |                       |  |  |
| arithmetic mean (standard deviation) | -2.7 (± 2.0)         | -3.8 (± 1.5)          |  |  |

**Statistical analyses**

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | Absolute change in TCS  |
| Statistical analysis description:<br>The primary endpoint is the absolute change in Total Clinical Score (TCS) of clinical signs (intensity of erythema, scaling and infiltration) from baseline to End of Treatment (EOT) was analyzed using a two-way ANOVA with subjects and treatments as factors. Treatment differences will be tested using Tukey's honestly significant difference method for correcting p-values. Ninety five percent (95%) confidence interval of differences between treatments will be calculated. |   |
| Comparison groups   | MC2-01 (calcipotriol) cream v MC2-01 vehicle v MC2-01 (Calcipotriol/betamethasone dipropionate) cream v Daivobet® ointment v Daivonex® cream v Daivonex® ointment |
| Number of subjects included in analysis   | 144   |
| Analysis specification  | Pre-specified   |
| Analysis type   | superiority <sup>[1]</sup>  |
| P-value   | ≤ 0.05  |
| Method  | ANOVA   |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |

Notes:

[1] - 24 subject were each treated with different treatments at 6 individual test sites, which add up to 144 test sites in total

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

AEs were collected/assessed from the time the informed consent form was signed. AEs assessed to reasonably possibly related to the trial medication had to be followed until it was resolved or until the medical condition of the subject was stable.

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

### Dictionary used

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

|                    |    |
|--------------------|----|
| Dictionary version | 19 |
|--------------------|----|

### Reporting groups

|                       |            |
|-----------------------|------------|
| Reporting group title | Test sites |
|-----------------------|------------|

Reporting group description:

Each patient received repeatedly applications with 6 products:

- MC2-01 (calcipotriol) cream
- MC2-01 (vehicle)
- MC2-01 (Calcipotriol/betamethasone dipropionate) cream
- Daivobet (Calcipotriol/betamethasone dipropionate) ointment
- Daivonex® (calcipotriol) cream
- Daivonex® (calcipotriol) ointment

The 6 products was randomly applied by a qualified person, under non-occlusive, using a sticker to define the areas of products application, once daily, except Sundays, for a total of 24 applications.

Reporting of AEs are done by SOC and preferred terms.

| Serious adverse events                            | Test sites     |  |  |
|---|----------------|--|--|
| Total subjects affected by serious adverse events |                |  |  |
| subjects affected / exposed                       | 0 / 24 (0.00%) |  |  |
| number of deaths (all causes)                     | 0              |  |  |
| number of deaths resulting from adverse events    | 0              |  |  |

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

| Non-serious adverse events                            | Test sites      |  |  |
|---|-----------------|--|--|
| Total subjects affected by non-serious adverse events |                 |  |  |
| subjects affected / exposed                           | 7 / 24 (29.17%) |  |  |
| Injury, poisoning and procedural complications        |                 |  |  |
| Fall  |                 |  |  |
| subjects affected / exposed                           | 1 / 24 (4.17%)  |  |  |
| occurrences (all)                                     | 1               |  |  |
| Nervous system disorders                              |                 |  |  |

|   |  |  |  |
|---|--|--|--|
| Syncope<br>subjects affected / exposed<br>occurrences (all)   | 1 / 24 (4.17%)<br>1                            |  |  |
| General disorders and administration<br>site conditions<br>Fewer<br>subjects affected / exposed<br>occurrences (all)  | 2 / 24 (8.33%)<br>2                            |  |  |
| Gastrointestinal disorders<br>Abdominal pain<br>subjects affected / exposed<br>occurrences (all)  | 1 / 24 (4.17%)<br>1                            |  |  |
| Respiratory, thoracic and mediastinal<br>disorders<br>Sore Throat<br>subjects affected / exposed<br>occurrences (all)   | 1 / 24 (4.17%)<br>1                            |  |  |
| Musculoskeletal and connective tissue<br>disorders<br>Shoulder pain<br>subjects affected / exposed<br>occurrences (all)   | 1 / 24 (4.17%)<br>1                            |  |  |
| Infections and infestations<br>Common cold<br>subjects affected / exposed<br>occurrences (all)<br><br>Flu-like symptoms<br>subjects affected / exposed<br>occurrences (all) | 1 / 24 (4.17%)<br>1<br><br>1 / 24 (4.17%)<br>1 |  |  |
| Metabolism and nutrition disorders<br>Hypoglycaemia<br>subjects affected / exposed<br>occurrences (all)   | 1 / 24 (4.17%)<br>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**

None reported