



## Clinical trial results:

### A PHASE IV, OPEN LABEL, PILOT STUDY OF THE TREATMENT OF CHILDREN WITH MODERATE TO SEVERE ATOPIC DERMATITIS (AD) USING LOCOBASE REPAIR® AS AN ADJUNCTIVE TO STANDARD TREATMENT

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

## Summary

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2006-006462-42    |
| Trial protocol           | GB                |
| Global end of trial date | 16 September 2008 |

## Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v2 (current) |
| This version publication date  | 19 May 2016  |
| First version publication date | 02 July 2015 |
| Version creation reason        |              |

## Trial information

### Trial identification

|                       |            |
|-----------------------|------------|
| Sponsor protocol code | REP-EC-001 |
|-----------------------|------------|

### Additional study identifiers

|                                    |                 |
|------------------------------------|-----------------|
| ISRCTN number                      | -               |
| ClinicalTrials.gov id (NCT number) | NCT00673725     |
| WHO universal trial number (UTN)   | -               |
| Other trial identifiers            | Acronym: REPAIR |

Notes:

## Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Astellas Pharma Europe B.V.  |
| Sponsor organisation address | P.O. Box 108, Leiderdorp, Netherlands, 2350 AC   |
| Public contact               | Clinical Trial Disclosure, Astellas Pharma Europe B.V.,<br>Astellas.resultsdisclosure@astellas.com |
| Scientific contact           | Clinical Trial Disclosure, Astellas Pharma Europe B.V.,<br>Astellas.resultsdisclosure@astellas.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                       | 16 September 2008 |
| Is this the analysis of the primary completion data? | Yes               |
| Primary completion date                              | 16 September 2008 |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 16 September 2008 |
| Was the trial ended prematurely?                     | No                |

Notes:

## General information about the trial

Main objective of the trial:

To assess the efficacy of Locobase REPAIR® when used in children with moderate to severe atopic dermatitis (AD)

Protection of trial subjects:

This clinical study was written, conducted and reported in accordance with the protocol, ICH GCP Guidelines, and applicable local regulations, including the European Directive 2001/20/EC, on the protection of human rights, and with the ethical principles that have their origin in the Declaration of Helsinki. Astellas ensures that the use and disclosure of protected health information (PHI) obtained during a research study complies with the federal, national and/or regional legislation related to the privacy and protection of personal information.

Background therapy: -

Evidence for comparator: -

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 26 March 2008 |
| 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 | United Kingdom: 49 |
| Worldwide total number of subjects   | 49                 |
| EEA total number of subjects         | 49                 |

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)  | 2  |
| Children (2-11 years)                     | 38 |
| Adolescents (12-17 years)                 | 9  |

|                      |   |
|----------------------|---|
| Adults (18-64 years) | 0 |
| From 65 to 84 years  | 0 |
| 85 years and over    | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Subjects must have continuously used a topical corticosteroid/Topical Calcineurin Inhibitor (TCI) as active treatment for AD, at least 4 weeks prior to screening. Subjects should have met following wash-out criteria prior to screening: Systemic corticosteroids - 2 weeks, Other investigational drugs - 2 weeks, Light Treatments (UVA, UVB) - 4 weeks.

### Period 1

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

Blinding implementation details:

Not applicable, this was an open label study.

### Arms

|                  |                              |
|------------------|------------------------------|
| <b>Arm title</b> | Locobase REPAIR® Twice daily |
|------------------|------------------------------|

Arm description:

Locobase REPAIR® cream to be applied twice daily to all areas with active lesions or dry skin either present at day 1 or that emerge during the study.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Locobase     |
| Investigational medicinal product code |              |
| Other name                             | REPAIR®      |
| Pharmaceutical forms                   | Cream        |
| Routes of administration               | Topical use  |

Dosage and administration details:

Locobase REPAIR® is a water-in-oil (W/O) cream with a relatively high percentage of Vaseline and some soft paraffin and carnauba wax. To this solid paraffin has been added in the form of nanoparticles (solid particles with a diameter <1000 nm). The skin lipid fraction of the formulation consists of cholesterol, oleic acid, palmitic acid and ceramide-III in relatively high concentrations. There is no active ingredient in Locobase REPAIR®. Locobase REPAIR® cream was to be applied topically twice daily to all areas with active lesions or dry skin either present at day 1 or that emerged during the study.

|                                       |                                 |
|---------------------------------------|---------------------------------|
| <b>Number of subjects in period 1</b> | Locobase REPAIR®<br>Twice daily |
| Started                               | 49                              |
| Completed                             | 34                              |
| Not completed                         | 15                              |
| Withdrawal of consent                 | 3                               |
| Lost to follow-up                     | 6                               |
| Adverse event (AE)                    | 4                               |
| Other (no adult to accompany patient) | 2                               |



## Baseline characteristics

### Reporting groups

|                       |                              |
|-----------------------|------------------------------|
| Reporting group title | Locobase REPAIR® Twice daily |
|-----------------------|------------------------------|

Reporting group description:

Locobase REPAIR® cream to be applied twice daily to all areas with active lesions or dry skin either present at day 1 or that emerge during the study.

| Reporting group values  | Locobase REPAIR®<br>Twice daily | Total |  |
|---|---------------------------------|-------|--|
| Number of subjects  | 49                              | 49    |  |
| Age categorical   |                                 |       |  |
| Units: Subjects   |                                 |       |  |
| In utero  |                                 | 0     |  |
| Preterm newborn infants<br>(gestational age < 37 wks)   |                                 | 0     |  |
| Newborns (0-27 days)  |                                 | 0     |  |
| Infants and toddlers (28 days-23<br>months)   |                                 | 0     |  |
| Children (2-11 years)   |                                 | 0     |  |
| Adolescents (12-17 years)   |                                 | 0     |  |
| Adults (18-64 years)  |                                 | 0     |  |
| From 65-84 years  |                                 | 0     |  |
| 85 years and over   |                                 | 0     |  |
| Age continuous  |                                 |       |  |
| Age values are based on the Safety Analysis Population (SAF). The SAF consisted of all enrolled patients who used Locobase REPAIR®. |                                 |       |  |
| Units: years  |                                 |       |  |
| arithmetic mean   | 7                               |       |  |
| standard deviation  | ± 4.1                           | -     |  |
| Gender categorical  |                                 |       |  |
| Gender values are based on the SAF.   |                                 |       |  |
| Units: Subjects   |                                 |       |  |
| Female  | 20                              | 20    |  |
| Male  | 29                              | 29    |  |

## End points

### End points reporting groups

|  |                                 |
|--|---------------------------------|
| Reporting group title  | Locobase REPAIR® Twice daily    |
| Reporting group description:<br>Locobase REPAIR® cream to be applied twice daily to all areas with active lesions or dry skin either present at day 1 or that emerge during the study.   |                                 |
| Subject analysis set title   | AD Cleared                      |
| Subject analysis set type  | Full analysis                   |
| Subject analysis set description:<br>The study analysis population for this endpoint consisted of the Full Analysis Set (FAS). The FAS consisted of all enrolled patients who used Locobase REPAIR® and had the baseline and a post-baseline Eczema Area and Severity Index (EASI) completed (i.e., the Physician's Assessments of Individual Signs (PAIS) and Affected Area and the Patient's Assessment of Itch (PAI) were completed). Last observation carried forward (LOCF) analysis. |                                 |
| Subject analysis set title   | Excellent Improvement in AD     |
| Subject analysis set type  | Full analysis                   |
| Subject analysis set description:<br>FAS, LOCF analysis.   |                                 |
| Subject analysis set title   | Marked Improvement in AD        |
| Subject analysis set type  | Full analysis                   |
| Subject analysis set description:<br>FAS, LOCF analysis.   |                                 |
| Subject analysis set title   | Moderate Improvement in AD      |
| Subject analysis set type  | Full analysis                   |
| Subject analysis set description:<br>FAS, LOCF analysis.   |                                 |
| Subject analysis set title   | Slight Improvement in AD        |
| Subject analysis set type  | Full analysis                   |
| Subject analysis set description:<br>FAS, LOCF analysis.   |                                 |
| Subject analysis set title   | AD Improvement Not Appreciable  |
| Subject analysis set type  | Full analysis                   |
| Subject analysis set description:<br>FAS, LOCF analysis.   |                                 |
| Subject analysis set title   | AD Worsened                     |
| Subject analysis set type  | Full analysis                   |
| Subject analysis set description:<br>FAS, LOCF analysis.   |                                 |
| Subject analysis set title   | Head and Neck Erythema Absent   |
| Subject analysis set type  | Full analysis                   |
| Subject analysis set description:<br>Physician's assessment of individual signs.   |                                 |
| Subject analysis set title   | Head and Neck Erythema Mild     |
| Subject analysis set type  | Full analysis                   |
| Subject analysis set description:<br>Physician's assessment of individual signs.   |                                 |
| Subject analysis set title   | Head and Neck Erythema Moderate |
| Subject analysis set type  | Full analysis                   |
| Subject analysis set description:<br>Physician's assessment of individual signs.   |                                 |
| Subject analysis set title   | Head and Neck Erythema Severe   |

|  |  |
|--|--|
| Subject analysis set type  | Full analysis                                      |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Head and Neck Edema/induration/papulation Absent   |
| Subject analysis set type  | Full analysis                                      |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Head and Neck Edema/induration/papulation Mild     |
| Subject analysis set type  | Full analysis                                      |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Head and Neck Edema/induration/papulation Moderate |
| Subject analysis set type  | Full analysis                                      |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Head and Neck Edema/induration/papulation Severe   |
| Subject analysis set type  | Full analysis                                      |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Head and Neck Excoriation Absent                   |
| Subject analysis set type  | Full analysis                                      |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Head and Neck Excoriation Mild                     |
| Subject analysis set type  | Full analysis                                      |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Head and Neck Excoriation Moderate                 |
| Subject analysis set type  | Full analysis                                      |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Head and Neck Excoriation Severe                   |
| Subject analysis set type  | Full analysis                                      |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Head and Neck Oozing/weeping/crusting Absent       |
| Subject analysis set type  | Full analysis                                      |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Head and Neck Oozing/weeping/crusting Mild         |
| Subject analysis set type  | Full analysis                                      |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Head and Neck Oozing/weeping/crusting Moderate     |
| Subject analysis set type  | Full analysis                                      |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Head and Neck Oozing/weeping/crusting Severe       |
| Subject analysis set type  | Full analysis                                      |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Head and Neck Scaling Absent                       |



