



## Clinical trial results:

### LEO 90100 aerosol foam compared to calcipotriol plus betamethasone dipropionate gel in subjects with psoriasis vulgaris

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2013-004686-14 |
| Trial protocol           | FR             |
| Global end of trial date | 04 March 2015  |

#### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 17 July 2016 |
| First version publication date | 17 July 2016 |

#### Trial information

##### Trial identification

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | LP0053-1003 |
|-----------------------|-------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02132936 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | LEO Pharma A/S  |
| Sponsor organisation address | Industriparken 55, Ballerup, Denmark, 2750  |
| Public contact               | Clinical Trial Disclosure Manager, LEO Pharma A/S, 45 44945888, ctr.disclosure@leo-pharma.com |
| Scientific contact           | Clinical Trial Disclosure Manager, LEO Pharma A/S, 45 44945888, ctr.disclosure@leo-pharma.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:

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**Results analysis stage**

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|  |                   |
|--|-------------------|
| Analysis stage                                       | Final             |
| Date of interim/final analysis                       | 11 September 2015 |
| Is this the analysis of the primary completion data? | Yes               |
| Primary completion date                              | 04 March 2015     |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 04 March 2015     |
| Was the trial ended prematurely?                     | No                |

Notes:

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**General information about the trial**

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Main objective of the trial:

To compare the efficacy of treatment with LEO 90100 at Week 4 to that of calcipotriol plus betamethasone dipropionate (BDP) gel at Week 8 in subjects with psoriasis vulgaris

Protection of trial subjects:

NA

Background therapy: -

Evidence for comparator: -

|   |              |
|---|--------------|
| Actual start date of recruitment                          | 30 June 2014 |
| Long term follow-up planned                               | No           |
| Independent data monitoring committee (IDMC) involvement? | No           |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |                     |
|--------------------------------------|---------------------|
| Country: Number of subjects enrolled | United Kingdom: 173 |
| Country: Number of subjects enrolled | France: 122         |
| Country: Number of subjects enrolled | United States: 168  |
| Worldwide total number of subjects   | 463                 |
| EEA total number of subjects         | 295                 |

Notes:

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**Subjects enrolled per age group**

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|   |     |
|---|-----|
| 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)                     | 0   |
| Adolescents (12-17 years)                 | 0   |
| Adults (18-64 years)                      | 341 |
| From 65 to 84 years                       | 121 |
| 85 years and over                         | 1   |

## Subject disposition

### Recruitment

Recruitment details:

The first subject was enrolled on 30-Jun-2014 and the last subject completed the trial (last visit, including followup) on 04-Mar-2015.

### Pre-assignment

Screening details:

504 subjects from 41 centres in the UK (15 centres), the US (15 centres) and France (11 centres) were enrolled into the trial.

41 enrolled subjects were not randomised due to the following reasons: screening failures (29 subjects); AE (1); protocol deviation (1); lost to follow-up (2); withdrawal by subject (3); other reasons (5).

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Overall trial (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Randomised - controlled        |
| Blinding used                | Single blind                   |
| Roles blinded                | Investigator <sup>[1]</sup>    |

Blinding implementation details:

The trial was investigator-blinded. As 2 of the treatments were in an aerosol foam formulation and 2 were in a gel formulation, the subjects knew if they received aerosol foam or gel but did not know if they received active treatment or vehicle. Furthermore, the trial medication was handed out to the subjects by a designated person (a study coordinator) so the investigator did not know which IP the subject received.

### Arms

|                              |                        |
|------------------------------|------------------------|
| Are arms mutually exclusive? | Yes                    |
| <b>Arm title</b>             | LEO 90100 aerosol foam |

Arm description:

Calcipotriol (as hydrate) 50 mcg/g and betamethasone 0.5 mg/g (as dipropionate), 60 g per can

|  |                |
|--|----------------|
| Arm type                               | Experimental   |
| Investigational medicinal product name | LEO 90100      |
| Investigational medicinal product code |                |
| Other name                             |                |
| Pharmaceutical forms                   | Cutaneous foam |
| Routes of administration               | Topical use    |

Dosage and administration details:

The investigational product (IP) was applied to psoriasis vulgaris affected areas on the trunk, arms and legs once daily for up to 12 weeks.

|                  |                      |
|------------------|----------------------|
| <b>Arm title</b> | Aerosol Foam Vehicle |
|------------------|----------------------|

Arm description:

Aerosol foam vehicle, 60 g per can

|  |                      |
|--|----------------------|
| Arm type                               | Placebo              |
| Investigational medicinal product name | Aerosol foam vehicle |
| Investigational medicinal product code |                      |
| Other name                             |                      |
| Pharmaceutical forms                   | Cutaneous foam       |
| Routes of administration               | Topical use          |

Dosage and administration details:

The IP was applied to psoriasis vulgaris affected areas on the trunk, arms and legs once daily for up to 12 weeks.

|                  |                      |
|------------------|----------------------|
| <b>Arm title</b> | Calcipotriol BDP Gel |
|------------------|----------------------|

Arm description:

Calcipotriol BDP gel, containing calcipotriol (as hydrate) 50 mcg/g and betamethasone 0.5 mg/g (as dipropionate), 60 g per bottle

|  |                      |
|--|----------------------|
| Arm type                               | Active comparator    |
| Investigational medicinal product name | Calcipotriol BDP Gel |
| Investigational medicinal product code |                      |
| Other name                             |                      |
| Pharmaceutical forms                   | Gel                  |
| Routes of administration               | Topical use          |

Dosage and administration details:

The IP was applied to psoriasis vulgaris affected areas on the trunk, arms and legs once daily for up to 12 weeks.

|                  |             |
|------------------|-------------|
| <b>Arm title</b> | Gel Vehicle |
|------------------|-------------|

Arm description:

Gel vehicle, 60 g per bottle

|  |             |
|--|-------------|
| Arm type                               | Placebo     |
| Investigational medicinal product name | Gel Vehicle |
| Investigational medicinal product code |             |
| Other name                             |             |
| Pharmaceutical forms                   | Gel         |
| Routes of administration               | Topical use |

Dosage and administration details:

The IP was applied to psoriasis vulgaris affected areas on the trunk, arms and legs once daily for up to 12 weeks.