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| Subject analysis set type  | Full analysis                                  |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Head and Neck Scaling Mild                     |
| Subject analysis set type  | Full analysis                                  |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Head and Neck Scaling Moderate                 |
| Subject analysis set type  | Full analysis                                  |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Head and Neck Scaling Severe                   |
| Subject analysis set type  | Full analysis                                  |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Head and Neck Lichenification Absent           |
| Subject analysis set type  | Full analysis                                  |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Head and Neck Lichenification Mild             |
| Subject analysis set type  | Full analysis                                  |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Head and Neck Lichenification Moderate         |
| Subject analysis set type  | Full analysis                                  |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Head and Neck Lichenification Severe           |
| Subject analysis set type  | Full analysis                                  |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Upper Limbs Erythema Absent                    |
| Subject analysis set type  | Full analysis                                  |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Upper Limbs Erythema Mild                      |
| Subject analysis set type  | Full analysis                                  |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Upper Limbs Erythema Moderate                  |
| Subject analysis set type  | Full analysis                                  |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Upper Limbs Erythema Severe                    |
| Subject analysis set type  | Full analysis                                  |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Upper Limbs Edema/induration/papulation Absent |
| Subject analysis set type  | Full analysis                                  |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Upper Limbs Edema/induration/papulation Mild   |

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|---|--|
| Subject analysis set type                   | Full analysis                                    |
| Subject analysis set description:           |  |
| Physician's assessment of individual signs. |  |
| Subject analysis set title                  | Upper Limbs Edema/induration/papulation Moderate |
| Subject analysis set type                   | Full analysis                                    |
| Subject analysis set description:           |  |
| Physician's assessment of individual signs. |  |
| Subject analysis set title                  | Upper Limbs Edema/induration/papulation Severe   |
| Subject analysis set type                   | Full analysis                                    |
| Subject analysis set description:           |  |
| Physician's assessment of individual signs. |  |
| Subject analysis set title                  | Upper Limbs Excoriation Absent                   |
| Subject analysis set type                   | Full analysis                                    |
| Subject analysis set description:           |  |
| Physician's assessment of individual signs. |  |
| Subject analysis set title                  | Upper Limbs Excoriation Mild                     |
| Subject analysis set type                   | Full analysis                                    |
| Subject analysis set description:           |  |
| Physician's assessment of individual signs. |  |
| Subject analysis set title                  | Upper Limbs Excoriation Moderate                 |
| Subject analysis set type                   | Full analysis                                    |
| Subject analysis set description:           |  |
| Physician's assessment of individual signs. |  |
| Subject analysis set title                  | Upper Limbs Excoriation Severe                   |
| Subject analysis set type                   | Full analysis                                    |
| Subject analysis set description:           |  |
| Physician's assessment of individual signs. |  |
| Subject analysis set title                  | Upper Limbs Oozing/weeping/crusting Absent       |
| Subject analysis set type                   | Full analysis                                    |
| Subject analysis set description:           |  |
| Physician's assessment of individual signs. |  |
| Subject analysis set title                  | Upper Limbs Oozing/weeping/crusting Mild         |
| Subject analysis set type                   | Full analysis                                    |
| Subject analysis set description:           |  |
| Physician's assessment of individual signs. |  |
| Subject analysis set title                  | Upper Limbs Oozing/weeping/crusting Moderate     |
| Subject analysis set type                   | Full analysis                                    |
| Subject analysis set description:           |  |
| Physician's assessment of individual signs. |  |
| Subject analysis set title                  | Upper Limbs Oozing/weeping/crusting Severe       |
| Subject analysis set type                   | Full analysis                                    |
| Subject analysis set description:           |  |
| Physician's assessment of individual signs. |  |
| Subject analysis set title                  | Upper Limbs Scaling Absent                       |
| Subject analysis set type                   | Full analysis                                    |
| Subject analysis set description:           |  |
| Physician's assessment of individual signs. |  |
| Subject analysis set title                  | Upper Limbs Scaling Mild                         |
| Subject analysis set type                   | Full analysis                                    |
| Subject analysis set description:           |  |
| Physician's assessment of individual signs. |  |
| Subject analysis set title                  | Upper Limbs Scaling Moderate                     |

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| Subject analysis set type  | Full analysis                              |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Upper Limbs Scaling Severe                 |
| Subject analysis set type  | Full analysis                              |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Upper Limbs Lichenification Absent         |
| Subject analysis set type  | Full analysis                              |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Upper Limbs Lichenification Mild           |
| Subject analysis set type  | Full analysis                              |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Upper Limbs Lichenification Moderate       |
| Subject analysis set type  | Full analysis                              |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Upper Limbs Lichenification Severe         |
| Subject analysis set type  | Full analysis                              |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Trunk Erythema Absent                      |
| Subject analysis set type  | Full analysis                              |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Trunk Erythema Mild                        |
| Subject analysis set type  | Full analysis                              |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Trunk Erythema Moderate                    |
| Subject analysis set type  | Full analysis                              |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Trunk Erythema Severe                      |
| Subject analysis set type  | Full analysis                              |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Trunk Edema/induration/papulation Absent   |
| Subject analysis set type  | Full analysis                              |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Trunk Edema/induration/papulation Mild     |
| Subject analysis set type  | Full analysis                              |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Trunk Edema/induration/papulation Moderate |

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| Subject analysis set type  | Full analysis                            |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Trunk Edema/induration/papulation Severe |
| Subject analysis set type  | Full analysis                            |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Trunk Excoriation Absent                 |
| Subject analysis set type  | Full analysis                            |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Trunk Excoriation Mild                   |
| Subject analysis set type  | Full analysis                            |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Trunk Excoriation Moderate               |
| Subject analysis set type  | Full analysis                            |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Trunk Excoriation Severe                 |
| Subject analysis set type  | Full analysis                            |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Trunk Oozing/weeping/crusting Absent     |
| Subject analysis set type  | Full analysis                            |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Trunk Oozing/weeping/crusting Mild       |
| Subject analysis set type  | Full analysis                            |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Trunk Oozing/weeping/crusting Moderate   |
| Subject analysis set type  | Full analysis                            |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Trunk Oozing/weeping/crusting Severe     |
| Subject analysis set type  | Full analysis                            |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Trunk Scaling Absent                     |
| Subject analysis set type  | Full analysis                            |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Trunk Scaling Mild                       |
| Subject analysis set type  | Full analysis                            |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Trunk Scaling Moderate                   |

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| Subject analysis set type  | Full analysis                                    |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Trunk Scaling Severe                             |
| Subject analysis set type  | Full analysis                                    |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Trunk Lichenification Absent                     |
| Subject analysis set type  | Full analysis                                    |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Trunk Lichenification Mild                       |
| Subject analysis set type  | Full analysis                                    |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Trunk Lichenification Moderate                   |
| Subject analysis set type  | Full analysis                                    |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Trunk Lichenification Severe                     |
| Subject analysis set type  | Full analysis                                    |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Lower Limbs Erythema Absent                      |
| Subject analysis set type  | Full analysis                                    |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Lower Limbs Erythema Mild                        |
| Subject analysis set type  | Full analysis                                    |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Lower Limbs Erythema Moderate                    |
| Subject analysis set type  | Full analysis                                    |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Lower Limbs Erythema Severe                      |
| Subject analysis set type  | Full analysis                                    |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Lower Limbs Edema/induration/papulation Absent   |
| Subject analysis set type  | Full analysis                                    |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Lower Limbs Edema/induration/papulation Mild     |
| Subject analysis set type  | Full analysis                                    |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Lower Limbs Edema/induration/papulation Moderate |
| Subject analysis set type  | Full analysis                                    |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Lower Limbs Edema/induration/papulation Severe   |

|   |  |
|---|--|
| Subject analysis set type                   | Full analysis                                |
| Subject analysis set description:           |  |
| Physician's assessment of individual signs. |  |
| Subject analysis set title                  | Lower Limbs Excoriation Absent               |
| Subject analysis set type                   | Full analysis                                |
| Subject analysis set description:           |  |
| Physician's assessment of individual signs. |  |
| Subject analysis set title                  | Lower Limbs Excoriation Mild                 |
| Subject analysis set type                   | Full analysis                                |
| Subject analysis set description:           |  |
| Physician's assessment of individual signs. |  |
| Subject analysis set title                  | Lower Limbs Excoriation Moderate             |
| Subject analysis set type                   | Full analysis                                |
| Subject analysis set description:           |  |
| Physician's assessment of individual signs. |  |
| Subject analysis set title                  | Lower Limbs Excoriation Severe               |
| Subject analysis set type                   | Full analysis                                |
| Subject analysis set description:           |  |
| Physician's assessment of individual signs. |  |
| Subject analysis set title                  | Lower Limbs Oozing/weeping/crusting Absent   |
| Subject analysis set type                   | Full analysis                                |
| Subject analysis set description:           |  |
| Physician's assessment of individual signs. |  |
| Subject analysis set title                  | Lower Limbs Oozing/weeping/crusting Mild     |
| Subject analysis set type                   | Full analysis                                |
| Subject analysis set description:           |  |
| Physician's assessment of individual signs. |  |
| Subject analysis set title                  | Lower Limbs Oozing/weeping/crusting Moderate |
| Subject analysis set type                   | Full analysis                                |
| Subject analysis set description:           |  |
| Physician's assessment of individual signs. |  |
| Subject analysis set title                  | Lower Limbs Oozing/weeping/crusting Severe   |
| Subject analysis set type                   | Full analysis                                |
| Subject analysis set description:           |  |
| Physician's assessment of individual signs. |  |
| Subject analysis set title                  | Lower Limbs Scaling Absent                   |
| Subject analysis set type                   | Full analysis                                |
| Subject analysis set description:           |  |
| Physician's assessment of individual signs. |  |
| Subject analysis set title                  | Lower Limbs Scaling Mild                     |
| Subject analysis set type                   | Full analysis                                |
| Subject analysis set description:           |  |
| Physician's assessment of individual signs. |  |
| Subject analysis set title                  | Lower Limbs Scaling Moderate                 |
| Subject analysis set type                   | Full analysis                                |
| Subject analysis set description:           |  |
| Physician's assessment of individual signs. |  |
| Subject analysis set title                  | Lower Limbs Scaling Severe                   |
| Subject analysis set type                   | Full analysis                                |
| Subject analysis set description:           |  |
| Physician's assessment of individual signs. |  |
| Subject analysis set title                  | Lower Limbs Lichenification Absent           |

|  |  |
|--|--|
| Subject analysis set type  | Full analysis                            |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Lower Limbs Lichenification Mild         |
| Subject analysis set type  | Full analysis                            |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Lower Limbs Lichenification Moderate     |
| Subject analysis set type  | Full analysis                            |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Lower Limbs Lichenification Severe       |
| Subject analysis set type  | Full analysis                            |
| Subject analysis set description:<br>Physician's assessment of individual signs. |  |
| Subject analysis set title   | Locobase REPAIR® Twice daily Week 3 LOCF |
| Subject analysis set type  | Full analysis                            |
| Subject analysis set description:<br>FAS population                              |  |
| Subject analysis set title   | Summary Statistics at Baseline           |
| Subject analysis set type  | Full analysis                            |
| Subject analysis set description:<br>FAS population.                             |  |
| Subject analysis set title   | Summary Statistics at Week 3             |
| Subject analysis set type  | Full analysis                            |
| Subject analysis set description:<br>FAS population.                             |  |
| Subject analysis set title   | Summary Statistics Week 3 LOCF           |
| Subject analysis set type  | Full analysis                            |
| Subject analysis set description:<br>FAS population.                             |  |
| Subject analysis set title   | AD Much Improved                         |
| Subject analysis set type  | Full analysis                            |
| Subject analysis set description:<br>FAS population.                             |  |
| Subject analysis set title   | AD Improved                              |
| Subject analysis set type  | Full analysis                            |
| Subject analysis set description:<br>FAS population.                             |  |
| Subject analysis set title   | AD Slightly Improved                     |
| Subject analysis set type  | Full analysis                            |
| Subject analysis set description:<br>FAS population.                             |  |
| Subject analysis set title   | AD Same                                  |
| Subject analysis set type  | Full analysis                            |
| Subject analysis set description:<br>FAS population.                             |  |
| Subject analysis set title   | AD Slightly Worse                        |
| Subject analysis set type  | Full analysis                            |
| Subject analysis set description:<br>FAS population.                             |  |
| Subject analysis set title   | AD Worse                                 |

|  |   |
|--|---|
| Subject analysis set type  | Full analysis   |
| Subject analysis set description:<br>FAS population.   |   |
| Subject analysis set title   | AD Much Worse   |
| Subject analysis set type  | Full analysis   |
| Subject analysis set description:<br>FAS population.   |   |
| Subject analysis set title   | Patients with at least one visit to a GP                    |
| Subject analysis set type  | Full analysis   |
| Subject analysis set description:<br>FAS population. General Practitioner (GP).  |   |
| Subject analysis set title   | Patients with at least one outpatient visit to a hospital   |
| Subject analysis set type  | Full analysis   |
| Subject analysis set description:<br>FAS population.   |   |
| Subject analysis set title   | Application site  |
| Subject analysis set type  | Safety analysis   |
| Subject analysis set description:<br>Safety Analysis Set (SAF) population. The SAF consisted of all enrolled patients who used Locobase REPAIR®. |   |
| Subject analysis set title   | Non-application site  |
| Subject analysis set type  | Safety analysis   |
| Subject analysis set description:<br>SAF population.   |   |
| Subject analysis set title   | Overall Participants with Treatment-Emergent Adverse Events |
| Subject analysis set type  | Safety analysis   |
| Subject analysis set description:<br>SAF population.   |   |

### **Primary: Change in the modified Eczema Area and Severity Index (mEASI) from baseline to Week 3**

|  |   |
|--|---|
| End point title  | Change in the modified Eczema Area and Severity Index (mEASI) from baseline to Week 3 |
| End point description:<br>The study analysis population for this endpoint consisted of the Full Analysis Set (FAS). The FAS consisted of all enrolled patients who used Locobase REPAIR® and had the baseline and a post-baseline EASI completed (i.e., the Physician's Assessments of Individual Signs (PAIS) and Affected Area and the Patient's Assessment of Itch (PAI) were completed). The mEASI is not an assessment but a score based on the PAIS and affected area and the PAI. The mEASI was calculated by the sponsor at the time of analysis. The modified EASI combined the EASI and the Itch Score (IS). The Investigator completed the Affected Area Scores (AAS) for each body region and the PAIS for signs of AD.<br>$\text{mEASI} (< 7 \text{ years old at baseline}) = \text{EASI} + \text{IS} \times (\text{AAS Head/Neck (H/N)} \times 0.2 + \text{AAS Upper Limbs (UL)} \times 0.2 + \text{AAS Trunk} \times 0.3 + \text{AAS Lower Limbs (LL)} \times 0.3)$ $\text{mEASI} (\geq 7 \text{ years old at baseline}) = \text{EASI} + \text{IS} \times (\text{AAS H/N} \times 0.1 + \text{AAS UL} \times 0.2 + \text{AAS Trunk} \times 0.3 + \text{AAS LL} \times 0.4)$ Highest possible score was: $72 + 18 = 90$ . |   |
| End point type   | Primary   |
| End point timeframe:<br>Baseline to Week 3.  |   |



| <b>End point values</b>              | Locobase REPAIR® Twice daily | Locobase REPAIR® Twice daily Week 3 LOCF | Summary Statistics at Baseline | Summary Statistics at Week 3 |
|--------------------------------------|------------------------------|--|--------------------------------|------------------------------|
| Subject group type                   | Reporting group              | Subject analysis set                     | Subject analysis set           | Subject analysis set         |
| Number of subjects analysed          | 30 <sup>[1]</sup>            | 41 <sup>[2]</sup>                        | 43 <sup>[3]</sup>              | 30 <sup>[4]</sup>            |
| Units: mEASI (see description)       |                              |  |                                |                              |
| arithmetic mean (standard deviation) | -7.77 (± 11.55)              | -6.73 (± 10.72)                          | 17.25 (± 12.78)                | 9.76 (± 8.63)                |

Notes:

[1] - Change in mEASI from baseline to Week 3.

[2] - Change in mEASI from baseline to Week 3 LOCF. Two patients had a missing mEASI at Week 3.

[3] - Summary Statistics at Baseline.

[4] - Summary Statistics at Week 3.

| <b>End point values</b>              | Summary Statistics Week 3 LOCF |  |  |  |
|--------------------------------------|--------------------------------|--|--|--|
| Subject group type                   | Subject analysis set           |  |  |  |
| Number of subjects analysed          | 41 <sup>[5]</sup>              |  |  |  |
| Units: mEASI (see description)       |                                |  |  |  |
| arithmetic mean (standard deviation) | 10.99 (± 10.06)                |  |  |  |

Notes:

[5] - Summary Statistics Week 3 LOCF. Two patients had a missing mEASI at Week 3.

## Statistical analyses

| <b>Statistical analysis title</b> | Statistical analysis 1 |
|-----------------------------------|------------------------|
|-----------------------------------|------------------------|

Statistical analysis description:

The hypothesis for the comparison is given as follows:

H0: There is no change in the mEASI at week 3 compared to baseline

H1: There is a change in the mEASI at week 3 compared to baseline

There were actually 30 subjects in this analysis, since the comparison includes the subjects at baseline and week 3.

|   |   |
|---|---|
| Comparison groups                       | Summary Statistics at Baseline v Summary Statistics at Week 3 |
| Number of subjects included in analysis | 73  |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | other <sup>[6]</sup>  |
| P-value                                 | = 0.0009 <sup>[7]</sup>                                       |
| Method                                  | t-test, 2-sided   |

Notes:

[6] - The primary variable was tested by use of a 2-sided paired t-test at a significance level of 5% on patients of the FAS who had a mEASI at week 3.

[7] - Two-sided paired t-test ( $\alpha=0.05$ )

t-value= -3.69

| <b>Statistical analysis title</b> | Statistical analysis 2 |
|-----------------------------------|------------------------|
|-----------------------------------|------------------------|

Statistical analysis description:

The hypothesis for the comparison is given as follows:

H0: There is no change in the mEASI at week 3 compared to baseline

H1: There is a change in the mEASI at week 3 compared to baseline

There were actually 41 subjects in this analysis, since the comparison includes the subjects at baseline and week 3 LOCF (Two patients had a missing mEASI at Week 3).

|   |   |
|---|---|
| Comparison groups                       | Summary Statistics at Baseline v Summary Statistics Week 3 LOCF |
| Number of subjects included in analysis | 84  |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | other <sup>[8]</sup>  |
| P-value                                 | = 0.0003 <sup>[9]</sup>   |
| Method                                  | t-test, 2-sided   |

Notes:

[8] - The primary variable was tested by use of a 2-sided paired t-test at a significance level of 5% on patients of the FAS who had a mEASI at week 3 (including data imputed using a LOCF approach). Two patients had a missing mEASI at Week 3.