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: The trial was investigator-blinded to ensure unbiased efficacy assessment.

Subjects knew if they were treated with a foam or gel formulation but did not know if they received active treatment or vehicle.

| Number of subjects in period 1 | LEO 90100 aerosol foam | Aerosol Foam Vehicle | Calcipotriol BDP Gel |
|--------------------------------|------------------------|----------------------|----------------------|
| Started                        | 185                    | 47                   | 188                  |
| Completed                      | 175                    | 38                   | 174                  |
| Not completed                  | 10                     | 9                    | 14                   |
| Consent withdrawn by subject   | 2                      | 1                    | -                    |
| Subject withdrew consent       | -                      | -                    | 2                    |
| Adverse event, non-fatal       | 3                      | 1                    | 3                    |
| Lost to follow-up              | 2                      | 2                    | 5                    |
| Lack of efficacy               | 1                      | 5                    | 4                    |
| Protocol deviation             | 2                      | -                    | -                    |

| Number of subjects in period 1 | Gel Vehicle |
|--------------------------------|-------------|
| Started                        | 43          |
| Completed                      | 29          |
| Not completed                  | 14          |
| Consent withdrawn by subject   | 4           |
| Subject withdrew consent       | -           |
| Adverse event, non-fatal       | -           |

|                    |   |
|--------------------|---|
| Lost to follow-up  | 1 |
| Lack of efficacy   | 9 |
| Protocol deviation | - |

## Baseline characteristics

### Reporting groups

|   |                        |
|---|------------------------|
| Reporting group title   | LEO 90100 aerosol foam |
| Reporting group description:  |                        |
| Calcipotriol (as hydrate) 50 mcg/g and betamethasone 0.5 mg/g (as dipropionate), 60 g per can                                     |                        |
| Reporting group title   | Aerosol Foam Vehicle   |
| Reporting group description:  |                        |
| Aerosol foam vehicle, 60 g per can  |                        |
| Reporting group title   | Calcipotriol BDP Gel   |
| Reporting group description:  |                        |
| Calcipotriol BDP gel, containing calcipotriol (as hydrate) 50 mcg/g and betamethasone 0.5 mg/g (as dipropionate), 60 g per bottle |                        |
| Reporting group title   | Gel Vehicle            |
| Reporting group description:  |                        |
| Gel vehicle, 60 g per bottle  |                        |

| Reporting group values                             | LEO 90100 aerosol foam | Aerosol Foam Vehicle | Calcipotriol BDP Gel |
|--|------------------------|----------------------|----------------------|
| Number of subjects                                 | 185                    | 47                   | 188                  |
| Age categorical                                    |                        |                      |                      |
| Units: Subjects                                    |                        |                      |                      |
| In utero   | 0                      | 0                    | 0                    |
| Preterm newborn infants (gestational age < 37 wks) | 0                      | 0                    | 0                    |
| Newborns (0-27 days)                               | 0                      | 0                    | 0                    |
| Infants and toddlers (28 days-23 months)           | 0                      | 0                    | 0                    |
| Children (2-11 years)                              | 0                      | 0                    | 0                    |
| Adolescents (12-17 years)                          | 0                      | 0                    | 0                    |
| Adults (18-64 years)                               | 137                    | 37                   | 134                  |
| From 65-84 years                                   | 48                     | 10                   | 53                   |
| 85 years and over                                  | 0                      | 0                    | 1                    |
| Gender categorical                                 |                        |                      |                      |
| Units: Subjects                                    |                        |                      |                      |
| Female   | 59                     | 18                   | 74                   |
| Male   | 126                    | 29                   | 114                  |

| Reporting group values                             | Gel Vehicle | Total |  |
|--|-------------|-------|--|
| Number of subjects                                 | 43          | 463   |  |
| Age categorical                                    |             |       |  |
| Units: Subjects                                    |             |       |  |
| In utero   | 0           | 0     |  |
| Preterm newborn infants (gestational age < 37 wks) | 0           | 0     |  |
| Newborns (0-27 days)                               | 0           | 0     |  |
| Infants and toddlers (28 days-23 months)           | 0           | 0     |  |
| Children (2-11 years)                              | 0           | 0     |  |
| Adolescents (12-17 years)                          | 0           | 0     |  |
| Adults (18-64 years)                               | 33          | 341   |  |

|                   |    |     |  |
|-------------------|----|-----|--|
| From 65-84 years  | 10 | 121 |  |
| 85 years and over | 0  | 1   |  |

|                    |    |     |  |
|--------------------|----|-----|--|
| Gender categorical |    |     |  |
| Units: Subjects    |    |     |  |
| Female             | 17 | 168 |  |
| Male               | 26 | 295 |  |