[9] - Two-sided paired t-test ( $\alpha=0.05$ )  
t-value=-4.02

### Secondary: Change in the mEASI from baseline to Day 10 and Week 6

|   |  |
|---|--|
| End point title   | Change in the mEASI from baseline to Day 10 and Week 6 |
| End point description:<br>The study analysis population for this endpoint consisted of the FAS. |  |
| End point type  | Secondary  |
| End point timeframe:<br>Baseline to Day 10 and Week 6.  |  |

| End point values                     | Locobase REPAIR®<br>Twice daily |  |  |  |
|--------------------------------------|---------------------------------|--|--|--|
| Subject group type                   | Reporting group                 |  |  |  |
| Number of subjects analysed          | 43                              |  |  |  |
| Units: mEASI                         |                                 |  |  |  |
| arithmetic mean (standard deviation) |                                 |  |  |  |
| Day 10 [n=36]                        | -7.5 (± 9.69)                   |  |  |  |
| Week 6 [n=28]                        | -7.5 (± 10.88)                  |  |  |  |
| Week 6 LOCF [n=42]                   | -7.31 (± 10.87)                 |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change in the Eczema Area and Severity Index (EASI) from baseline to Day 10, Week 3 and Week 6

|                 |  |
|-----------------|--|
| End point title | Change in the Eczema Area and Severity Index (EASI) from baseline to Day 10, Week 3 and Week 6 |
|-----------------|--|

End point description:

The study analysis population for this endpoint consisted of the FAS. The EASI is not an assessment but a score based on the Physician's Assessment of Individual Signs (for four signs of atopic dermatitis: Erythema, Edema/Induration/Papulation, Excoriation, Lichenification) and the Affected Area Assessment (for each of four defined body regions: Head/Neck, Upper Limbs, Trunk, Lower Limbs).

EASI CALCULATION

TOTAL EASI (<7 years old at baseline) = Head/Neck (Subtotal) x 0.2 + Upper Limbs (Subtotal) x 0.2 + Trunk (Subtotal) x 0.3 + Lower Limbs (Subtotal) x 0.3

TOTAL EASI ( $\geq 7$  years old at baseline) = Head/Neck (Subtotal) x 0.1 + Upper Limbs (Subtotal) x 0.2 + Trunk (Subtotal) x 0.3 + Lower Limbs (Subtotal) x 0.4

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

End point timeframe:

Baseline to Day 10, Week 3 and Week 6.

| End point values                     | Locobase<br>REPAIR®<br>Twice daily |  |  |  |
|--------------------------------------|------------------------------------|--|--|--|
| Subject group type                   | Reporting group                    |  |  |  |
| Number of subjects analysed          | 43                                 |  |  |  |
| Units: EASI (see description)        |                                    |  |  |  |
| arithmetic mean (standard deviation) |                                    |  |  |  |
| Day 10 [n=37]                        | -4.79 (± 6.65)                     |  |  |  |
| Week 3 [n=30]                        | -4.88 (± 7.72)                     |  |  |  |
| Week 3 LOCF [n=42]                   | -4.13 (± 7.13)                     |  |  |  |
| Week 6 [n=30]                        | -4.09 (± 7.29)                     |  |  |  |
| Week 6 LOCF [n=43]                   | -4.46 (± 7.39)                     |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change in Patient's Assessment of Itch from baseline to Day 10, Week 3 and Week 6

|                 |   |
|-----------------|---|
| End point title | Change in Patient's Assessment of Itch from baseline to Day 10, Week 3 and Week 6 |
|-----------------|---|

End point description:

The study analysis population for this endpoint consisted of the FAS. Itch was assessed by the subject on a 10 cm visual analogue scale (VAS). The distance between the upper end of the scale ("No Itch") and the subject's mark on the scale was measured by the sponsor. The calculation was based on a modified EASI, the distance was categorized to values 0, 1, 2 and 3 as follows:

Itch score measured distance

0 0 - <2.5 cm

1 2.5 - <5 cm

2 5 - <7.5 cm

3 7.5 - 10 cm

Summary statistics for the observed value at each visit, including LOCF, and changes from baseline for the Itch Score (the classified itch assessment in 0, 1, 2 3) were not analyzed.

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

End point timeframe:

Baseline to Day 10, Week 3 and Week 6.

|                                      |                                    |  |  |  |
|--------------------------------------|------------------------------------|--|--|--|
| <b>End point values</b>              | Locobase<br>REPAIR®<br>Twice daily |  |  |  |
| Subject group type                   | Reporting group                    |  |  |  |
| Number of subjects analysed          | 43                                 |  |  |  |
| Units: Itch VAS (cm)                 |                                    |  |  |  |
| arithmetic mean (standard deviation) |                                    |  |  |  |
| Day 10 [n=36]                        | -2.12 (± 2.91)                     |  |  |  |
| Week 3 [n=30]                        | -2.42 (± 3.17)                     |  |  |  |
| Week 3 LOCF [n=41]                   | -2.1 (± 3.26)                      |  |  |  |
| Week 6 [n=28]                        | -2.76 (± 3.28)                     |  |  |  |
| Week 6 LOCF [n=42]                   | -2.34 (± 3.25)                     |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change in Physician's Global Evaluation of Clinical Response from baseline to Day 10, Week 3 and Week 6

|                 |   |
|-----------------|---|
| End point title | Change in Physician's Global Evaluation of Clinical Response from baseline to Day 10, Week 3 and Week 6 |
|-----------------|---|

End point description:

The study analysis population for this endpoint consisted of the FAS. The Physician's Global Evaluation of Clinical Response rates the change for all areas affected on the whole body on day 1 compared to defined visits. The physician completed the following at defined visits during the course of the study:

"Consider the patient's atopic dermatitis as a whole, how it looks, how it feels, how others react to it, etc. Since the patient started his/her first treatment with the study substance, do you think the condition is/shows":

% Improvement (Except for residual discolouration)

Cleared: 100

Excellent Improvement: 90-99

Marked Improvement: 75-89

Moderate Improvement: 50-74

Slight Improvement: 30-49

No Appreciable Improvement: 0-29

Worse: < 0

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

End point timeframe:

Baseline to Day 10, Week 3 and Week 6.

| <b>End point values</b>           | AD Cleared           | Excellent Improvement in AD | Marked Improvement in AD | Moderate Improvement in AD |
|-----------------------------------|----------------------|-----------------------------|--------------------------|----------------------------|
| Subject group type                | Subject analysis set | Subject analysis set        | Subject analysis set     | Subject analysis set       |
| Number of subjects analysed       | 43                   | 43                          | 43                       | 43                         |
| Units: percentage of participants |                      |                             |                          |                            |
| number (not applicable)           |                      |                             |                          |                            |
| Day 10 [n=37]                     | 2.7                  | 5.4                         | 29.7                     | 16.2                       |
| Week 3 [n=30]                     | 0                    | 10                          | 23.3                     | 23.3                       |
| Week 3 LOCF [n=42]                | 2.4                  | 7.1                         | 21.4                     | 21.4                       |
| Week 6 [n=30]                     | 0                    | 13.3                        | 30                       | 33.3                       |

|                    |   |      |      |      |
|--------------------|---|------|------|------|
| Week 6 LOCF [n=43] | 0 | 11.6 | 25.6 | 27.9 |
|--------------------|---|------|------|------|

| End point values                  | Slight Improvement in AD | AD Improvement Not Appreciable | AD Worsened          |  |
|-----------------------------------|--------------------------|--------------------------------|----------------------|--|
| Subject group type                | Subject analysis set     | Subject analysis set           | Subject analysis set |  |
| Number of subjects analysed       | 43                       | 43                             | 43                   |  |
| Units: percentage of participants |                          |                                |                      |  |
| number (not applicable)           |                          |                                |                      |  |
| Day 10 [n=37]                     | 24.3                     | 18.9                           | 2.7                  |  |
| Week 3 [n=30]                     | 20                       | 10                             | 13.3                 |  |
| Week 3 LOCF [n=42]                | 19                       | 16.7                           | 11.9                 |  |
| Week 6 [n=30]                     | 3.3                      | 10                             | 10                   |  |
| Week 6 LOCF [n=43]                | 11.6                     | 14                             | 9.3                  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change in Total Affected Body Surface Area from baseline to Day 10, Week 3 and Week 6

|                 |   |
|-----------------|---|
| End point title | Change in Total Affected Body Surface Area from baseline to Day 10, Week 3 and Week 6 |
|-----------------|---|

End point description:

The study analysis population for this endpoint consisted of the FAS.

Grading Scale: (Physician`s Assessment of Individual Signs)

0 = None

1 = Mild

2 = Moderate

3 = Severe

Sum of Erythema/Induration/Papulation,Excoriation, Lichenification on defined body regions Head/Neck, Upper Limbs, Trunk, Lower Limbs

Affected Area Score:

Score 0 1 2 3 4 5 6

Affected Area (%) 0 1-9 10-29 30-49 50-69 70-89 90-100

4 Subtotal = Sum2 x Affected Area Score (0-6)^3

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

End point timeframe:

Baseline to Day 10, Week 3 and Week 6.

|                                      |                                    |  |  |  |
|--------------------------------------|------------------------------------|--|--|--|
| <b>End point values</b>              | Locobase<br>REPAIR®<br>Twice daily |  |  |  |
| Subject group type                   | Reporting group                    |  |  |  |
| Number of subjects analysed          | 43                                 |  |  |  |
| Units: percentage of participants    |                                    |  |  |  |
| arithmetic mean (standard deviation) |                                    |  |  |  |
| Day 10 [n=37]                        | -5.49 (± 11.95)                    |  |  |  |
| Week 3 [n=30]                        | -4.86 (± 14.87)                    |  |  |  |
| Week 3 LOCF [n=42]                   | -4.13 (± 13.74)                    |  |  |  |
| Week 6 [n=30]                        | -7.56 (± 16.6)                     |  |  |  |
| Week 6 LOCF [n=43]                   | -6.88 (± 14.62)                    |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Physician's Assessment of Individual Signs

|                 |  |
|-----------------|--|
| End point title | Physician's Assessment of Individual Signs |
|-----------------|--|

End point description:

The study analysis population for this endpoint consisted of the FAS.