## End points

### End points reporting groups

|   |                        |
|---|------------------------|
| Reporting group title   | LEO 90100 aerosol foam |
| Reporting group description:<br>Calcipotriol (as hydrate) 50 mcg/g and betamethasone 0.5 mg/g (as dipropionate), 60 g per can                                     |                        |
| Reporting group title   | Aerosol Foam Vehicle   |
| Reporting group description:<br>Aerosol foam vehicle, 60 g per can  |                        |
| Reporting group title   | Calcipotriol BDP Gel   |
| Reporting group description:<br>Calcipotriol BDP gel, containing calcipotriol (as hydrate) 50 mcg/g and betamethasone 0.5 mg/g (as dipropionate), 60 g per bottle |                        |
| Reporting group title   | Gel Vehicle            |
| Reporting group description:<br>Gel vehicle, 60 g per bottle  |                        |

### Primary: Treatment Success According to the PGA

|  |   |
|--|---|
| End point title  | Treatment Success According to the PGA <sup>[1]</sup> |
| End point description:<br>To compare the efficacy of treatment of LEO 90100 at Week 4 to that of calcipotriol BDP gel at Week 8 in subjects with psoriasis vulgaris.<br>The severity of psoriasis vulgaris on the trunk and limbs was assessed using the Physician's Global Assessment of disease severity (PGA). A five-point scale (clear, almost clear, mild, moderate, and severe) was used.<br>'Treatment success' was defined as achieving 'clear' or 'almost clear' for subjects with at least 'moderate' disease at baseline and 'clear' for subjects with 'mild' disease at baseline. |   |
| End point type   | Primary   |
| End point timeframe:<br>Week 4 for LEO 90100 and Week 8 for calcipotriol BDP gel   |   |

#### Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.  
Justification: The statistical analysis of the primary endpoint was planned and performed to compare the 2 active treatments.

| End point values              | LEO 90100 aerosol foam | Calcipotriol BDP Gel |  |  |
|-------------------------------|------------------------|----------------------|--|--|
| Subject group type            | Reporting group        | Reporting group      |  |  |
| Number of subjects analysed   | 185                    | 188                  |  |  |
| Units: Percentage of subjects |                        |                      |  |  |
| number (not applicable)       | 38.3                   | 22.5                 |  |  |

### Statistical analyses

|  |  |
|--|--|
| Statistical analysis title   | Treatment Success According to the PGA |
| Statistical analysis description:<br>Mantel-Haenszel odds of treatment success in LEO 90100 group relative to calcipotriol BDP gel group, adjusted for pooled centre and baseline PGA.<br>Multiple imputation was used to handle missing PGA values. |  |



|   |   |
|---|---|
| Comparison groups                       | LEO 90100 aerosol foam v Calcipotriol BDP Gel |
| Number of subjects included in analysis | 373   |
| Analysis specification                  | Pre-specified                                 |
| Analysis type                           | superiority                                   |
| P-value                                 | < 0.001                                       |
| Method                                  | Mantel-Haenszel                               |
| Parameter estimate                      | Odds ratio (OR)                               |
| Point estimate                          | 2.55  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided                                       |
| lower limit                             | 1.46  |
| upper limit                             | 4.46  |

### Secondary: Subjects With PASI 75 at Week 4 for LEO 90100 and at Week 8 for Calcipotriol BDP Gel

|                 |   |
|-----------------|---|
| End point title | Subjects With PASI 75 at Week 4 for LEO 90100 and at Week 8 for Calcipotriol BDP Gel <sup>[2]</sup> |
|-----------------|---|

End point description:

Subjects with PASI 75 (a 75% reduction in the modified Psoriasis Area and Severity Index) at Week 4 for LEO 90100 and at Week 8 for calcipotriol BDP gel.

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

End point timeframe:

Week 4 for LEO 90100 and Week 8 for calcipotriol BDP gel

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The statistical analysis of this secondary endpoint was planned and performed for the 2 active treatments.

| End point values              | LEO 90100 aerosol foam | Calcipotriol BDP Gel |  |  |
|-------------------------------|------------------------|----------------------|--|--|
| Subject group type            | Reporting group        | Reporting group      |  |  |
| Number of subjects analysed   | 185                    | 188                  |  |  |
| Units: Percentage of subjects |                        |                      |  |  |
| number (not applicable)       | 52.1                   | 34.6                 |  |  |

### Statistical analyses

|                            |                       |
|----------------------------|-----------------------|
| Statistical analysis title | Subjects With PASI 75 |
|----------------------------|-----------------------|

Statistical analysis description:

Mantel-Haenszel odds of having PASI 75 in LEO 90100 group relative to calcipotriol BDP gel group, adjusted for pooled centre and baseline PGA.

Multiple imputation was used to handle missing data.

|                   |   |
|-------------------|---|
| Comparison groups | LEO 90100 aerosol foam v Calcipotriol BDP Gel |
|-------------------|---|

|   |                 |
|---|-----------------|
| Number of subjects included in analysis | 373             |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | superiority     |
| P-value                                 | = 0.001         |
| Method                                  | Mantel-Haenszel |
| Parameter estimate                      | Odds ratio (OR) |
| Point estimate                          | 2.18            |
| Confidence interval                     |                 |
| level                                   | 95 %            |
| sides                                   | 2-sided         |
| lower limit                             | 1.37            |
| upper limit                             | 3.47            |

## Secondary: Time to 'Treatment Success' According to PGA.

|                 |  |
|-----------------|--|
| End point title | Time to 'Treatment Success' According to PGA. <sup>[3]</sup> |
|-----------------|--|

End point description:

Definition for 'treatment success' is given under the primary endpoint.