Grading Scale: (Physician's Assessment of Individual Signs)

0 = None

1 = Mild

2 = Moderate

3 = Severe

Sum of Erythema/Induration/Papulation, Excoriation, Lichenification on defined body regions Head/Neck, Upper Limbs, Trunk, Lower Limbs

Affected Area Score:

Score 0 1 2 3 4 5 6

Affected Area (%) 0 1-9 10-29 30-49 50-69 70-89 90-100

4 Subtotal = Sum2 x Affected Area Score (0-6)^3

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

End point timeframe:

Baseline, Day 10, Week 3 and Week 6.

| <b>End point values</b>           | Head and Neck<br>Erythema<br>Absent | Head and Neck<br>Erythema Mild | Head and Neck<br>Erythema<br>Moderate | Head and Neck<br>Erythema<br>Severe |
|-----------------------------------|-------------------------------------|--------------------------------|---------------------------------------|-------------------------------------|
| Subject group type                | Subject analysis set                | Subject analysis set           | Subject analysis set                  | Subject analysis set                |
| Number of subjects analysed       | 43                                  | 43                             | 43                                    | 43                                  |
| Units: percentage of participants |                                     |                                |                                       |                                     |
| number (not applicable)           |                                     |                                |                                       |                                     |
| Baseline [n=43]                   | 34.9                                | 39.5                           | 23.3                                  | 2.3                                 |
| Day 10 [n=37]                     | 51.4                                | 43.2                           | 5.4                                   | 0                                   |

|                    |      |      |     |   |
|--------------------|------|------|-----|---|
| Week 3 [n=30]      | 50   | 43.3 | 6.7 | 0 |
| Week 3 LOCF [n=42] | 45.2 | 45.2 | 9.5 | 0 |
| Week 6 [n=30]      | 60   | 36.7 | 3.3 | 0 |
| Week 6 LOCF [n=43] | 53.5 | 37.2 | 9.3 | 0 |

| End point values                  | Head and Neck<br>Edema/induration/papulation<br>Absent | Head and Neck<br>Edema/induration/papulation<br>Mild | Head and Neck<br>Edema/induration/papulation<br>Moderate | Head and Neck<br>Edema/induration/papulation<br>Severe |
|-----------------------------------|--|--|--|--|
| Subject group type                | Subject analysis set                                   | Subject analysis set                                 | Subject analysis set                                     | Subject analysis set                                   |
| Number of subjects analysed       | 43   | 43   | 43   | 43   |
| Units: percentage of participants |  |  |  |  |
| number (not applicable)           |  |  |  |  |
| Baseline [n=43]                   | 51.2   | 37.2   | 11.6   | 0  |
| Day 10 [n=37]                     | 75.7   | 24.3   | 0  | 0  |
| Week 3 [n=30]                     | 70   | 26.7   | 3.3  | 0  |
| Week 3 LOCF [n=42]                | 71.4   | 26.2   | 2.4  | 0  |
| Week 6 [n=30]                     | 80   | 20   | 0  | 0  |
| Week 6 LOCF [n=43]                | 74.4   | 23.3   | 2.3  | 0  |

| End point values                  | Head and Neck<br>Excoriation<br>Absent | Head and Neck<br>Excoriation<br>Mild | Head and Neck<br>Excoriation<br>Moderate | Head and Neck<br>Excoriation<br>Severe |
|-----------------------------------|--|--------------------------------------|--|--|
| Subject group type                | Subject analysis set                   | Subject analysis set                 | Subject analysis set                     | Subject analysis set                   |
| Number of subjects analysed       | 43                                     | 43                                   | 43                                       | 43                                     |
| Units: percentage of participants |  |                                      |  |  |
| number (not applicable)           |  |                                      |  |  |
| Baseline [n=43]                   | 60.5                                   | 27.9                                 | 11.6                                     | 0                                      |
| Day 10 [n=37]                     | 83.8                                   | 16.2                                 | 0  | 0                                      |
| Week 3 [n=30]                     | 76.7                                   | 20                                   | 3.3                                      | 0                                      |
| Week 3 LOCF [n=42]                | 78.6                                   | 19                                   | 2.4                                      | 0                                      |
| Week 6 [n=30]                     | 83.3                                   | 16.7                                 | 0  | 0                                      |
| Week 6 LOCF [n=43]                | 76.7                                   | 20.9                                 | 2.3                                      | 0                                      |

| End point values                  | Head and Neck<br>Oozing/weeping/crusting<br>Absent | Head and Neck<br>Oozing/weeping/crusting<br>Mild | Head and Neck<br>Oozing/weeping/crusting<br>Moderate | Head and Neck<br>Oozing/weeping/crusting<br>Severe |
|-----------------------------------|--|--|--|--|
| Subject group type                | Subject analysis set                               | Subject analysis set                             | Subject analysis set                                 | Subject analysis set                               |
| Number of subjects analysed       | 43   | 43   | 43   | 43   |
| Units: percentage of participants |  |  |  |  |
| number (not applicable)           |  |  |  |  |
| Baseline [n=43]                   | 86   | 9.3  | 4.7  | 0  |
| Day 10 [n=37]                     | 94.6   | 5.4  | 0  | 0  |
| Week 3 [n=30]                     | 100  | 0  | 0  | 0  |
| Week 3 LOCF [n=42]                | 97.6   | 2.4  | 0  | 0  |

|                    |      |     |   |   |
|--------------------|------|-----|---|---|
| Week 6 [n=30]      | 100  | 0   | 0 | 0 |
| Week 6 LOCF [n=43] | 97.7 | 2.3 | 0 | 0 |

| End point values                  | Head and Neck<br>Scaling Absent | Head and Neck<br>Scaling Mild | Head and Neck<br>Scaling<br>Moderate | Head and Neck<br>Scaling Severe |
|-----------------------------------|---------------------------------|-------------------------------|--------------------------------------|---------------------------------|
| Subject group type                | Subject analysis set            | Subject analysis set          | Subject analysis set                 | Subject analysis set            |
| Number of subjects analysed       | 43                              | 43                            | 43                                   | 43                              |
| Units: percentage of participants |                                 |                               |                                      |                                 |
| number (not applicable)           |                                 |                               |                                      |                                 |
| Baseline [n=43]                   | 60.5                            | 39.5                          | 0                                    | 0                               |
| Day 10 [n=37]                     | 75.7                            | 24.3                          | 0                                    | 0                               |
| Week 3 [n=30]                     | 73.3                            | 26.7                          | 0                                    | 0                               |
| Week 3 LOCF [n=42]                | 69                              | 31                            | 0                                    | 0                               |
| Week 6 [n=30]                     | 90                              | 10                            | 0                                    | 0                               |
| Week 6 LOCF [n=43]                | 79.1                            | 20.9                          | 0                                    | 0                               |

| End point values                  | Head and Neck<br>Lichenification<br>Absent | Head and Neck<br>Lichenification<br>Mild | Head and Neck<br>Lichenification<br>Moderate | Head and Neck<br>Lichenification<br>Severe |
|-----------------------------------|--|--|--|--|
| Subject group type                | Subject analysis set                       | Subject analysis set                     | Subject analysis set                         | Subject analysis set                       |
| Number of subjects analysed       | 43   | 43                                       | 43   | 43   |
| Units: percentage of participants |  |  |  |  |
| number (not applicable)           |  |  |  |  |
| Baseline [n=43]                   | 74.4                                       | 25.6                                     | 0  | 0  |
| Day 10 [n=37]                     | 81.1                                       | 18.9                                     | 0  | 0  |
| Week 3 [n=30]                     | 90   | 10                                       | 0  | 0  |
| Week 3 LOCF [n=42]                | 85.7                                       | 14.3                                     | 0  | 0  |
| Week 6 [n=30]                     | 90   | 10                                       | 0  | 0  |
| Week 6 LOCF [n=43]                | 88.4                                       | 11.6                                     | 0  | 0  |

| End point values                  | Upper Limbs<br>Erythema<br>Absent | Upper Limbs<br>Erythema Mild | Upper Limbs<br>Erythema<br>Moderate | Upper Limbs<br>Erythema<br>Severe |
|-----------------------------------|-----------------------------------|------------------------------|-------------------------------------|-----------------------------------|
| Subject group type                | Subject analysis set              | Subject analysis set         | Subject analysis set                | Subject analysis set              |
| Number of subjects analysed       | 43                                | 43                           | 43                                  | 43                                |
| Units: percentage of participants |                                   |                              |                                     |                                   |
| number (not applicable)           |                                   |                              |                                     |                                   |
| Baseline [n=43]                   | 2.3                               | 41.9                         | 48.8                                | 7                                 |
| Day 10 [n=37]                     | 8.1                               | 62.2                         | 29.7                                | 0                                 |
| Week 3 [n=30]                     | 0                                 | 76.7                         | 20                                  | 3.3                               |
| Week 3 LOCF [n=42]                | 2.4                               | 71.4                         | 23.8                                | 2.4                               |
| Week 6 [n=30]                     | 20                                | 56.7                         | 20                                  | 3.3                               |
| Week 6 LOCF [n=43]                | 14                                | 60.5                         | 20.9                                | 4.7                               |



| <b>End point values</b>           | Upper Limbs<br>Edema/induration/<br>papulation<br>Absent | Upper Limbs<br>Edema/induration/<br>papulation<br>Mild | Upper Limbs<br>Edema/induration/<br>papulation<br>Moderate | Upper Limbs<br>Edema/induration/<br>papulation<br>Severe |
|-----------------------------------|--|--|--|--|
| Subject group type                | Subject analysis set                                     | Subject analysis set                                   | Subject analysis set                                       | Subject analysis set                                     |
| Number of subjects analysed       | 43   | 43   | 43   | 43   |
| Units: percentage of participants |  |  |  |  |
| number (not applicable)           |  |  |  |  |
| Baseline [n=43]                   | 9.3  | 46.5   | 39.5   | 4.7  |
| Day 10 [n=37]                     | 27   | 67.6   | 5.4  | 0  |
| Week 3 [n=30]                     | 30   | 53.3   | 16.7   | 0  |
| Week 3 LOCF [n=42]                | 35.7   | 50   | 14.3   | 0  |
| Week 6 [n=30]                     | 46.7   | 36.7   | 13.3   | 3.3  |
| Week 6 LOCF [n=43]                | 39.5   | 46.5   | 11.6   | 2.3  |