Time to treatment success was calculated as the number of weeks from baseline to the visit where the subject first achieved treatment success.

LEO 90100 (n=185)

Time to treatment success (median): 6 weeks

Lower quartile: 4

Upper quartile: NA (could not be estimated as less than 75% of subjects achieved treatment success)

Calcipotriol BDP gel (n=188)

Time to treatment success (median): NA (could not be estimated for the group as less than 50% of subjects achieved treatment success)

Lower quartile: 6

Upper quartile: NA (could not be estimated as less than 75% of subjects achieved treatment success)

In the table below, measure type is set to 'number' instead of 'median', and precision type is set to 'not applicable' instead of 'inter-quartile range', as the database does not accept NA values for intra-quartile range to a median number.

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

End point timeframe:

Baseline to Week 12

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The statistical analysis of this secondary endpoint was planned and performed for the 2 active treatments.

| End point values            | LEO 90100 aerosol foam | Calcipotriol BDP Gel |  |  |
|-----------------------------|------------------------|----------------------|--|--|
| Subject group type          | Reporting group        | Reporting group      |  |  |
| Number of subjects analysed | 185                    | 188                  |  |  |
| Units: Weeks                |                        |                      |  |  |
| number (not applicable)     | 6                      | 0                    |  |  |

## Statistical analyses

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Time to 'Treatment Success' According to PGA. |
| Comparison groups                       | Calcipotriol BDP Gel v LEO 90100 aerosol foam |
| Number of subjects included in analysis | 373   |
| Analysis specification                  | Pre-specified                                 |
| Analysis type                           | superiority                                   |
| P-value                                 | < 0.001                                       |
| Method                                  | Logrank                                       |
| Parameter estimate                      | Hazard ratio (HR)                             |
| Point estimate                          | 1.97  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided                                       |
| lower limit                             | 1.46  |
| upper limit                             | 2.65  |

## Secondary: Change in Itch as Assessed on a VAS Scale (LEO 90100 vs. the Foam Vehicle Group)

|                 |   |
|-----------------|---|
| End point title | Change in Itch as Assessed on a VAS Scale (LEO 90100 vs. the Foam Vehicle Group) <sup>[4]</sup> |
|-----------------|---|

End point description:

Maximum itch during the previous 24 hours was assessed on a Visual Analogue Scale (VAS) - range from 0 (no itch at all) to 100 mm (worst itch one could imagine).

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

End point timeframe:

Baseline to Week 4

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The statistical analysis of this secondary endpoint was planned and performed to compare LEO 90100 with its vehicle.

| End point values                          | LEO 90100 aerosol foam | Aerosol Foam Vehicle  |  |  |
|---|------------------------|-----------------------|--|--|
| Subject group type                        | Reporting group        | Reporting group       |  |  |
| Number of subjects analysed               | 185                    | 47                    |  |  |
| Units: Units on a scale                   |                        |                       |  |  |
| arithmetic mean (confidence interval 95%) | -30.5 (-33.4 to -27.5) | -15.9 (-21.3 to 10.5) |  |  |

## Statistical analyses

|                                   |   |
|-----------------------------------|---|
| <b>Statistical analysis title</b> | Change in Itch (LEO 90100 vs. the Foam Vehicle) |
| Comparison groups                 | LEO 90100 aerosol foam v Aerosol Foam Vehicle   |

|   |                                |
|---|--------------------------------|
| Number of subjects included in analysis | 232                            |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           | superiority <sup>[5]</sup>     |
| P-value                                 | < 0.001                        |
| Method                                  | ANCOVA                         |
| Parameter estimate                      | Mean difference (final values) |
| Point estimate                          | -14.6                          |
| Confidence interval                     |                                |
| level                                   | 95 %                           |
| sides                                   | 2-sided                        |
| lower limit                             | -20.64                         |
| upper limit                             | -8.55                          |

Notes:

[5] - Mean change in itch adjusted for pooled centre, baseline PGA and baseline itch. Multiple imputation used for missing data.

### **Secondary: Change in Itch as Assessed on a VAS Scale From Baseline to Week 4 (LEO 90100) vs. Week 8 (Calcipotriol BDP Gel).**

|                 |   |
|-----------------|---|
| End point title | Change in Itch as Assessed on a VAS Scale From Baseline to Week 4 (LEO 90100) vs. Week 8 (Calcipotriol BDP Gel). <sup>[6]</sup> |
|-----------------|---|

End point description:

Maximum itch during the previous 24 hours was assessed on a Visual Analogue Scale - range from 0 (no itch at all) to 100 mm (worst itch one could imagine).

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

End point timeframe:

Baseline to Week 4 for LEO 90100 and Baseline to Week 8 for calcipotriol BDP gel

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The statistical analysis of this secondary endpoint was planned and performed for the 2 active treatments.

| <b>End point values</b>                   | LEO 90100 aerosol foam | Calcipotriol BDP Gel   |  |  |
|---|------------------------|------------------------|--|--|
| Subject group type                        | Reporting group        | Reporting group        |  |  |
| Number of subjects analysed               | 185                    | 188                    |  |  |
| Units: Units on a scale                   |                        |                        |  |  |
| arithmetic mean (confidence interval 95%) | -30.5 (-33.4 to -27.5) | -28.5 (-31.4 to -25.6) |  |  |

### **Statistical analyses**

|                                   |  |
|-----------------------------------|--|
| <b>Statistical analysis title</b> | Change in Itch (LEO 90100 vs. Calcipotriol BDP Ge) |
|-----------------------------------|--|

Statistical analysis description:

Mean change in itch adjusted for pooled centre, baseline PGA and baseline itch. Multiple imputation used for missing data.

|                   |   |
|-------------------|---|
| Comparison groups | LEO 90100 aerosol foam v Calcipotriol BDP Gel |
|-------------------|---|

|   |                                |
|---|--------------------------------|
| Number of subjects included in analysis | 373                            |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           | superiority                    |
| P-value                                 | = 0.33                         |
| Method                                  | ANCOVA                         |
| Parameter estimate                      | Mean difference (final values) |
| Point estimate                          | -1.93                          |
| Confidence interval                     |                                |
| level                                   | 95 %                           |
| sides                                   | 2-sided                        |
| lower limit                             | -5.78                          |
| upper limit                             | 1.93                           |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Day 0 until week 12

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 15.1 |
|--------------------|------|

### Reporting groups

|                       |           |
|-----------------------|-----------|
| Reporting group title | LEO 90100 |
|-----------------------|-----------|

Reporting group description: -

|                       |                      |
|-----------------------|----------------------|
| Reporting group title | Aerosol Foam Vehicle |
|-----------------------|----------------------|

Reporting group description: -

|                       |                      |
|-----------------------|----------------------|
| Reporting group title | Calcipotriol BDP Gel |
|-----------------------|----------------------|

Reporting group description: -

|                       |             |
|-----------------------|-------------|
| Reporting group title | Gel Vehicle |
|-----------------------|-------------|

Reporting group description: -

| Serious adverse events  | LEO 90100       | Aerosol Foam Vehicle | Calcipotriol BDP Gel |
|---|-----------------|----------------------|----------------------|
| Total subjects affected by serious adverse events                   |                 |                      |                      |
| subjects affected / exposed   | 8 / 185 (4.32%) | 0 / 47 (0.00%)       | 3 / 188 (1.60%)      |
| number of deaths (all causes)                                       | 0               | 0                    | 0                    |
| number of deaths resulting from adverse events                      | 0               | 0                    | 0                    |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                 |                      |                      |
| Prostate cancer   |                 |                      |                      |
| subjects affected / exposed   | 1 / 185 (0.54%) | 0 / 47 (0.00%)       | 0 / 188 (0.00%)      |
| occurrences causally related to treatment / all                     | 0 / 1           | 0 / 0                | 0 / 0                |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0                | 0 / 0                |
| Injury, poisoning and procedural complications                      |                 |                      |                      |
| Post procedural haemorrhage   |                 |                      |                      |
| subjects affected / exposed   | 0 / 185 (0.00%) | 0 / 47 (0.00%)       | 1 / 188 (0.53%)      |
| occurrences causally related to treatment / all                     | 0 / 0           | 0 / 0                | 0 / 1                |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0                | 0 / 0                |
| Cardiac disorders   |                 |                      |                      |
| Cardiac failure congestive  |                 |                      |                      |

|   |                 |                |                 |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed                     | 1 / 185 (0.54%) | 0 / 47 (0.00%) | 0 / 188 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| <b>Nervous system disorders</b>                 |                 |                |                 |
| Ischaemic stroke                                |                 |                |                 |
| subjects affected / exposed                     | 0 / 185 (0.00%) | 0 / 47 (0.00%) | 1 / 188 (0.53%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| <b>Gastrointestinal disorders</b>               |                 |                |                 |
| Gastrooesophageal reflux disease                |                 |                |                 |
| subjects affected / exposed                     | 1 / 185 (0.54%) | 0 / 47 (0.00%) | 0 / 188 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| <b>Hepatobiliary disorders</b>                  |                 |                |                 |
| Cholecystitis                                   |                 |                |                 |
| subjects affected / exposed                     | 0 / 185 (0.00%) | 0 / 47 (0.00%) | 0 / 188 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| <b>Skin and subcutaneous tissue disorders</b>   |                 |                |                 |
| Psoriasis                                       |                 |                |                 |
| subjects affected / exposed                     | 1 / 185 (0.54%) | 0 / 47 (0.00%) | 0 / 188 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| <b>Metabolism and nutrition disorders</b>       |                 |                |                 |
| Type 2 diabetes mellitus                        |                 |                |                 |
| subjects affected / exposed                     | 0 / 185 (0.00%) | 0 / 47 (0.00%) | 1 / 188 (0.53%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |

|   |                |  |  |
|---|----------------|--|--|
| <b>Serious adverse events</b>                                       | Gel Vehicle    |  |  |
| Total subjects affected by serious adverse events                   |                |  |  |
| subjects affected / exposed   | 1 / 43 (2.33%) |  |  |
| number of deaths (all causes)                                       | 0              |  |  |
| number of deaths resulting from adverse events                      | 0              |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                |  |  |

|   |                |  |  |
|---|----------------|--|--|
| Prostate cancer                                 |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Injury, poisoning and procedural complications  |                |  |  |
| Post procedural haemorrhage                     |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Cardiac disorders                               |                |  |  |
| Cardiac failure congestive                      |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Nervous system disorders                        |                |  |  |
| Ischaemic stroke                                |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Gastrointestinal disorders                      |                |  |  |
| Gastrooesophageal reflux disease                |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Hepatobiliary disorders                         |                |  |  |
| Cholecystitis                                   |                |  |  |
| subjects affected / exposed                     | 1 / 43 (2.33%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Skin and subcutaneous tissue disorders          |                |  |  |
| Psoriasis                                       |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Metabolism and nutrition disorders              |                |  |  |



|   |                |  |  |
|---|----------------|--|--|
| Type 2 diabetes mellitus<br>subjects affected / exposed | 0 / 43 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all      | 0 / 0          |  |  |
| deaths causally related to<br>treatment / all           | 0 / 0          |  |  |