| <b>End point values</b>           | Upper Limbs<br>Excoriation<br>Absent | Upper Limbs<br>Excoriation<br>Mild | Upper Limbs<br>Excoriation<br>Moderate | Upper Limbs<br>Excoriation<br>Severe |
|-----------------------------------|--------------------------------------|------------------------------------|--|--------------------------------------|
| Subject group type                | Subject analysis set                 | Subject analysis set               | Subject analysis set                   | Subject analysis set                 |
| Number of subjects analysed       | 43                                   | 43                                 | 43                                     | 43                                   |
| Units: percentage of participants |                                      |                                    |  |                                      |
| number (not applicable)           |                                      |                                    |  |                                      |
| Baseline [n=43]                   | 7                                    | 46.5                               | 39.5                                   | 7                                    |
| Day 10 [n=37]                     | 13.5                                 | 64.9                               | 21.6                                   | 0                                    |
| Week 3 [n=30]                     | 26.7                                 | 53.3                               | 20                                     | 0                                    |
| Week 3 LOCF [n=42]                | 26.2                                 | 52.4                               | 21.4                                   | 0                                    |
| Week 6 [n=30]                     | 23.3                                 | 53.3                               | 23.3                                   | 0                                    |
| Week 6 LOCF [n=43]                | 23.3                                 | 51.2                               | 25.6                                   | 0                                    |

| <b>End point values</b>           | Upper Limbs<br>Oozing/weeping/<br>crusting<br>Absent | Upper Limbs<br>Oozing/weeping/<br>crusting Mild | Upper Limbs<br>Oozing/weeping/<br>crusting<br>Moderate | Upper Limbs<br>Oozing/weeping/<br>crusting<br>Severe |
|-----------------------------------|--|---|--|--|
| Subject group type                | Subject analysis set                                 | Subject analysis set                            | Subject analysis set                                   | Subject analysis set                                 |
| Number of subjects analysed       | 43   | 43  | 43   | 43   |
| Units: percentage of participants |  |   |  |  |
| number (not applicable)           |  |   |  |  |
| Baseline [n=43]                   | 55.8   | 32.6  | 11.6   | 0  |
| Day 10 [n=37]                     | 73   | 24.3  | 2.7  | 0  |
| Week 3 [n=30]                     | 80   | 20  | 0  | 0  |
| Week 3 LOCF [n=42]                | 83.3   | 14.3  | 2.4  | 0  |
| Week 6 [n=30]                     | 80   | 20  | 0  | 0  |
| Week 6 LOCF [n=43]                | 81.4   | 16.3  | 2.3  | 0  |

| <b>End point values</b>           | Upper Limbs<br>Scaling Absent | Upper Limbs<br>Scaling Mild | Upper Limbs<br>Scaling<br>Moderate | Upper Limbs<br>Scaling Severe |
|-----------------------------------|-------------------------------|-----------------------------|------------------------------------|-------------------------------|
| Subject group type                | Subject analysis set          | Subject analysis set        | Subject analysis set               | Subject analysis set          |
| Number of subjects analysed       | 43                            | 43                          | 43                                 | 43                            |
| Units: percentage of participants |                               |                             |                                    |                               |
| number (not applicable)           |                               |                             |                                    |                               |
| Baseline [n=43]                   | 30.2                          | 55.8                        | 14                                 | 0                             |
| Day 10 [n=37]                     | 45.9                          | 51.4                        | 2.7                                | 0                             |
| Week 3 [n=30]                     | 46.7                          | 50                          | 3.3                                | 0                             |
| Week 3 LOCF [n=42]                | 45.2                          | 52.4                        | 2.4                                | 0                             |
| Week 6 [n=30]                     | 56.7                          | 43.3                        | 0                                  | 0                             |
| Week 6 LOCF [n=43]                | 46.5                          | 51.2                        | 2.3                                | 0                             |

| <b>End point values</b>           | Upper Limbs<br>Lichenification<br>Absent | Upper Limbs<br>Lichenification<br>Mild | Upper Limbs<br>Lichenification<br>Moderate | Upper Limbs<br>Lichenification<br>Severe |
|-----------------------------------|--|--|--|--|
| Subject group type                | Subject analysis set                     | Subject analysis set                   | Subject analysis set                       | Subject analysis set                     |
| Number of subjects analysed       | 43                                       | 43                                     | 43   | 43                                       |
| Units: percentage of participants |  |  |  |  |
| number (not applicable)           |  |  |  |  |
| Baseline [n=43]                   | 23.3                                     | 55.8                                   | 20.9                                       | 0  |
| Day 10 [n=37]                     | 40.5                                     | 51.4                                   | 8.1  | 0  |
| Week 3 [n=30]                     | 43.3                                     | 56.7                                   | 0  | 0  |
| Week 3 LOCF [n=42]                | 40.5                                     | 52.4                                   | 7.1  | 0  |
| Week 6 [n=30]                     | 43.3                                     | 50                                     | 6.7  | 0  |
| Week 6 LOCF [n=43]                | 41.9                                     | 51.2                                   | 7  | 0  |

| <b>End point values</b>           | Trunk<br>Erythema<br>Absent | Trunk<br>Erythema Mild | Trunk<br>Erythema<br>Moderate | Trunk<br>Erythema<br>Severe |
|-----------------------------------|-----------------------------|------------------------|-------------------------------|-----------------------------|
| Subject group type                | Subject analysis set        | Subject analysis set   | Subject analysis set          | Subject analysis set        |
| Number of subjects analysed       | 43                          | 43                     | 43                            | 43                          |
| Units: percentage of participants |                             |                        |                               |                             |
| number (not applicable)           |                             |                        |                               |                             |
| Baseline [n=43]                   | 34.9                        | 53.5                   | 11.6                          | 0                           |
| Day 10 [n=37]                     | 56.8                        | 35.1                   | 8.1                           | 0                           |
| Week 3 [n=30]                     | 60                          | 30                     | 10                            | 0                           |
| Week 3 LOCF [n=42]                | 54.8                        | 35.7                   | 9.5                           | 0                           |
| Week 6 [n=30]                     | 63.3                        | 30                     | 6.7                           | 0                           |
| Week 6 LOCF [n=43]                | 53.5                        | 37.2                   | 9.3                           | 0                           |

| <b>End point values</b>           | Trunk<br>Edema/induration/papulation<br>Absent | Trunk<br>Edema/induration/papulation<br>Mild | Trunk<br>Edema/induration/papulation<br>Moderate | Trunk<br>Edema/induration/papulation<br>Severe |
|-----------------------------------|--|--|--|--|
| Subject group type                | Subject analysis set                           | Subject analysis set                         | Subject analysis set                             | Subject analysis set                           |
| Number of subjects analysed       | 43   | 43   | 43   | 43   |
| Units: percentage of participants |  |  |  |  |
| number (not applicable)           |  |  |  |  |
| Baseline [n=43]                   | 62.8   | 30.2   | 7  | 0  |
| Day 10 [n=37]                     | 78.4   | 21.6   | 0  | 0  |
| Week 3 [n=30]                     | 73.3   | 20   | 6.7  | 0  |
| Week 3 LOCF [n=42]                | 71.4   | 23.8   | 4.8  | 0  |
| Week 6 [n=30]                     | 80   | 16.7   | 3.3  | 0  |
| Week 6 LOCF [n=43]                | 76.7   | 16.3   | 7  | 0  |

| <b>End point values</b>           | Trunk<br>Excoriation<br>Absent | Trunk<br>Excoriation<br>Mild | Trunk<br>Excoriation<br>Moderate | Trunk<br>Excoriation<br>Severe |
|-----------------------------------|--------------------------------|------------------------------|----------------------------------|--------------------------------|
| Subject group type                | Subject analysis set           | Subject analysis set         | Subject analysis set             | Subject analysis set           |
| Number of subjects analysed       | 43                             | 43                           | 43                               | 43                             |
| Units: percentage of participants |                                |                              |                                  |                                |
| number (not applicable)           |                                |                              |                                  |                                |
| Baseline [n=43]                   | 65.1                           | 20.9                         | 9.3                              | 4.7                            |
| Day 10 [n=37]                     | 73                             | 27                           | 0                                | 0                              |
| Week 3 [n=30]                     | 70                             | 23.3                         | 6.7                              | 0                              |
| Week 3 LOCF [n=42]                | 69                             | 26.2                         | 4.8                              | 0                              |
| Week 6 [n=30]                     | 73.3                           | 23.3                         | 3.3                              | 0                              |
| Week 6 LOCF [n=43]                | 69.8                           | 23.3                         | 7                                | 0                              |

| <b>End point values</b>           | Trunk<br>Oozing/weeping/crusting<br>Absent | Trunk<br>Oozing/weeping/crusting<br>Mild | Trunk<br>Oozing/weeping/crusting<br>Moderate | Trunk<br>Oozing/weeping/crusting<br>Severe |
|-----------------------------------|--|--|--|--|
| Subject group type                | Subject analysis set                       | Subject analysis set                     | Subject analysis set                         | Subject analysis set                       |
| Number of subjects analysed       | 43   | 43                                       | 43   | 43   |
| Units: percentage of participants |  |  |  |  |
| number (not applicable)           |  |  |  |  |
| Baseline [n=43]                   | 86   | 9.3                                      | 4.7  | 0  |
| Day 10 [n=37]                     | 91.9                                       | 8.1                                      | 0  | 0  |
| Week 3 [n=30]                     | 93.3                                       | 6.7                                      | 0  | 0  |
| Week 3 LOCF [n=42]                | 92.9                                       | 7.1                                      | 0  | 0  |
| Week 6 [n=30]                     | 93.3                                       | 6.7                                      | 0  | 0  |
| Week 6 LOCF [n=43]                | 93   | 7  | 0  | 0  |

| <b>End point values</b> | Trunk Scaling<br>Absent | Trunk Scaling<br>Mild | Trunk Scaling<br>Moderate | Trunk Scaling<br>Severe |
|-------------------------|-------------------------|-----------------------|---------------------------|-------------------------|
|-------------------------|-------------------------|-----------------------|---------------------------|-------------------------|

| Subject group type                | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
|-----------------------------------|----------------------|----------------------|----------------------|----------------------|
| Number of subjects analysed       | 43                   | 43                   | 43                   | 43                   |
| Units: percentage of participants |                      |                      |                      |                      |
| number (not applicable)           |                      |                      |                      |                      |
| Baseline [n=43]                   | 60.5                 | 39.5                 | 0                    | 0                    |
| Day 10 [n=37]                     | 78.4                 | 21.6                 | 0                    | 0                    |
| Week 3 [n=30]                     | 90                   | 10                   | 0                    | 0                    |
| Week 3 LOCF [n=42]                | 83.3                 | 16.7                 | 0                    | 0                    |
| Week 6 [n=30]                     | 86.7                 | 13.3                 | 0                    | 0                    |
| Week 6 LOCF [n=43]                | 81.4                 | 18.6                 | 0                    | 0                    |