Frequency threshold for reporting non-serious adverse events: 2 %

| <b>Non-serious adverse events</b>                                      | LEO 90100         | Aerosol Foam<br>Vehicle | Calcipotriol BDP Gel |
|--|-------------------|-------------------------|----------------------|
| Total subjects affected by non-serious<br>adverse events               |                   |                         |                      |
| subjects affected / exposed  | 77 / 185 (41.62%) | 25 / 47 (53.19%)        | 60 / 188 (31.91%)    |
| Neoplasms benign, malignant and<br>unspecified (incl cysts and polyps) |                   |                         |                      |
| Colon adenoma  |                   |                         |                      |
| subjects affected / exposed  | 0 / 185 (0.00%)   | 0 / 47 (0.00%)          | 0 / 188 (0.00%)      |
| occurrences (all)  | 0                 | 0                       | 0                    |
| Vascular disorders   |                   |                         |                      |
| Haematoma  |                   |                         |                      |
| subjects affected / exposed  | 0 / 185 (0.00%)   | 0 / 47 (0.00%)          | 0 / 188 (0.00%)      |
| occurrences (all)  | 0                 | 0                       | 0                    |
| Hypertension   |                   |                         |                      |
| subjects affected / exposed  | 2 / 185 (1.08%)   | 0 / 47 (0.00%)          | 7 / 188 (3.72%)      |
| occurrences (all)  | 2                 | 0                       | 7                    |
| General disorders and administration<br>site conditions                |                   |                         |                      |
| Application site pain  |                   |                         |                      |
| subjects affected / exposed  | 0 / 185 (0.00%)   | 1 / 47 (2.13%)          | 0 / 188 (0.00%)      |
| occurrences (all)  | 0                 | 1                       | 0                    |
| Application site pruritus  |                   |                         |                      |
| subjects affected / exposed  | 1 / 185 (0.54%)   | 2 / 47 (4.26%)          | 1 / 188 (0.53%)      |
| occurrences (all)  | 1                 | 2                       | 1                    |
| Feeling cold   |                   |                         |                      |
| subjects affected / exposed  | 0 / 185 (0.00%)   | 1 / 47 (2.13%)          | 0 / 188 (0.00%)      |
| occurrences (all)  | 0                 | 1                       | 0                    |
| Influenza like illness   |                   |                         |                      |
| subjects affected / exposed  | 3 / 185 (1.62%)   | 0 / 47 (0.00%)          | 2 / 188 (1.06%)      |
| occurrences (all)  | 3                 | 0                       | 2                    |
| Respiratory, thoracic and mediastinal<br>disorders                     |                   |                         |                      |

|  |                      |                     |                      |
|--|----------------------|---------------------|----------------------|
| Cough<br>subjects affected / exposed<br>occurrences (all)  | 1 / 185 (0.54%)<br>1 | 1 / 47 (2.13%)<br>1 | 2 / 188 (1.06%)<br>2 |
| Nasal congestion<br>subjects affected / exposed<br>occurrences (all)                                       | 0 / 185 (0.00%)<br>0 | 1 / 47 (2.13%)<br>1 | 0 / 188 (0.00%)<br>0 |
| Pulmonary congestion<br>subjects affected / exposed<br>occurrences (all)                                   | 0 / 185 (0.00%)<br>0 | 1 / 47 (2.13%)<br>1 | 0 / 188 (0.00%)<br>0 |
| Sinus congestion<br>subjects affected / exposed<br>occurrences (all)                                       | 0 / 185 (0.00%)<br>0 | 1 / 47 (2.13%)<br>1 | 0 / 188 (0.00%)<br>0 |
| Investigations<br>Vitamin D decreased<br>subjects affected / exposed<br>occurrences (all)                  | 2 / 185 (1.08%)<br>2 | 1 / 47 (2.13%)<br>1 | 3 / 188 (1.60%)<br>3 |
| Injury, poisoning and procedural complications<br>Fall<br>subjects affected / exposed<br>occurrences (all) | 0 / 185 (0.00%)<br>0 | 0 / 47 (0.00%)<br>0 | 1 / 188 (0.53%)<br>1 |
| Cardiac disorders<br>Angina pectoris<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 185 (0.00%)<br>0 | 1 / 47 (2.13%)<br>1 | 0 / 188 (0.00%)<br>0 |
| Atrial fibrillation<br>subjects affected / exposed<br>occurrences (all)                                    | 0 / 185 (0.00%)<br>0 | 0 / 47 (0.00%)<br>0 | 0 / 188 (0.00%)<br>0 |
| Nervous system disorders<br>Headache<br>subjects affected / exposed<br>occurrences (all)                   | 2 / 185 (1.08%)<br>2 | 2 / 47 (4.26%)<br>2 | 1 / 188 (0.53%)<br>1 |
| Gastrointestinal disorders<br>Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all)     | 0 / 185 (0.00%)<br>0 | 0 / 47 (0.00%)<br>0 | 0 / 188 (0.00%)<br>0 |
| Diarrhoea  |                      |                     |                      |