| End point values                  | Trunk<br>Lichenification<br>Absent | Trunk<br>Lichenification<br>Mild | Trunk<br>Lichenification<br>Moderate | Trunk<br>Lichenification<br>Severe |
|-----------------------------------|------------------------------------|----------------------------------|--------------------------------------|------------------------------------|
| Subject group type                | Subject analysis set               | Subject analysis set             | Subject analysis set                 | Subject analysis set               |
| Number of subjects analysed       | 43                                 | 43                               | 43                                   | 43                                 |
| Units: percentage of participants |                                    |                                  |                                      |                                    |
| number (not applicable)           |                                    |                                  |                                      |                                    |
| Baseline [n=43]                   | 72.1                               | 25.6                             | 2.3                                  | 0                                  |
| Day 10 [n=37]                     | 81.1                               | 18.9                             | 0                                    | 0                                  |
| Week 3 [n=30]                     | 80.8                               | 20                               | 0                                    | 0                                  |
| Week 3 LOCF [n=42]                | 78.6                               | 21.4                             | 0                                    | 0                                  |
| Week 6 [n=30]                     | 80                                 | 16.7                             | 3.3                                  | 0                                  |
| Week 6 LOCF [n=43]                | 81.4                               | 16.3                             | 2.3                                  | 0                                  |

| End point values                  | Lower Limbs<br>Erythema<br>Absent | Lower Limbs<br>Erythema Mild | Lower Limbs<br>Erythema<br>Moderate | Lower Limbs<br>Erythema<br>Severe |
|-----------------------------------|-----------------------------------|------------------------------|-------------------------------------|-----------------------------------|
| Subject group type                | Subject analysis set              | Subject analysis set         | Subject analysis set                | Subject analysis set              |
| Number of subjects analysed       | 43                                | 43                           | 43                                  | 43                                |
| Units: percentage of participants |                                   |                              |                                     |                                   |
| number (not applicable)           |                                   |                              |                                     |                                   |
| Baseline [n=43]                   | 4.7                               | 23.3                         | 55.8                                | 16.3                              |
| Day 10 [n=37]                     | 8.1                               | 56.8                         | 35.1                                | 0                                 |
| Week 3 [n=30]                     | 3.3                               | 46.7                         | 43.3                                | 6.7                               |
| Week 3 LOCF [n=42]                | 4.8                               | 42.9                         | 47.6                                | 4.8                               |
| Week 6 [n=30]                     | 10                                | 46.7                         | 33.3                                | 10                                |
| Week 6 LOCF [n=43]                | 7                                 | 44.2                         | 39.5                                | 9.3                               |

| End point values                  | Lower Limbs<br>Edema/induration/papulation<br>Absent | Lower Limbs<br>Edema/induration/papulation<br>Mild | Lower Limbs<br>Edema/induration/papulation<br>Moderate | Lower Limbs<br>Edema/induration/papulation<br>Severe |
|-----------------------------------|--|--|--|--|
| Subject group type                | Subject analysis set                                 | Subject analysis set                               | Subject analysis set                                   | Subject analysis set                                 |
| Number of subjects analysed       | 43   | 43   | 43   | 43   |
| Units: percentage of participants |  |  |  |  |

|                         |      |      |      |     |
|-------------------------|------|------|------|-----|
| number (not applicable) |      |      |      |     |
| Baseline [n=43]         | 14   | 30.2 | 48.8 | 7   |
| Day 10 [n=37]           | 21.6 | 56.8 | 18.9 | 2.7 |
| Week 3 [n=30]           | 23.3 | 43.3 | 33.3 | 0   |
| Week 3 LOCF [n=42]      | 23.8 | 38.1 | 35.7 | 2.4 |
| Week 6 [n=30]           | 33.3 | 40   | 16.7 | 10  |
| Week 6 LOCF [n=43]      | 25.6 | 39.5 | 27.9 | 7   |

| End point values                  | Lower Limbs<br>Excoriation<br>Absent | Lower Limbs<br>Excoriation<br>Mild | Lower Limbs<br>Excoriation<br>Moderate | Lower Limbs<br>Excoriation<br>Severe |
|-----------------------------------|--------------------------------------|------------------------------------|--|--------------------------------------|
| Subject group type                | Subject analysis set                 | Subject analysis set               | Subject analysis set                   | Subject analysis set                 |
| Number of subjects analysed       | 43                                   | 43                                 | 43                                     | 43                                   |
| Units: percentage of participants |                                      |                                    |  |                                      |
| number (not applicable)           |                                      |                                    |  |                                      |
| Baseline [n=43]                   | 14                                   | 27.9                               | 48.8                                   | 9.3                                  |
| Day 10 [n=37]                     | 13.5                                 | 70.3                               | 16.2                                   | 0                                    |
| Week 3 [n=30]                     | 26.7                                 | 46.7                               | 23.3                                   | 3.3                                  |
| Week 3 LOCF [n=42]                | 23.8                                 | 45.2                               | 28.6                                   | 2.4                                  |
| Week 6 [n=30]                     | 20                                   | 53.3                               | 20                                     | 6.7                                  |
| Week 6 LOCF [n=43]                | 20.9                                 | 48.8                               | 23.3                                   | 7                                    |

| End point values                  | Lower Limbs<br>Oozing/weepin<br>g/crusting<br>Absent | Lower Limbs<br>Oozing/weepin<br>g/crusting Mild | Lower Limbs<br>Oozing/weepin<br>g/crusting<br>Moderate | Lower Limbs<br>Oozing/weepin<br>g/crusting<br>Severe |
|-----------------------------------|--|---|--|--|
| Subject group type                | Subject analysis set                                 | Subject analysis set                            | Subject analysis set                                   | Subject analysis set                                 |
| Number of subjects analysed       | 43   | 43  | 43   | 43   |
| Units: percentage of participants |  |   |  |  |
| number (not applicable)           |  |   |  |  |
| Baseline [n=43]                   | 53.5   | 34.9  | 11.6   | 0  |
| Day 10 [n=37]                     | 78.4   | 21.6  | 0  | 0  |
| Week 3 [n=30]                     | 66.7   | 26.7  | 6.7  | 0  |
| Week 3 LOCF [n=42]                | 71.4   | 23.8  | 4.8  | 0  |
| Week 6 [n=30]                     | 70   | 23.3  | 6.7  | 0  |
| Week 6 LOCF [n=43]                | 74.4   | 20.9  | 4.7  | 0  |

| End point values                  | Lower Limbs<br>Scaling Absent | Lower Limbs<br>Scaling Mild | Lower Limbs<br>Scaling<br>Moderate | Lower Limbs<br>Scaling Severe |
|-----------------------------------|-------------------------------|-----------------------------|------------------------------------|-------------------------------|
| Subject group type                | Subject analysis set          | Subject analysis set        | Subject analysis set               | Subject analysis set          |
| Number of subjects analysed       | 43                            | 43                          | 43                                 | 43                            |
| Units: percentage of participants |                               |                             |                                    |                               |
| number (not applicable)           |                               |                             |                                    |                               |
| Baseline [n=43]                   | 23.3                          | 60.5                        | 16.3                               | 0                             |
| Day 10 [n=37]                     | 40.5                          | 51.4                        | 8.1                                | 0                             |

|                    |      |      |      |   |
|--------------------|------|------|------|---|
| Week 3 [n=30]      | 40   | 53.3 | 6.7  | 0 |
| Week 3 LOCF [n=42] | 42.9 | 50   | 7.1  | 0 |
| Week 6 [n=30]      | 56.7 | 33.3 | 10   | 0 |
| Week 6 LOCF [n=43] | 48.8 | 39.5 | 11.5 | 0 |

| End point values                  | Lower Limbs<br>Lichenification<br>Absent | Lower Limbs<br>Lichenification<br>Mild | Lower Limbs<br>Lichenification<br>Moderate | Lower Limbs<br>Lichenification<br>Severe |
|-----------------------------------|--|--|--|--|
| Subject group type                | Subject analysis set                     | Subject analysis set                   | Subject analysis set                       | Subject analysis set                     |
| Number of subjects analysed       | 43                                       | 43                                     | 43   | 43                                       |
| Units: percentage of participants |  |  |  |  |
| number (not applicable)           |  |  |  |  |
| Baseline [n=43]                   | 30.2                                     | 48.8                                   | 18.6                                       | 2.3                                      |
| Day 10 [n=37]                     | 40.5                                     | 43.2                                   | 16.2                                       | 0  |
| Week 3 [n=30]                     | 40                                       | 53.3                                   | 6.7  | 0  |
| Week 3 LOCF [n=42]                | 35.7                                     | 50                                     | 14.3                                       | 0  |
| Week 6 [n=30]                     | 40                                       | 43.3                                   | 16.7                                       | 0  |
| Week 6 LOCF [n=43]                | 39.5                                     | 41.9                                   | 18.6                                       | 0  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Patient's/Guardian's/Parent(s) Assessment of Global Response

|                 |  |
|-----------------|--|
| End point title | Patient's/Guardian's/Parent(s) Assessment of Global Response |
|-----------------|--|

End point description:

The study analysis population for this endpoint consisted of the FAS. Patient's/Guardian's/Parent(s) Assessment of Global Response: The patient/guardian/parent(s) was instructed to answer the following questions at day 10, week 3 & week 6 (visits 3-5). "Consider your atopic dermatitis as a whole, how it looks, how it feels, how others react to it etc. Since the time you started treatment with the study substance, do you think the condition is":

Much Improved  
Improved  
Slightly Improved  
Same  
Slightly Worse  
Worse  
Much Worse

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

End point timeframe:

Day 10, Week 3 and Week 6.