|   |                 |                |                 |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed                     | 4 / 185 (2.16%) | 0 / 47 (0.00%) | 2 / 188 (1.06%) |
| occurrences (all)                               | 4               | 0              | 2               |
| Gastrooesophageal reflux disease                |                 |                |                 |
| subjects affected / exposed                     | 2 / 185 (1.08%) | 1 / 47 (2.13%) | 1 / 188 (0.53%) |
| occurrences (all)                               | 2               | 1              | 1               |
| Nausea  |                 |                |                 |
| subjects affected / exposed                     | 2 / 185 (1.08%) | 0 / 47 (0.00%) | 2 / 188 (1.06%) |
| occurrences (all)                               | 2               | 0              | 2               |
| Gastroentirits                                  |                 |                |                 |
| subjects affected / exposed                     | 1 / 185 (0.54%) | 1 / 47 (2.13%) | 1 / 188 (0.53%) |
| occurrences (all)                               | 1               | 1              | 1               |
| Skin and subcutaneous tissue disorders          |                 |                |                 |
| Blister   |                 |                |                 |
| subjects affected / exposed                     | 1 / 185 (0.54%) | 1 / 47 (2.13%) | 0 / 188 (0.00%) |
| occurrences (all)                               | 1               | 1              | 0               |
| Dermatitis contact                              |                 |                |                 |
| subjects affected / exposed                     | 0 / 185 (0.00%) | 1 / 47 (2.13%) | 0 / 188 (0.00%) |
| occurrences (all)                               | 0               | 1              | 0               |
| Dry skin  |                 |                |                 |
| subjects affected / exposed                     | 1 / 185 (0.54%) | 1 / 47 (2.13%) | 0 / 188 (0.00%) |
| occurrences (all)                               | 1               | 1              | 0               |
| Erythema  |                 |                |                 |
| subjects affected / exposed                     | 1 / 185 (0.54%) | 1 / 47 (2.13%) | 0 / 188 (0.00%) |
| occurrences (all)                               | 1               | 1              | 0               |
| Pruritus  |                 |                |                 |
| subjects affected / exposed                     | 5 / 185 (2.70%) | 1 / 47 (2.13%) | 2 / 188 (1.06%) |
| occurrences (all)                               | 6               | 1              | 2               |
| Psoriasis                                       |                 |                |                 |
| subjects affected / exposed                     | 4 / 185 (2.16%) | 1 / 47 (2.13%) | 7 / 188 (3.72%) |
| occurrences (all)                               | 4               | 1              | 8               |
| Renal and urinary disorders                     |                 |                |                 |
| Renal failure chronic                           |                 |                |                 |
| subjects affected / exposed                     | 0 / 185 (0.00%) | 1 / 47 (2.13%) | 1 / 188 (0.53%) |
| occurrences (all)                               | 0               | 1              | 1               |
| Musculoskeletal and connective tissue disorders |                 |                |                 |

|   |                      |                     |                      |
|---|----------------------|---------------------|----------------------|
| Back pain<br>subjects affected / exposed<br>occurrences (all)                         | 5 / 185 (2.70%)<br>5 | 1 / 47 (2.13%)<br>1 | 3 / 188 (1.60%)<br>3 |
| Joint swelling<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 185 (0.00%)<br>0 | 0 / 47 (0.00%)<br>0 | 1 / 188 (0.53%)<br>1 |
| Infections and infestations   |                      |                     |                      |
| Cellulitis<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 185 (0.00%)<br>0 | 0 / 47 (0.00%)<br>0 | 0 / 188 (0.00%)<br>0 |
| Intertrigo candida<br>subjects affected / exposed<br>occurrences (all)                | 0 / 185 (0.00%)<br>0 | 1 / 47 (2.13%)<br>1 | 0 / 188 (0.00%)<br>0 |
| Lower respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 4 / 185 (2.16%)<br>4 | 0 / 47 (0.00%)<br>0 | 1 / 188 (0.53%)<br>1 |
| Nail infection<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 185 (0.00%)<br>0 | 0 / 47 (0.00%)<br>0 | 0 / 188 (0.00%)<br>0 |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)                   | 7 / 185 (3.78%)<br>7 | 0 / 47 (0.00%)<br>0 | 4 / 188 (2.13%)<br>4 |
| Sinusitis<br>subjects affected / exposed<br>occurrences (all)                         | 2 / 185 (1.08%)<br>2 | 0 / 47 (0.00%)<br>0 | 3 / 188 (1.60%)<br>3 |
| Tooth abscess<br>subjects affected / exposed<br>occurrences (all)                     | 1 / 185 (0.54%)<br>1 | 1 / 47 (2.13%)<br>1 | 1 / 188 (0.53%)<br>1 |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 5 / 185 (2.70%)<br>6 | 1 / 47 (2.13%)<br>1 | 9 / 188 (4.79%)<br>9 |
| Metabolism and nutrition disorders  |                      |                     |                      |
| Vitamin D deficiency<br>subjects affected / exposed<br>occurrences (all)              | 6 / 185 (3.24%)<br>6 | 0 / 47 (0.00%)<br>0 | 5 / 188 (2.66%)<br>5 |

|                                   |             |  |  |
|-----------------------------------|-------------|--|--|
| <b>Non-serious adverse events</b> | Gel Vehicle |  |  |
|-----------------------------------|-------------|--|--|