| End point values                  | AD Much Improved     | AD Improved          | AD Slightly Improved | AD Same              |
|-----------------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type                | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed       | 43                   | 43                   | 43                   | 43                   |
| Units: percentage of participants |                      |                      |                      |                      |
| number (not applicable)           |                      |                      |                      |                      |
| Day 10 [n=36]                     | 36.1                 | 19.4                 | 27.8                 | 11.1                 |
| Week 3 [n=30]                     | 33.3                 | 23.3                 | 13.3                 | 10                   |
| Week 3 LOCF [n=41]                | 34.1                 | 19.5                 | 17.1                 | 9.8                  |
| Week 6 [n=28]                     | 39.3                 | 28.6                 | 3.6                  | 17.9                 |
| Week 6 LOCF [n=42]                | 33.3                 | 31                   | 4.8                  | 16.7                 |

| End point values                  | AD Slightly Worse    | AD Worse             | AD Much Worse        |  |
|-----------------------------------|----------------------|----------------------|----------------------|--|
| Subject group type                | Subject analysis set | Subject analysis set | Subject analysis set |  |
| Number of subjects analysed       | 43                   | 43                   | 43                   |  |
| Units: percentage of participants |                      |                      |                      |  |
| number (not applicable)           |                      |                      |                      |  |
| Day 10 [n=36]                     | 2.8                  | 0                    | 2.8                  |  |
| Week 3 [n=30]                     | 16.7                 | 0                    | 3.3                  |  |
| Week 3 LOCF [n=41]                | 14.6                 | 0                    | 4.9                  |  |
| Week 6 [n=28]                     | 7.1                  | 3.6                  | 0                    |  |
| Week 6 LOCF [n=42]                | 9.5                  | 2.4                  | 2.4                  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change in Euroqol 5 Dimensions Questionnaire (EQ-5D) from baseline to Week 6

|                 |  |
|-----------------|--|
| End point title | Change in Euroqol 5 Dimensions Questionnaire (EQ-5D) from baseline to Week 6 |
|-----------------|--|

End point description:

The study analysis population for this endpoint consisted of the FAS. The EQ-5D comprises five dimensions of health (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) and each dimension comprises three levels (1=no problems, 2=some/moderate problems, 3=extreme problems). The EQ-5D VAS records the respondents-rated health status on a vertical graduated VAS ranging from 0 indicating the worst imaginable state to 100 indicating the best imaginable state of the patient's health. EQ-5D questionnaire was used to calculate the utility of an individual patient and produces a utility value of between 0 (death) and 1 (perfect health). The EQ-5D was not completed for children less than 3 years of age.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Baseline to Week 6.  |           |

|                                      |                                    |  |  |  |
|--------------------------------------|------------------------------------|--|--|--|
| <b>End point values</b>              | Locobase<br>REPAIR®<br>Twice daily |  |  |  |
| Subject group type                   | Reporting group                    |  |  |  |
| Number of subjects analysed          | 23                                 |  |  |  |
| Units: EQ-5D VAS and Utility Scores  |                                    |  |  |  |
| arithmetic mean (standard deviation) |                                    |  |  |  |
| EQ-5D VAS                            | 7.7 (± 12.2)                       |  |  |  |
| EQ-5D Utility Score TTO UK           | 0.13 (± 0.24)                      |  |  |  |
| EQ-5D Utility Score VAS UK           | 0.13 (± 0.2)                       |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change in Children's Dermatology Life Quality Index (CDLQI) ] from baseline to Week 6

|  |   |
|--|---|
| End point title  | Change in Children's Dermatology Life Quality Index (CDLQI) ] from baseline to Week 6 |
| End point description:   |   |
| The study analysis population for this endpoint consisted of the FAS. The CDLQI consists of 10 questions and was completed by the patients themselves with help from their parent(s)/guardian where necessary. The CDLQI was calculated by summing the score of each question resulting in a total score between 0 and 30. Furthermore, six subscores were calculated. The higher the score, the more QoL is impaired. Children under 5 years of age were not asked to complete the CDLQI. |   |
| End point type   | Secondary   |
| End point timeframe:   |   |
| Baseline to Week 6.  |   |

|   |                                    |  |  |  |
|---|------------------------------------|--|--|--|
| <b>End point values</b>                     | Locobase<br>REPAIR®<br>Twice daily |  |  |  |
| Subject group type                          | Reporting group                    |  |  |  |
| Number of subjects analysed                 | 43                                 |  |  |  |
| Units: CDLQI Scores                         |                                    |  |  |  |
| arithmetic mean (standard deviation)        |                                    |  |  |  |
| CDLQI Total Score [n=16]                    | -5.1 (± 6.5)                       |  |  |  |
| CDLQI Subscore Symptoms and Feelings [n=17] | -1.6 (± 1.6)                       |  |  |  |
| CDLQI Subscore Leisure [n=17]               | -1.2 (± 2.2)                       |  |  |  |
| CDLQI Subscore School and Holiday [n=3]     | -0.7 (± 1.2)                       |  |  |  |
| CDLQI Subscore Personal Relationship [n=16] | -0.4 (± 1.7)                       |  |  |  |
| CDLQI Subscore Sleep [n=15]                 | -0.7 (± 1)                         |  |  |  |
| CDLQI Subscore Treatment [n=16]             | -0.6 (± 0.8)                       |  |  |  |



## Statistical analyses

No statistical analyses for this end point

### Secondary: Resource Utilization Questionnaire

|                 |                                    |
|-----------------|------------------------------------|
| End point title | Resource Utilization Questionnaire |
|-----------------|------------------------------------|

End point description:

The study analysis population for this endpoint consisted of the FAS. The Resource Utilization Questionnaire was used to record the patients' visits to a general practitioner (GP) for AD, the patients' hospital outpatient visits and the patients' admissions due to AD during the study. Patients completed a resource utilization questionnaire at all visits.

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

End point timeframe:

Baseline, Day 10, Week 3 and Week 6.

| End point values                                  | Patients with at least one visit to a GP | Patients with at least one outpatient visit to a hospital |  |  |
|---|--|---|--|--|
| Subject group type                                | Subject analysis set                     | Subject analysis set                                      |  |  |
| Number of subjects analysed                       | 43                                       | 43  |  |  |
| Units: percentage of participants                 |  |   |  |  |
| number (not applicable)                           |  |   |  |  |
| Up to 91 days before Baseline - ≥ Baseline [n=43] | 41.9                                     | 9.3   |  |  |
| > Baseline - ≤ Day 10 [n=43]                      | 16.3                                     | 4.7   |  |  |
| > Baseline - ≤ Week 3 [n=43]                      | 16.3                                     | 4.7   |  |  |
| > Baseline - ≤ Week 6 [n=43]                      | 16.3                                     | 4.7   |  |  |
| > Day 10 - ≤ Week 3 [n=30]                        | 3.3                                      | 3.3   |  |  |
| > Week 3 - ≤ Week 6 [n=31]                        | 3.2                                      | 0   |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Safety as assessed by recording adverse events, and laboratory assessments

|                 |  |
|-----------------|--|
| End point title | Safety as assessed by recording adverse events, and laboratory assessments |
|-----------------|--|

End point description:

The study analysis population for this endpoint consisted of the Safety analysis set (SAF). The SAF consisted of all enrolled patients who used Locobase REPAIR®. Treatment emergent adverse events (TEAE) were those events that commenced on the day or after the first day that study medication was dispensed, unless indicated by the investigator as before first application of study drug.

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

End point timeframe:

Up to Week 6.

| <b>End point values</b>       | Application site     | Non-application site | Overall Participants with Treatment-Emergent Adverse Events |  |
|-------------------------------|----------------------|----------------------|---|--|
| Subject group type            | Subject analysis set | Subject analysis set | Subject analysis set  |  |
| Number of subjects analysed   | 49                   | 49                   | 49  |  |
| Units: Participants           |                      |                      |   |  |
| Total TEAEs                   | 8                    | 10                   | 16  |  |
| Serious Adverse Events (SAEs) | 0                    | 1                    | 1   |  |
| Deaths                        | 0                    | 0                    | 0   |  |
| Discontinued due to AEs       | 3                    | 2                    | 4   |  |
| TEAEs Mild                    | 4                    | 5                    | 8   |  |
| TEAEs Moderate                | 4                    | 4                    | 7   |  |
| TEAEs Severe                  | 0                    | 1                    | 1   |  |
| Treatment related AEs         | 4                    | 0                    | 4   |  |
| Total treatment-related AEs   | 8                    | 0                    | 8   |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information<sup>[1]</sup>

Timeframe for reporting adverse events:

TEAEs were those events that commenced on the day or after the first day that study medication was dispensed, unless indicated by the investigator as before first application of study drug.

Adverse event reporting additional description:

An adverse event was defined as any untoward medical occurrence in a patient entered into the study, which did not necessarily have a causal relationship with the treatment. The study analysis population for this endpoint consisted of the SAF.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 1.10 |
|--------------------|------|

### Reporting groups

|                       |                              |
|-----------------------|------------------------------|
| Reporting group title | Locobase REPAIR® Twice daily |
|-----------------------|------------------------------|

Reporting group description:

Locobase REPAIR® cream to be applied twice daily to all areas with active lesions or dry skin either present at day 1 or that emerge during the study.

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: There were no non-serious adverse events within the 5% or more frequency threshold for reporting non-serious adverse events.

| Serious adverse events                            | Locobase REPAIR®<br>Twice daily |  |  |
|---|---------------------------------|--|--|
| Total subjects affected by serious adverse events |                                 |  |  |
| subjects affected / exposed                       | 1 / 49 (2.04%)                  |  |  |
| number of deaths (all causes)                     | 0                               |  |  |
| number of deaths resulting from adverse events    | 0                               |  |  |
| Infections and infestations                       |                                 |  |  |
| Urinary tract infection                           |                                 |  |  |
| subjects affected / exposed                       | 1 / 49 (2.04%)                  |  |  |
| occurrences causally related to treatment / all   | 0 / 1                           |  |  |
| deaths causally related to treatment / all        | 0 / 0                           |  |  |

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

| Non-serious adverse events                            | Locobase REPAIR®<br>Twice daily |  |  |
|---|---------------------------------|--|--|
| Total subjects affected by non-serious adverse events |                                 |  |  |
| subjects affected / exposed                           | 0 / 49 (0.00%)                  |  |  |



## 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