|  |  |  |  |
|--|--|--|--|
| Total subjects affected by non-serious adverse events<br>subjects affected / exposed   | 28 / 43 (65.12%)   |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps)<br>Colon adenoma<br>subjects affected / exposed<br>occurrences (all)   | 1 / 43 (2.33%)<br>1  |  |  |
| Vascular disorders<br>Haematoma<br>subjects affected / exposed<br>occurrences (all)<br><br>Hypertension<br>subjects affected / exposed<br>occurrences (all)  | 1 / 43 (2.33%)<br>1<br><br>0 / 43 (0.00%)<br>0   |  |  |
| General disorders and administration site conditions<br>Application site pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Application site pruritus<br>subjects affected / exposed<br>occurrences (all)<br><br>Feeling cold<br>subjects affected / exposed<br>occurrences (all)<br><br>Influenza like illness<br>subjects affected / exposed<br>occurrences (all) | 1 / 43 (2.33%)<br>1<br><br>1 / 43 (2.33%)<br>1<br><br>0 / 43 (0.00%)<br>0<br><br>1 / 43 (2.33%)<br>1 |  |  |
| Respiratory, thoracic and mediastinal disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all)<br><br>Nasal congestion<br>subjects affected / exposed<br>occurrences (all)<br><br>Pulmonary congestion<br>subjects affected / exposed<br>occurrences (all)   | 1 / 43 (2.33%)<br>1<br><br>0 / 43 (0.00%)<br>0<br><br>0 / 43 (0.00%)<br>0                            |  |  |

|  |  |  |  |
|--|--|--|--|
| Sinus congestion<br>subjects affected / exposed<br>occurrences (all)   | 0 / 43 (0.00%)<br>0  |  |  |
| Investigations<br>Vitamin D decreased<br>subjects affected / exposed<br>occurrences (all)  | 1 / 43 (2.33%)<br>1  |  |  |
| Injury, poisoning and procedural complications<br>Fall<br>subjects affected / exposed<br>occurrences (all)   | 1 / 43 (2.33%)<br>1  |  |  |
| Cardiac disorders<br>Angina pectoris<br>subjects affected / exposed<br>occurrences (all)<br><br>Atrial fibrillation<br>subjects affected / exposed<br>occurrences (all)  | 0 / 43 (0.00%)<br>0<br><br>1 / 43 (2.33%)<br>1   |  |  |
| Nervous system disorders<br>Headache<br>subjects affected / exposed<br>occurrences (all)   | 1 / 43 (2.33%)<br>1  |  |  |
| Gastrointestinal disorders<br>Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all)<br><br>Diarrhoea<br>subjects affected / exposed<br>occurrences (all)<br><br>Gastrooesophageal reflux disease<br>subjects affected / exposed<br>occurrences (all)<br><br>Nausea<br>subjects affected / exposed<br>occurrences (all)<br><br>Gastroenteritis | 1 / 43 (2.33%)<br>1<br><br>2 / 43 (4.65%)<br>2<br><br>0 / 43 (0.00%)<br>0<br><br>1 / 43 (2.33%)<br>1 |  |  |

|  |                     |  |  |
|--|---------------------|--|--|
| subjects affected / exposed<br>occurrences (all) | 0 / 43 (0.00%)<br>0 |  |  |
| Skin and subcutaneous tissue disorders           |                     |  |  |
| Blister  |                     |  |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 43 (0.00%)<br>0 |  |  |
| Dermatitis contact                               |                     |  |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 43 (0.00%)<br>0 |  |  |
| Dry skin   |                     |  |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 43 (0.00%)<br>0 |  |  |
| Erythema   |                     |  |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 43 (0.00%)<br>0 |  |  |
| Pruritus   |                     |  |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 43 (0.00%)<br>0 |  |  |
| Psoriasis  |                     |  |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 43 (0.00%)<br>0 |  |  |
| Renal and urinary disorders                      |                     |  |  |
| Renal failure chronic                            |                     |  |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 43 (0.00%)<br>0 |  |  |
| Musculoskeletal and connective tissue disorders  |                     |  |  |
| Back pain  |                     |  |  |
| subjects affected / exposed<br>occurrences (all) | 2 / 43 (4.65%)<br>2 |  |  |
| Joint swelling                                   |                     |  |  |
| subjects affected / exposed<br>occurrences (all) | 1 / 43 (2.33%)<br>1 |  |  |
| Infections and infestations                      |                     |  |  |
| Cellulitis                                       |                     |  |  |
| subjects affected / exposed<br>occurrences (all) | 1 / 43 (2.33%)<br>1 |  |  |

|  |                     |  |  |
|--|---------------------|--|--|
| Intertrigo candida<br>subjects affected / exposed<br>occurrences (all)   | 0 / 43 (0.00%)<br>0 |  |  |
| Lower respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)                          | 1 / 43 (2.33%)<br>1 |  |  |
| Nail infection<br>subjects affected / exposed<br>occurrences (all)   | 1 / 43 (2.33%)<br>1 |  |  |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)  | 2 / 43 (4.65%)<br>2 |  |  |
| Sinusitis<br>subjects affected / exposed<br>occurrences (all)  | 1 / 43 (2.33%)<br>1 |  |  |
| Tooth abscess<br>subjects affected / exposed<br>occurrences (all)  | 1 / 43 (2.33%)<br>1 |  |  |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)                          | 2 / 43 (4.65%)<br>2 |  |  |
| Metabolism and nutrition disorders<br>Vitamin D deficiency<br>subjects affected / exposed<br>occurrences (all) | 2 / 43 (4.65%)<br>2 |  |  |



## 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.

|    |
|----|
| NA |
|----|

Notes: