



## Clinical trial results:

**A randomised, double-blind, placebo-controlled, parallel-group, multi-centre trial to evaluate the efficacy, safety, and tolerability of tralokinumab monotherapy in adolescent subjects with moderate-to-severe atopic dermatitis who are candidates for systemic therapy - ECZTRA 6 (ECZema TRAlokinumab trial no.6)**

### Summary

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2017-005143-33    |
| Trial protocol           | FR PL DE NL BE GB |
| Global end of trial date | 16 March 2021     |

### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v1              |
| This version publication date  | 01 October 2021 |
| First version publication date | 01 October 2021 |

### Trial information

#### Trial identification

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | LP0162-1334 |
|-----------------------|-------------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03526861 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | LEO Pharma A/S  |
| Sponsor organisation address | Industriparken 55, Ballerup, Denmark, 2750  |
| Public contact               | Clinical Disclosure Specialist, LEO Pharma A/S<br>, +45 44945888, disclosure@leo-pharma.com |
| Scientific contact           | Clinical Disclosure Specialist, LEO Pharma A/S<br>, +45 44945888, disclosure@leo-pharma.com |

Notes:

### Paediatric regulatory details

|  |                     |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP)       | Yes                 |
| EMA paediatric investigation plan number(s)                          | EMA-001900-PIP02-17 |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No                  |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | Yes                 |

Notes:

## Results analysis stage

|  |               |
|--|---------------|
| Analysis stage                                       | Final         |
| Date of interim/final analysis                       | 12 May 2021   |
| Is this the analysis of the primary completion data? | No            |
| Global end of trial reached?                         | Yes           |
| Global end of trial date                             | 16 March 2021 |
| Was the trial ended prematurely?                     | No            |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the efficacy of subcutaneous administration of tralokinumab compared with placebo in treating adolescent subjects (age 12 to <18 years) with moderate-to-severe atopic dermatitis.

Protection of trial subjects:

This clinical trial was conducted to conform to the principles of the Declaration of Helsinki as adopted by the 18th World Medical Association General Assembly, 1964, and subsequent amendments. Subjects and their legally acceptable representative received written and verbal information concerning the clinical trial and were given an opportunity to ask questions and sufficient time to consider before consenting. Subjects not of legal age assented to participation in the trial, and for such subjects, one or more legally authorised representatives provided consent. Subjects or legally authorised representatives were asked to consent to their personal data being recorded, collected, processed and transferred to EU and non-EU countries in accordance with any national legislation regulating privacy and data protection. Some subjects were randomised to initial treatment with placebo, and subjects who achieved a clinical response at Week 16 with placebo were assigned to continue placebo treatment until Week 52. If medically necessary (i.e. to control intolerable atopic dermatitis [AD] symptoms), rescue treatment for AD could be provided to subjects throughout the trial, both during the initial treatment period and the maintenance treatment period, at the discretion of the investigator. For the first 3 investigational medicinal product (IMP) dosing visits in both the initial treatment period (i.e. Weeks 0, 2, and 4) and in open-label treatment, subjects were monitored after IMP administration for immediate drug reactions for a minimum of 2 hours with vital signs taken every 30 minutes or until stable, whichever was later. Vital signs were documented in the electronic case report forms. Appropriate drugs, such as epinephrine, antihistamines, corticosteroids, etc., and medical equipment to treat acute anaphylactic reactions were immediately available at trial sites, and trial personnel was trained to recognise and respond to anaphylaxis according to local guidelines

Background therapy:

All subjects were to use an emollient twice daily (or more, as needed) for at least 14 days before randomisation and were to continue this treatment throughout the trial.

Evidence for comparator: -

|   |              |
|---|--------------|
| Actual start date of recruitment                          | 13 July 2018 |
| Long term follow-up planned                               | No           |
| Independent data monitoring committee (IDMC) involvement? | Yes          |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | United States: 105 |
| Country: Number of subjects enrolled | Canada: 52         |
| Country: Number of subjects enrolled | Australia: 14      |
| Country: Number of subjects enrolled | Japan: 32          |
| Country: Number of subjects enrolled | Netherlands: 13    |

|                                      |                   |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Poland: 54        |
| Country: Number of subjects enrolled | United Kingdom: 4 |
| Country: Number of subjects enrolled | Belgium: 8        |
| Country: Number of subjects enrolled | France: 8         |
| Country: Number of subjects enrolled | Germany: 11       |
| Worldwide total number of subjects   | 301               |
| EEA total number of subjects         | 94                |

Notes:

| <b>Subjects enrolled per age group</b>    |     |
|---|-----|
| In utero                                  | 0   |
| Preterm newborn - gestational age < 37 wk | 0   |
| Newborns (0-27 days)                      | 0   |
| Infants and toddlers (28 days-23 months)  | 0   |
| Children (2-11 years)                     | 0   |
| Adolescents (12-17 years)                 | 301 |
| Adults (18-64 years)                      | 0   |
| From 65 to 84 years                       | 0   |
| 85 years and over                         | 0   |

## Subject disposition

### Recruitment

Recruitment details:

Trial start date: 13-Jul-2018. Primary completion date: 15-Apr-2020, Trial completion date: March 16 2021. The trial was conducted in 10 countries: United States, Australia, Canada, United Kingdom, Poland, Belgium, Germany, France, Japan, and the Netherlands.

### Pre-assignment

Screening details:

The screening period was 2 to 6 weeks and included 1 or 2 visits. The exact duration depended on the washout period defined by the exclusion criteria. If no wash-out or only a 2-week wash-out was required, screening Visits 1 and 2 were combined. Eligibility was assessed at the (first) screening visit and on Day 0 prior to randomisation.

### Period 1

|                              |   |
|------------------------------|---|
| Period 1 title               | Initial treatment period                                      |
| Is this the baseline period? | Yes   |
| Allocation method            | Randomised - controlled                                       |
| Blinding used                | Double blind  |
| Roles blinded                | Subject, Investigator, Monitor, Data analyst, Carer, Assessor |

Blinding implementation details:

This was a double-blind trial in which tralokinumab and placebo were visually distinct from each other. The IMP was handled and administered by a qualified, unblinded healthcare professional (HCP) at the site who was not involved in the management of trial subjects and who did not perform any of the assessments.

### Arms

|                              |  |
|------------------------------|--|
| Are arms mutually exclusive? | Yes  |
| <b>Arm title</b>             | Initial treatment period - Tralokinumab 300 mg Q2W |

Arm description:

Subjects in the initial treatment period (Week 0 to Week 16) treated with tralokinumab 300 mg every second week (Q2W)

|  |  |
|--|--|
| Arm type                               | Experimental                                 |
| Investigational medicinal product name | Tralokinumb 300 mg Q2W                       |
| Investigational medicinal product code |  |
| Other name                             |  |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use                             |

Dosage and administration details:

At Day 0, each subject received 4 subcutaneous injections (each 1.0 mL) of 150 mg tralokinumab to receive a total loading dose of 600 mg tralokinumab (4.0 mL). At subsequent visits (Q2W) each subject received 2 SC injections (each 1.0 mL) of 150 mg tralokinumab to receive a total dose of 300 mg tralokinumab. IMP was administered by a qualified, unblinded HCP. The injections were administered into the subcutaneous tissue of the upper arm, anterior thigh, or abdomen.

|                  |  |
|------------------|--|
| <b>Arm title</b> | Initial treatment period - Tralokinumab 150 mg Q2W |
|------------------|--|

Arm description:

Subjects in the initial treatment period (Week 0 to Week 16) treated with tralokinumab 150 mg every second week (Q2W)

|          |              |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

|  |  |
|--|--|
| Investigational medicinal product name | Tralokinumb 150 mg Q2W                       |
| Investigational medicinal product code |  |
| Other name                             |  |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use                             |

**Dosage and administration details:**

At Day 0, each subject received 2 subcutaneous injections (each 1.0 mL) of 150 mg tralokinumab and 2 SC injections (each 1.0 mL) of placebo to receive a total loading dose of 300 mg tralokinumab (4.0 mL). At subsequent visits (Q2W) each subject received 1 SC injection (1.0 mL) of 150 mg tralokinumab and 1 SC injection (1.0 mL) of placebo to receive a total dose of 150 mg tralokinumab. IMP was administered by a qualified, unblinded HCP. The injections were administered into the subcutaneous tissue of the upper arm, anterior thigh, or abdomen.

|                  |  |
|------------------|--|
| <b>Arm title</b> | Initial treatment period - Placebo Q2W |
|------------------|--|

**Arm description:**

Subjects in the initial treatment period (Week 0 to Week 16) treated with placebo every second week (Q2W).

|  |  |
|--|--|
| Arm type                               | Placebo                                      |
| Investigational medicinal product name | Placebo Q2W                                  |
| Investigational medicinal product code |  |
| Other name                             |  |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use                             |

**Dosage and administration details:**

At Day 0, each subject received 4 subcutaneous injections (each 1.0 mL) of placebo to receive a total loading dose (4.0 mL). At subsequent visits (Q2W) each subject received 2 SC injections (each 1.0 mL) of placebo. IMP was administered by a qualified, unblinded HCP. The injections were administered into the subcutaneous tissue of the upper arm, anterior thigh, or abdomen.

| <b>Number of subjects in period 1</b>             | Initial treatment period - Tralokinumab 300 mg Q2W | Initial treatment period - Tralokinumab 150 mg Q2W | Initial treatment period - Placebo Q2W |
|---|--|--|--|
| Started   | 101  | 100  | 100                                    |
| Completed   | 94   | 93   | 86                                     |
| Not completed                                     | 7  | 7  | 14                                     |
| Excluded from trial+FAS due to quality/GCP issues | 3  | 1  | 5                                      |
| Discontinued IMP before Week 16                   | 3  | 5  | 8                                      |
| Not dosed   | 1  | 1  | 1                                      |

**Period 2**

|                              |                             |
|------------------------------|-----------------------------|
| Period 2 title               | Open-label treatment period |
| Is this the baseline period? | No                          |
| Allocation method            | Not applicable              |
| Blinding used                | Not blinded                 |

## Arms

|           |   |
|-----------|---|
| Arm title | Open-label Treatment - Tralokinumab 300 mg Q2W + optional TCS |
|-----------|---|

### Arm description:

Subjects in the open-label treatment period (Week 16 to Week 52) treated with tralokinumab every second week (Q2W) + optional TCS. Subjects transferred to open-label treatment at Week 16 if they did not achieve protocol-defined clinical response at Week 16 without use of rescue medication from Week 2 to Week 16 OR after Week 16 if they lost clinical response during the maintenance treatment period.

Loss of clinical response during the maintenance treatment period was defined as:

-IGA of at least 2 and not achieving EASI75 over at least a 4-week period (3 consecutive visits) for subjects with IGA=0 at Week 16

-IGA of at least 3 and not achieving EASI75 over at least a 4-week period (3 consecutive visits) for subjects with IGA=1 at Week 16

-Not achieving EASI75 over at least a 4-week period (3 consecutive visits) for subjects with IGA>1 at Week 1

|  |  |
|--|--|
| Arm type                               | Experimental                                 |
| Investigational medicinal product name | Tralokinumb 300 mg Q2W                       |
| Investigational medicinal product code |  |
| Other name                             |  |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use                             |

### Dosage and administration details:

At each visit, subject received 2 subcutaneous injections (each 1.0 mL) of 150 mg tralokinumab Q2W to receive a total dose of 300 mg. IMP was administered by a qualified HCP. The injections were administered into the subcutaneous tissue of the upper arm, anterior thigh, or abdomen.

| Number of subjects in period 2 <sup>[1]</sup>     | Open-label Treatment - Tralokinumab 300 mg Q2W + optional TCS |
|---|---|
| Started   | 242   |
| Completed   | 214   |
| Not completed                                     | 28  |
| Excluded from trial+FAS due to quality/GCP issues | 8   |
| Discontinued IMP before Week 52                   | 19  |
| Received IMP and withdrew from trial at Week 50   | 1   |

### Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: The open-label treatment period was in parallel to the maintenance treatment period. Subjects from the initial treatment period entered either into the open-label treatment period or maintenance treatment period.

## Period 3

|                              |   |
|------------------------------|---|
| Period 3 title               | Maintenance treatment period                                  |
| Is this the baseline period? | No  |
| Allocation method            | Randomised - controlled                                       |
| Blinding used                | Double blind  |
| Roles blinded                | Subject, Investigator, Monitor, Data analyst, Carer, Assessor |

### Blinding implementation details:

This was a double-blind trial in which tralokinumab and placebo were visually distinct from each other.

The IMP was handled and administered by a qualified, unblinded HCP at the site who was not involved in the management of trial subjects and who did not perform any of the assessments. Maintenance treatment period was in parallel to the Open-label treatment period.

## Arms

|                              |  |
|------------------------------|--|
| Are arms mutually exclusive? | Yes  |
| <b>Arm title</b>             | Maintenance Treatment Period - Tralokinumab 300 mg Q2W |

### Arm description:

Subjects initially randomised to tralokinumab 300 mg Q2W, achieving a clinical response (defined as Investigator's Global Assessment score of 0 or 1, or at least 75% reduction in Eczema Area and Severity Index) at Week 16 without use of rescue medication from Week 2 to Week 16, and re-randomised to tralokinumab 300 mg Q2W maintenance treatment.

|  |  |
|--|--|
| Arm type                               | Experimental                                 |
| Investigational medicinal product name | Tralokinumb 300 mg Q2W                       |
| Investigational medicinal product code |  |
| Other name                             |  |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use                             |

### Dosage and administration details:

At each visit, subject received 2 subcutaneous injections (each 1.0 mL) of 150 mg tralokinumab Q2W to receive a total dose of 300 mg tralokinumab. IMP was administered by a qualified, unblinded HCP. The injections were administered into the subcutaneous tissue of the upper arm, anterior thigh, or abdomen.

|                  |  |
|------------------|--|
| <b>Arm title</b> | Maintenance Treatment Period - Tralokinumab 300 mg Q4W |
|------------------|--|

### Arm description:

Subjects initially randomised to tralokinumab 300 mg Q2W, achieving a clinical response (defined as Investigator's Global Assessment score of 0 or 1, or at least 75% reduction in Eczema Area and Severity Index) at Week 16 without use of rescue medication from Week 2 to Week 16, and re-randomised to tralokinumab 300 mg Q4W maintenance treatment.

|  |  |
|--|--|
| Arm type                               | Experimental                                 |
| Investigational medicinal product name | Tralokinumb 300 mg Q4W                       |
| Investigational medicinal product code |  |
| Other name                             |  |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use                             |

### Dosage and administration details:

At each visit, subject received alternating dose administrations: 2 subcutaneous injections (each 1.0 mL) of 150 mg tralokinumab Q2W to receive a total dose of 300 mg tralokinumab or 2 subcutaneous injections (each 1.0 mL) of placebo. IMP was administered by a qualified, unblinded HCP. The injections were administered into the subcutaneous tissue of the upper arm, anterior thigh, or abdomen.

|                  |  |
|------------------|--|
| <b>Arm title</b> | Maintenance Treatment Period - Tralokinumab 150 mg Q2W |
|------------------|--|

### Arm description:

Subjects initially randomised to tralokinumab 150 mg Q2W, achieving a clinical response (defined as Investigator's Global Assessment score of 0 or 1, or at least 75% reduction in Eczema Area and Severity Index) at Week 16 without use of rescue medication from Week 2 to Week 16, and re-randomised to tralokinumab 150 mg Q2W maintenance treatment.

|  |  |
|--|--|
| Arm type                               | Experimental                                 |
| Investigational medicinal product name | Tralokinumb 150 mg Q2W                       |
| Investigational medicinal product code |  |
| Other name                             |  |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use                             |

### Dosage and administration details:

At each visit, subject received 1 subcutaneous injection (1.0 mL) of 150 mg tralokinumab and 1 subcutaneous injection (1.0 mL) of placebo Q2W to receive a total dose of 150 mg tralokinumab. IMP was administered by a qualified, unblinded HCP. The injections were administered into the subcutaneous

tissue of the upper arm, anterior thigh, or abdomen.

|  |  |
|--|--|
| <b>Arm title</b>   | Maintenance Treatment Period - Tralokinumab 150 mg Q4W |
| Arm description:<br>Subjects initially randomised to tralokinumab 150 mg Q2W, achieving a clinical response (defined as Investigator's Global Assessment score of 0 or 1, or at least 75% reduction in Eczema Area and Severity Index) at Week 16 without use of rescue medication from Week 2 to Week 16, and re-randomised to tralokinumab 150 mg Q4W maintenance treatment. |  |
| Arm type   | Experimental   |
| Investigational medicinal product name   | Tralokinumb 150 mg Q4W                                 |
| Investigational medicinal product code   |  |
| Other name   |  |
| Pharmaceutical forms   | Solution for injection in pre-filled syringe           |
| Routes of administration   | Subcutaneous use                                       |

**Dosage and administration details:**

At each visit, subject received alternating dose administrations: 1 subcutaneous injection (1.0 mL) of 150 mg tralokinumab and 1 subcutaneous injection (1.0 mL) of placebo to receive a total dose of 300 mg tralokinumab or 2 subcutaneous injections (each 1.0 mL) of placebo. IMP was administered by a qualified, unblinded HCP. The injections were administered into the subcutaneous tissue of the upper arm, anterior thigh, or abdomen.

|  |  |
|--|--|
| <b>Arm title</b>   | Maintenance Treatment Period - Placebo Q2W   |
| Arm description:<br>Subjects initially randomised to placebo, achieving a clinical response (defined as Investigator's Global Assessment score of 0 or 1, or at least 75% reduction in Eczema Area and Severity Index) at Week 16 without use of rescue medication from Week 2 to Week 16, and re-assigned to placebo maintenance treatment. |  |
| Arm type   | Experimental                                 |
| Investigational medicinal product name   | Placebo Q2W                                  |
| Investigational medicinal product code   |  |
| Other name   |  |
| Pharmaceutical forms   | Solution for injection in pre-filled syringe |
| Routes of administration   | Subcutaneous use                             |

**Dosage and administration details:**

At each visit, subject received 2 SC injections (each 1.0 mL) of placebo. IMP was administered by a qualified, unblinded HCP. The injections were administered into the SC tissue of the upper arm, anterior thigh, or abdomen, separated by at least 3 cm.

| <b>Number of subjects in period 3<sup>[2]</sup></b> | Maintenance Treatment Period - Tralokinumab 300 mg Q2W | Maintenance Treatment Period - Tralokinumab 300 mg Q4W | Maintenance Treatment Period - Tralokinumab 150 mg Q2W |
|---|--|--|--|
| Started   | 13   | 14   | 12   |
| Completed   | 5  | 8  | 8  |
| Not completed                                       | 8  | 6  | 4  |
| Transferred to open-label treatment                 | 6  | 5  | 4  |
| Excluded from trial+FAS due to quality/GCP issues   | 1  | -  | -  |
| Discontinued IMP before Week 52                     | 1  | 1  | -  |



| Number of subjects in period<br>3 <sup>[2]</sup>     | Maintenance<br>Treatment Period -<br>Tralokinumab 150<br>mg Q4W | Maintenance<br>Treatment Period -<br>Placebo Q2W |
|--|---|--|
|  |   |  |
| Started  | 14  | 6  |
| Completed  | 8   | 4  |
| Not completed  | 6   | 2  |
| Transferred to open-label treatment                  | 5   | 2  |
| Excluded from trial+FAS due to<br>quality/GCP issues | -   | -  |
| Discontinued IMP before Week 52                      | 1   | -  |

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Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: The maintenance treatment period was in parallel to the open-label treatment period. Subjects from the initial treatment phase entered either into the maintenance treatment period or the open-label treatment period.

## Baseline characteristics

### Reporting groups

|   |  |
|---|--|
| Reporting group title   | Initial treatment period - Tralokinumab 300 mg Q2W |
| Reporting group description:  |  |
| Subjects in the initial treatment period (Week 0 to Week 16) treated with tralokinumab 300 mg every second week (Q2W) |  |
| Reporting group title   | Initial treatment period - Tralokinumab 150 mg Q2W |
| Reporting group description:  |  |
| Subjects in the initial treatment period (Week 0 to Week 16) treated with tralokinumab 150 mg every second week (Q2W) |  |
| Reporting group title   | Initial treatment period - Placebo Q2W             |
| Reporting group description:  |  |
| Subjects in the initial treatment period (Week 0 to Week 16) treated with placebo every second week (Q2W).            |  |

| Reporting group values   | Initial treatment period - Tralokinumab 300 mg Q2W | Initial treatment period - Tralokinumab 150 mg Q2W | Initial treatment period - Placebo Q2W |
|--|--|--|--|
| Number of subjects   | 101  | 100  | 100                                    |
| Age categorical<br>Units: Subjects   |  |  |  |
| Adolescents (12-17 years)  | 101  | 100  | 100                                    |
| Age continuous<br>Units: years   |  |  |  |
| arithmetic mean  | 14.6   | 14.8   | 14.4                                   |
| standard deviation   | ± 1.8  | ± 1.7  | ± 1.6                                  |
| Gender categorical<br>Units: Subjects  |  |  |  |
| Female   | 52   | 48   | 46                                     |
| Male   | 49   | 52   | 54                                     |
| Race<br>Units: Subjects  |  |  |  |
| White  | 59   | 56   | 58                                     |
| Black or African American  | 14   | 8  | 12                                     |
| Asian  | 21   | 28   | 23                                     |
| American Indian or Alaska native   | 0  | 2  | 1                                      |
| Native Hawaiian or other Pacific islander  | 2  | 0  | 2                                      |
| Other  | 5  | 6  | 4                                      |
| Ethnicity<br>Units: Subjects   |  |  |  |
| Hispanic or Latino   | 12   | 10   | 10                                     |
| Not Hispanic or Latino   | 89   | 90   | 90                                     |
| Unknown or Not Reported  | 0  | 0  | 0                                      |
| Investigator's Global Assessment   |  |  |  |
| The Investigator's Global Assessment (IGA) is an instrument used in clinical trials to rate the severity of the subject's global atopic dermatitis and is based on a 5-point scale ranging from 0 (clear) to 4 (severe). |  |  |  |
| Units: Subjects  |  |  |  |
| Clear  | 0  | 0  | 0                                      |

|   |         |         |         |
|---|---------|---------|---------|
| Almost Clear  | 0       | 0       | 0       |
| Mild  | 0       | 0       | 0       |
| Moderate  | 52      | 55      | 54      |
| Severe  | 48      | 44      | 45      |
| Missing   | 1       | 1       | 1       |
| Eczema Area and Severity Index  |         |         |         |
| Measure description: The Eczema Area and Severity Index (EASI) is a validated measure used in clinical practice and clinical trials to assess the severity and extent of atopic dermatitis. The EASI is a composite index with scores ranging from 0 to 72, with higher values indicating more severe and/or more extensive condition.  |         |         |         |
| Units: Units on a scale   |         |         |         |
| arithmetic mean   | 31.90   | 31.89   | 31.25   |
| standard deviation  | ± 13.74 | ± 12.97 | ± 14.19 |
| Scoring Atopic Dermatitis   |         |         |         |
| The Scoring Atopic Dermatitis (SCORAD) is a validated tool to evaluate the extent and severity of AD lesions, along with subjective symptoms. The maximum total score is 103, with higher values indicating more severe disease.  |         |         |         |
| Units: Units on a scale   |         |         |         |
| arithmetic mean   | 68.41   | 67.42   | 67.70   |
| standard deviation  | ± 13.51 | ± 14.51 | ± 14.77 |
| Children's Dermatology Life Quality Index   |         |         |         |
| The Children's Dermatology Life Quality Index (CDLQI) consists of 10 items addressing the subject's perception of the impact of their skin disease on various aspects of their quality of life (QoL) over the last week such as dermatology-related symptoms and feelings, leisure, school or holidays, personal relationships, sleep, and the treatment. Each item is scored on a 4-point Likert scale (0 = 'not at all'; 1 = 'only a little'; 2 = 'quite a lot'; 3 = 'very much'). The total score is the sum of the 10 items (0 to 30); a high score is indicative of a poor health-related quality of life. |         |         |         |
| Units: units on a scale   |         |         |         |
| arithmetic mean   | 13.29   | 12.86   | 13.14   |
| standard deviation  | ± 7.18  | ± 6.27  | ± 5.99  |
| Adolescent Worst Pruritus NRS (weekly average)  |         |         |         |
| Subjects assessed their worst itch severity over the past 24 hours using an 11-point numeric rating scale ('Adolescent Worst Pruritus NRS') each morning, with 0 indicating 'no itch' and 10 indicating 'worst itch possible'.  |         |         |         |
| Units: units on a scale   |         |         |         |
| arithmetic mean   | 7.79    | 7.49    | 7.45    |
| standard deviation  | ± 1.53  | ± 1.58  | ± 1.62  |
| Body surface area affected by atopic dermatitis (AD)  |         |         |         |
| Units: percentage affected  |         |         |         |
| arithmetic mean   | 49.8    | 52.0    | 50.9    |
| standard deviation  | ± 23.0  | ± 22.5  | ± 23.5  |
| Age of onset of atopic dermatitis (AD)  |         |         |         |
| Units: years  |         |         |         |
| arithmetic mean   | 2.5     | 2.1     | 2.4     |
| standard deviation  | ± 3.5   | ± 3.3   | ± 3.5   |
| Duration of atopic dermatitis (AD)  |         |         |         |
| Units: years  |         |         |         |
| arithmetic mean   | 12.1    | 12.7    | 12.0    |
| standard deviation  | ± 3.7   | ± 3.7   | ± 3.4   |
| <b>Reporting group values</b>   |         |         |         |
| Number of subjects  | 301     |         |         |

|  |     |  |  |
|--|-----|--|--|
| Age categorical  |     |  |  |
| Units: Subjects  |     |  |  |
| Adolescents (12-17 years)  | 301 |  |  |
| Age continuous   |     |  |  |
| Units: years   |     |  |  |
| arithmetic mean  |     |  |  |
| standard deviation   | -   |  |  |
| Gender categorical   |     |  |  |
| Units: Subjects  |     |  |  |
| Female   | 146 |  |  |
| Male   | 155 |  |  |
| Race   |     |  |  |
| Units: Subjects  |     |  |  |
| White  | 173 |  |  |
| Black or African American  | 34  |  |  |
| Asian  | 72  |  |  |
| American Indian or Alaska native   | 3   |  |  |
| Native Hawaiian or other Pacific islander  | 4   |  |  |
| Other  | 15  |  |  |
| Ethnicity  |     |  |  |
| Units: Subjects  |     |  |  |
| Hispanic or Latino   | 32  |  |  |
| Not Hispanic or Latino   | 269 |  |  |
| Unknown or Not Reported  | 0   |  |  |
| Investigator's Global Assessment   |     |  |  |
| The Investigator's Global Assessment (IGA) is an instrument used in clinical trials to rate the severity of the subject's global atopic dermatitis and is based on a 5-point scale ranging from 0 (clear) to 4 (severe).   |     |  |  |
| Units: Subjects  |     |  |  |
| Clear  | 0   |  |  |
| Almost Clear   | 0   |  |  |
| Mild   | 0   |  |  |
| Moderate   | 161 |  |  |
| Severe   | 137 |  |  |
| Missing  | 3   |  |  |
| Eczema Area and Severity Index   |     |  |  |
| Measure description: The Eczema Area and Severity Index (EASI) is a validated measure used in clinical practice and clinical trials to assess the severity and extent of atopic dermatitis. The EASI is a composite index with scores ranging from 0 to 72, with higher values indicating more severe and/or more extensive condition. |     |  |  |
| Units: Units on a scale  |     |  |  |
| arithmetic mean  |     |  |  |
| standard deviation   | -   |  |  |
| Scoring Atopic Dermatitis  |     |  |  |
| The Scoring Atopic Dermatitis (SCORAD) is a validated tool to evaluate the extent and severity of AD lesions, along with subjective symptoms. The maximum total score is 103, with higher values indicating more severe disease.   |     |  |  |
| Units: Units on a scale  |     |  |  |
| arithmetic mean  |     |  |  |
| standard deviation   | -   |  |  |
| Children's Dermatology Life Quality Index  |     |  |  |

|  |   |  |  |
|--|---|--|--|
| <p>The Children's Dermatology Life Quality Index (CDLQI) consists of 10 items addressing the subject's perception of the impact of their skin disease on various aspects of their quality of life (QoL) over the last week such as dermatology-related symptoms and feelings, leisure, school or holidays, personal relationships, sleep, and the treatment. Each item is scored on a 4-point Likert scale (0 = 'not at all'; 1 = 'only a little'; 2 = 'quite a lot'; 3 = 'very much'). The total score is the sum of the 10 items (0 to 30); a high score is indicative of a poor health-related quality of life.</p> |   |  |  |
| Units: units on a scale<br>arithmetic mean<br>standard deviation   | - |  |  |
| Adolescent Worst Pruritus NRS (weekly average)   |   |  |  |
| <p>Subjects assessed their worst itch severity over the past 24 hours using an 11-point numeric rating scale ('Adolescent Worst Pruritus NRS') each morning, with 0 indicating 'no itch' and 10 indicating 'worst itch possible'.</p>  |   |  |  |
| Units: units on a scale<br>arithmetic mean<br>standard deviation   | - |  |  |
| Body surface area affected by atopic dermatitis (AD)<br>Units: percentage affected<br>arithmetic mean<br>standard deviation  | - |  |  |
| Age of onset of atopic dermatitis (AD)<br>Units: years<br>arithmetic mean<br>standard deviation  | - |  |  |
| Duration of atopic dermatitis (AD)<br>Units: years<br>arithmetic mean<br>standard deviation  | - |  |  |

## End points

### End points reporting groups

|   |   |
|---|---|
| Reporting group title   | Initial treatment period - Tralokinumab 300 mg Q2W            |
| Reporting group description:<br>Subjects in the initial treatment period (Week 0 to Week 16) treated with tralokinumab 300 mg every second week (Q2W)   |   |
| Reporting group title   | Initial treatment period - Tralokinumab 150 mg Q2W            |
| Reporting group description:<br>Subjects in the initial treatment period (Week 0 to Week 16) treated with tralokinumab 150 mg every second week (Q2W)   |   |
| Reporting group title   | Initial treatment period - Placebo Q2W                        |
| Reporting group description:<br>Subjects in the initial treatment period (Week 0 to Week 16) treated with placebo every second week (Q2W).  |   |
| Reporting group title   | Open-label Treatment - Tralokinumab 300 mg Q2W + optional TCS |
| Reporting group description:<br>Subjects in the open-label treatment period (Week 16 to Week 52) treated with tralokinumab every second week (Q2W) + optional TCS. Subjects transferred to open-label treatment at Week 16 if they did not achieve protocol-defined clinical response at Week 16 without use of rescue medication from Week 2 to Week 16 OR after Week 16 if they lost clinical response during the maintenance treatment period. Loss of clinical response during the maintenance treatment period was defined as:<br>-IGA of at least 2 and not achieving EASI75 over at least a 4-week period (3 consecutive visits) for subjects with IGA=0 at Week 16<br>-IGA of at least 3 and not achieving EASI75 over at least a 4-week period (3 consecutive visits) for subjects with IGA=1 at Week 16<br>-Not achieving EASI75 over at least a 4-week period (3 consecutive visits) for subjects with IGA>1 at Week 1 |   |
| Reporting group title   | Maintenance Treatment Period - Tralokinumab 300 mg Q2W        |
| Reporting group description:<br>Subjects initially randomised to tralokinumab 300 mg Q2W, achieving a clinical response (defined as Investigator's Global Assessment score of 0 or 1, or at least 75% reduction in Eczema Area and Severity Index) at Week 16 without use of rescue medication from Week 2 to Week 16, and re-randomised to tralokinumab 300 mg Q2W maintenance treatment.  |   |
| Reporting group title   | Maintenance Treatment Period - Tralokinumab 300 mg Q4W        |
| Reporting group description:<br>Subjects initially randomised to tralokinumab 300 mg Q2W, achieving a clinical response (defined as Investigator's Global Assessment score of 0 or 1, or at least 75% reduction in Eczema Area and Severity Index) at Week 16 without use of rescue medication from Week 2 to Week 16, and re-randomised to tralokinumab 300 mg Q4W maintenance treatment.  |   |
| Reporting group title   | Maintenance Treatment Period - Tralokinumab 150 mg Q2W        |
| Reporting group description:<br>Subjects initially randomised to tralokinumab 150 mg Q2W, achieving a clinical response (defined as Investigator's Global Assessment score of 0 or 1, or at least 75% reduction in Eczema Area and Severity Index) at Week 16 without use of rescue medication from Week 2 to Week 16, and re-randomised to tralokinumab 150 mg Q2W maintenance treatment.  |   |
| Reporting group title   | Maintenance Treatment Period - Tralokinumab 150 mg Q4W        |
| Reporting group description:<br>Subjects initially randomised to tralokinumab 150 mg Q2W, achieving a clinical response (defined as Investigator's Global Assessment score of 0 or 1, or at least 75% reduction in Eczema Area and Severity Index) at Week 16 without use of rescue medication from Week 2 to Week 16, and re-randomised to tralokinumab 150 mg Q4W maintenance treatment.  |   |
| Reporting group title   | Maintenance Treatment Period - Placebo Q2W                    |
| Reporting group description:<br>Subjects initially randomised to placebo, achieving a clinical response (defined as Investigator's Global Assessment score of 0 or 1, or at least 75% reduction in Eczema Area and Severity Index) at Week 16 without use of rescue medication from Week 2 to Week 16, and re-assigned to placebo maintenance treatment.  |   |

**Primary: Subjects With Investigator's Global Assessment (IGA) Score of 0 (Clear) or 1 (Almost Clear) at Week 16**

|                 |  |
|-----------------|--|
| End point title | Subjects With Investigator's Global Assessment (IGA) Score of 0 (Clear) or 1 (Almost Clear) at Week 16 |
|-----------------|--|

## End point description:

The IGA is an instrument used in clinical trials to rate the severity of the subject's global AD and is based on a 5-point scale ranging from 0 (clear) to 4 (severe).

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

## End point timeframe:

At Week 16

| End point values                        | Initial treatment period - Tralokinumab 300 mg Q2W | Initial treatment period - Tralokinumab 150 mg Q2W | Initial treatment period - Placebo Q2W |  |
|---|--|--|--|--|
| Subject group type                      | Reporting group                                    | Reporting group                                    | Reporting group                        |  |
| Number of subjects analysed             | 97   | 98   | 94                                     |  |
| Units: Number of subjects with response | 17   | 21   | 4                                      |  |

**Statistical analyses**

|                            |  |
|----------------------------|--|
| Statistical analysis title | Tralokinumab 300 mg Q2W versus Placebo |
|----------------------------|--|

## Statistical analysis description:

Subjects with IGA score of 0 (clear) or 1 (almost clear) at Week 16 were considered responders. Subjects with missing data or subjects who received rescue medication from Week 2 to Week 16 were considered non-responders. Analysis was performed using Cochran-Mantel-Haenszel test stratified by region and baseline disease severity. The null hypothesis of no difference in response rate between tralokinumab 300 mg Q2W and placebo was tested against the 2-sided alternative that there is a difference.

|   |   |
|---|---|
| Comparison groups                       | Initial treatment period - Tralokinumab 300 mg Q2W v Initial treatment period - Placebo Q2W |
| Number of subjects included in analysis | 191   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | superiority <sup>[1]</sup>  |
| P-value                                 | = 0.002 <sup>[2]</sup>  |
| Method                                  | Cochran-Mantel-Haenszel   |
| Parameter estimate                      | Risk difference (RD)  |
| Point estimate                          | 13.8  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | 5.3   |
| upper limit                             | 22.3  |

## Notes:

[1] - Primary endpoint tested sequentially at a 5% significance level.

[2] - Based on the primary analysis of the primary estimand 'composite'.

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | Tralokinumab 150 mg Q2W versus Placebo  |
| Statistical analysis description:   |   |
| Subjects with IGA score of 0 (clear) or 1 (almost clear) at Week 16 were considered responders. Subjects with missing data or subjects who received rescue medication from Week 2 to Week 16 were considered non-responders. Analysis was performed using Cochran-Mantel-Haenszel test stratified by region and baseline disease severity. The null hypothesis of no difference in response rate between tralokinumab 150 mg Q2W and placebo was tested against the 2-sided alternative that there is a difference. |   |
| Comparison groups   | Initial treatment period - Tralokinumab 150 mg Q2W v Initial treatment period - Placebo Q2W |
| Number of subjects included in analysis   | 192   |
| Analysis specification  | Pre-specified   |
| Analysis type   | superiority <sup>[3]</sup>  |
| P-value   | < 0.001 <sup>[4]</sup>  |
| Method  | Cochran-Mantel-Haenszel   |
| Parameter estimate  | Risk difference (RD)  |
| Point estimate  | 17.5  |
| Confidence interval   |   |
| level   | 95 %  |
| sides   | 2-sided   |
| lower limit   | 8.4   |
| upper limit   | 26.6  |

Notes:

[3] - Primary endpoint tested sequentially at a 5% significance level.

[4] - Based on the primary analysis of the primary estimand 'composite'.

### **Primary: Subjects With at Least 75% Reduction in Eczema Area and Severity Index (EASI75) at Week 16**

|   |  |
|---|--|
| End point title   | Subjects With at Least 75% Reduction in Eczema Area and Severity Index (EASI75) at Week 16 |
| End point description:  |  |
| The EASI is a validated measure used in clinical practice and clinical trials to assess the severity and extent of AD. The EASI is a composite index with scores ranging from 0 to 72, with higher values indicating more severe and/or more extensive condition. |  |
| End point type  | Primary  |
| End point timeframe:  |  |
| At Week 16  |  |

| <b>End point values</b>                 | Initial treatment period - Tralokinumab 300 mg Q2W | Initial treatment period - Tralokinumab 150 mg Q2W | Initial treatment period - Placebo Q2W |  |
|---|--|--|--|--|
| Subject group type                      | Reporting group                                    | Reporting group                                    | Reporting group                        |  |
| Number of subjects analysed             | 97   | 98   | 94                                     |  |
| Units: Number of subjects with response | 27   | 28   | 6                                      |  |



## Statistical analyses

| Statistical analysis title  | Tralokinumab 300 mg Q2W versus Placebo  |
|---|---|
| Statistical analysis description:   |   |
| Subjects who achieved at least 75% reduction in EASI at Week 16 were considered responders. Subjects with missing data or subjects who received rescue medication from Week 2 to Week 16 were considered non-responders. Analysis was performed using Cochran-Mantel-Haenszel test stratified by region and baseline disease severity. The null hypothesis of no difference in response rate between tralokinumab 300 mg Q2W and placebo was tested against the 2-sided alternative that there is a difference. |   |
| Comparison groups   | Initial treatment period - Tralokinumab 300 mg Q2W v Initial treatment period - Placebo Q2W |
| Number of subjects included in analysis   | 191   |
| Analysis specification  | Pre-specified   |
| Analysis type   | superiority <sup>[5]</sup>  |
| P-value   | > 0.001 <sup>[6]</sup>  |
| Method  | Cochran-Mantel-Haenszel   |
| Parameter estimate  | Risk difference (RD)  |
| Point estimate  | 22  |
| Confidence interval   |   |
| level   | 95 %  |
| sides   | 2-sided   |
| lower limit   | 12  |
| upper limit   | 32  |

Notes:

[5] - Primary endpoint tested sequentially at a 5% significance level.

[6] - Based on the primary analysis of the primary estimand 'composite'.

| Statistical analysis title  | Tralokinumab 150 mg Q2W versus Placebo  |
|---|---|
| Statistical analysis description:   |   |
| Subjects who achieved at least 75% reduction in EASI at Week 16 were considered responders. Subjects with missing data or subjects who received rescue medication from Week 2 to Week 16 were considered non-responders. Analysis was performed using Cochran-Mantel-Haenszel test stratified by region and baseline disease severity. The null hypothesis of no difference in response rate between tralokinumab 150 mg Q2W and placebo was tested against the 2-sided alternative that there is a difference. |   |
| Comparison groups   | Initial treatment period - Tralokinumab 150 mg Q2W v Initial treatment period - Placebo Q2W |
| Number of subjects included in analysis   | 192   |
| Analysis specification  | Pre-specified   |
| Analysis type   | superiority <sup>[7]</sup>  |
| P-value   | < 0.001 <sup>[8]</sup>  |
| Method  | Cochran-Mantel-Haenszel   |
| Parameter estimate  | Risk difference (RD)  |
| Point estimate  | 22.5  |
| Confidence interval   |   |
| level   | 95 %  |
| sides   | 2-sided   |
| lower limit   | 12.4  |
| upper limit   | 32.6  |

Notes:

[7] - Primary endpoint tested sequentially at a 5% significance level.

[8] - Based on the primary analysis of the primary estimand 'composite'.

## Secondary: Subjects With Reduction of Adolescent Worst Pruritus Numeric Rating Scale (NRS) (Weekly Average) of at Least 4 From Baseline to Week 16

|                 |   |
|-----------------|---|
| End point title | Subjects With Reduction of Adolescent Worst Pruritus Numeric Rating Scale (NRS) (Weekly Average) of at Least 4 From |
|-----------------|---|

## End point description:

The Adolescent Worst Pruritus NRS is used by subjects to assess their worst itch over the past 24 hours using an 11-point NRS with 0 indicating 'no itch' and 10 indicating 'worst itch possible'.

## End point type

Secondary

## End point timeframe:

At Week 16

| End point values                        | Initial treatment period - Tralokinumab 300 mg Q2W | Initial treatment period - Tralokinumab 150 mg Q2W | Initial treatment period - Placebo Q2W |  |
|---|--|--|--|--|
| Subject group type                      | Reporting group                                    | Reporting group                                    | Reporting group                        |  |
| Number of subjects analysed             | 96 <sup>[9]</sup>                                  | 95 <sup>[10]</sup>                                 | 90 <sup>[11]</sup>                     |  |
| Units: Number of subjects with response | 24   | 22   | 3                                      |  |

## Notes:

[9] - Subjects in the full analysis set with baseline Adolescent Worst Pruritus weekly average  $\geq 4$ .

[10] - Subjects in the full analysis set with baseline Adolescent Worst Pruritus weekly average  $\geq 4$ .

[11] - Subjects in the full analysis set with baseline Adolescent Worst Pruritus weekly average  $\geq 4$ .

## Statistical analyses

| Statistical analysis title | Tralokinumab 300 mg Q2W versus Placebo |
|----------------------------|--|
|----------------------------|--|

## Statistical analysis description:

Subjects with at least 4-point reduction in Adolescent Worst Pruritus NRS were considered responders. Subjects with missing data or who received rescue medication from Week 2 to Week 16 were considered non-responders.

Analysis was performed using Cochran-Mantel-Haenszel test stratified by region and baseline disease severity. The null hypothesis of no difference in response rate between tralokinumab 300 mg Q2W and placebo was tested against the 2-sided alternative that there is a difference.

|   |   |
|---|---|
| Comparison groups                       | Initial treatment period - Tralokinumab 300 mg Q2W v Initial treatment period - Placebo Q2W |
| Number of subjects included in analysis | 186   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | superiority <sup>[12]</sup>   |
| P-value                                 | < 0.001 <sup>[13]</sup>   |
| Method                                  | Cochran-Mantel-Haenszel   |
| Parameter estimate                      | Risk difference (RD)  |
| Point estimate                          | 21.7  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | 12.3  |
| upper limit                             | 31.1  |

## Notes:

[12] - This secondary endpoint was tested sequentially using the Holm-Bonferroni method for multiplicity adjustment at a 2.5% significance level after the sequential testing of the primary endpoints.

[13] - Based on the primary analysis of the primary estimand 'composite'.

| Statistical analysis title | Tralokinumab 150 mg Q2W versus Placebo |
|----------------------------|--|
|----------------------------|--|

## Statistical analysis description:

Subjects with at least 4-point reduction in Adolescent Worst Pruritus NRS were considered responders.

Subjects with missing data or who received rescue medication from Week 2 to Week 16 were considered non-responders. Analysis was performed using Cochran-Mantel-Haenszel test stratified by region and baseline disease severity. The null hypothesis of no difference in response rate between tralokinumab 150 mg Q2W and placebo was tested against the 2-sided alternative that there is a difference.

|   |   |
|---|---|
| Comparison groups                       | Initial treatment period - Tralokinumab 150 mg Q2W v Initial treatment period - Placebo Q2W |
| Number of subjects included in analysis | 185   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | superiority <sup>[14]</sup>   |
| P-value                                 | < 0.001 <sup>[15]</sup>   |
| Method                                  | Cochran-Mantel-Haenszel   |
| Parameter estimate                      | Risk difference (RD)  |
| Point estimate                          | 19.9  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | 10.6  |
| upper limit                             | 29.2  |

Notes:

[14] - This secondary endpoint was tested sequentially using the Holm-Bonferroni method for multiplicity adjustment at a 5% significance level after the sequential testing of the primary endpoints.

[15] - Based on the primary analysis of the primary estimand 'composite'.

## Secondary: Change in Scoring Atopic Dermatitis (SCORAD) From Baseline to Week 16

|  |   |
|--|---|
| End point title  | Change in Scoring Atopic Dermatitis (SCORAD) From Baseline to Week 16 |
| End point description:   |   |
| The SCORAD is a validated tool to evaluate the extent and severity of AD lesions, along with subjective symptoms. The maximum total score is 103, with higher values indicating more severe disease. |   |
| End point type   | Secondary   |
| End point timeframe:   |   |
| From Week 0 to Week 16   |   |

| End point values                    | Initial treatment period - Tralokinumab 300 mg Q2W | Initial treatment period - Tralokinumab 150 mg Q2W | Initial treatment period - Placebo Q2W |  |
|-------------------------------------|--|--|--|--|
| Subject group type                  | Reporting group                                    | Reporting group                                    | Reporting group                        |  |
| Number of subjects analysed         | 98   | 97   | 94                                     |  |
| Units: Adjusted mean change         |  |  |  |  |
| least squares mean (standard error) | -29.1 (± 2.4)                                      | -27.5 (± 2.4)                                      | -9.5 (± 3.0)                           |  |

## Statistical analyses

|                            |  |
|----------------------------|--|
| Statistical analysis title | Tralokinumab 300 mg Q2W versus Placebo |
|----------------------------|--|

Statistical analysis description:

Repeated measurements model on post-baseline data. In case of no post-baseline assessments before initiation of rescue medication, the Week 2 change was imputed as 0. Data collected after permanent discontinuation of IMP or after use of rescue treatment from Week 2 to Week 16 were not included in

the analysis.

|   |   |
|---|---|
| Comparison groups                       | Initial treatment period - Tralokinumab 300 mg Q2W v Initial treatment period - Placebo Q2W |
| Number of subjects included in analysis | 192   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | superiority <sup>[16]</sup>   |
| P-value                                 | < 0.001 <sup>[17]</sup>   |
| Method                                  | Repeated measurements model   |
| Parameter estimate                      | Difference of least square means  |
| Point estimate                          | -19.7   |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -27.1   |
| upper limit                             | -12.2   |

Notes:

[16] - This secondary endpoint was tested sequentially using the Holm-Bonferroni method for multiplicity adjustment at a 2.5% significance level after the sequential testing of the primary endpoints.

[17] - Based on the primary analysis of the primary estimand 'hypothetical'.

|                                   |  |
|-----------------------------------|--|
| <b>Statistical analysis title</b> | Tralokinumab 150 mg Q2W versus Placebo |
|-----------------------------------|--|

Statistical analysis description:

Repeated measurements model on post-baseline data. In case of no post-baseline assessments before initiation of rescue medication, the Week 2 change was imputed as 0. Data collected after permanent discontinuation of IMP or after use of rescue treatment from Week 2 to Week 16 were not included in the analysis.

|   |   |
|---|---|
| Comparison groups                       | Initial treatment period - Tralokinumab 150 mg Q2W v Initial treatment period - Placebo Q2W |
| Number of subjects included in analysis | 191   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | superiority <sup>[18]</sup>   |
| P-value                                 | < 0.001 <sup>[19]</sup>   |
| Method                                  | Repeated measurements model   |
| Parameter estimate                      | Difference of least square means  |
| Point estimate                          | -18   |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -25.6   |
| upper limit                             | -10.4   |

Notes:

[18] - This secondary endpoint was tested sequentially using the Holm-Bonferroni method for multiplicity adjustment at a 5% significance level after the sequential testing of the primary endpoints.

[19] - Based on the primary analysis of the primary estimand 'hypothetical'.

### **Secondary: Change in Children's Dermatology Life Quality Index (CDLQI) Score From Baseline to Week 16**

|                 |  |
|-----------------|--|
| End point title | Change in Children's Dermatology Life Quality Index (CDLQI) Score From Baseline to Week 16 |
|-----------------|--|

End point description:

The CDLQI is a validated questionnaire with content specific to those with dermatology conditions. It consists of 10 items addressing the subject's perception of the impact of their skin disease on various aspects of their quality of life over the last week such as dermatology-related symptoms and feelings, leisure, school or holidays, personal relationships, sleep, and the treatment. Each item is scored on a 4-point Likert scale (0 = 'not at all'; 1 = 'only a little'; 2 = 'quite a lot'; 3 = 'very much'). Item 7 (on school time) has one additional response category 'prevented school', which is also scored '3'. The total

score of the CDLQI is the sum of the 10 items (0 to 30); a high score is indicative of a poor quality of life.

|                        |           |
|------------------------|-----------|
| End point type         | Secondary |
| End point timeframe:   |           |
| From Week 0 to Week 16 |           |

| End point values                    | Initial treatment period - Tralokinumab 300 mg Q2W | Initial treatment period - Tralokinumab 150 mg Q2W | Initial treatment period - Placebo Q2W |  |
|-------------------------------------|--|--|--|--|
| Subject group type                  | Reporting group                                    | Reporting group                                    | Reporting group                        |  |
| Number of subjects analysed         | 94 <sup>[20]</sup>                                 | 95 <sup>[21]</sup>                                 | 89 <sup>[22]</sup>                     |  |
| Units: Adjusted mean change         |  |  |  |  |
| least squares mean (standard error) | -6.7 (± 0.6)                                       | -6.1 (± 0.6)                                       | -4.1 (± 0.7)                           |  |

Notes:

[20] - Subjects in the full analysis set with non-missing baseline CDLQI score

[21] - Subjects in the full analysis set with non-missing baseline CDLQI score

[22] - Subjects in the full analysis set with non-missing baseline CDLQI score

## Statistical analyses

|                                   |  |
|-----------------------------------|--|
| <b>Statistical analysis title</b> | Tralokinumab 300 mg Q2W versus Placebo |
|-----------------------------------|--|

Statistical analysis description:

Repeated measurements model on post-baseline data. In case of no post-baseline assessments before initiation of rescue medication, the Week 2 change was imputed as 0. Data collected after permanent discontinuation of IMP or after use of rescue treatment from Week 2 to Week 16 were not included in the analysis.

|   |   |
|---|---|
| Comparison groups                       | Initial treatment period - Tralokinumab 300 mg Q2W v Initial treatment period - Placebo Q2W |
| Number of subjects included in analysis | 183   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | superiority <sup>[23]</sup>   |
| P-value                                 | = 0.007 <sup>[24]</sup>   |
| Method                                  | Repeated measurements model   |
| Parameter estimate                      | Difference of least square means  |
| Point estimate                          | -2.6  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -4.5  |
| upper limit                             | -0.7  |

Notes:

[23] - This secondary endpoint was tested sequentially using the Holm-Bonferroni method for multiplicity adjustment at a 2.5% significance level after the sequential testing of the primary endpoints.

[24] - Based on the primary analysis of the primary estimand 'hypothetical'.

|                                   |  |
|-----------------------------------|--|
| <b>Statistical analysis title</b> | Tralokinumab 150 mg Q2W versus Placebo |
|-----------------------------------|--|

Statistical analysis description:

Repeated measurements model on post-baseline data. In case of no post-baseline assessments before initiation of rescue medication, the Week 2 change was imputed as 0. Data collected after permanent discontinuation of IMP or after use of rescue treatment from Week 2 to Week 16 were not included in the analysis.

|   |   |
|---|---|
| Comparison groups                       | Initial treatment period - Tralokinumab 150 mg Q2W v Initial treatment period - Placebo Q2W |
| Number of subjects included in analysis | 184   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | superiority <sup>[25]</sup>   |
| P-value                                 | = 0.04 <sup>[26]</sup>  |
| Method                                  | Repeated measurements model   |
| Parameter estimate                      | Difference of least square means  |
| Point estimate                          | -2  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -3.9  |
| upper limit                             | -0.1  |

Notes:

[25] - This secondary endpoint was tested sequentially using the Holm-Bonferroni method for multiplicity adjustment at a 5% significance level after the sequential testing of the primary endpoints.

[26] - Based on the primary analysis of the primary estimand 'hypothetical'.

### Secondary: Number of Adverse Events

|   |                          |
|---|--------------------------|
| End point title   | Number of Adverse Events |
| End point description:  |                          |
| Overall number of AEs during the Initial treatment period is presented. For a complete description of AEs and SAEs by MedDRA system organ class (SOC) and preferred term (PT) during the initial treatment period, maintenance treatment period, open-label treatment period, and safety follow-up period, see the Adverse Events Overview section. |                          |
| End point type  | Secondary                |
| End point timeframe:  |                          |
| From Week 0 to Week 16  |                          |

| End point values                | Initial treatment period - Tralokinumab 300 mg Q2W | Initial treatment period - Tralokinumab 150 mg Q2W | Initial treatment period - Placebo Q2W |  |
|---------------------------------|--|--|--|--|
| Subject group type              | Reporting group                                    | Reporting group                                    | Reporting group                        |  |
| Number of subjects analysed     | 97   | 98   | 94                                     |  |
| Units: Number of adverse events | 130  | 175  | 134                                    |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Presence of Anti-drug Antibodies

|   |                                  |
|---|----------------------------------|
| End point title   | Presence of Anti-drug Antibodies |
| End point description:  |                                  |
| Anti-tralokinumab antibody levels were analysed using a validated bioanalytical method. |                                  |
| End point type  | Secondary                        |

End point timeframe:  
From Week 0 to Week 16

| End point values            | Initial treatment period - Tralokinumab 300 mg Q2W | Initial treatment period - Tralokinumab 150 mg Q2W | Initial treatment period - Placebo Q2W |  |
|-----------------------------|--|--|--|--|
| Subject group type          | Reporting group                                    | Reporting group                                    | Reporting group                        |  |
| Number of subjects analysed | 97   | 98   | 94                                     |  |
| Units: Number of subjects   | 1  | 7  | 2                                      |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Subjects With at Least 50% Reduction in Eczema Area and Severity Index (EASI50) at Week 16.

|   |   |
|---|---|
| End point title   | Subjects With at Least 50% Reduction in Eczema Area and Severity Index (EASI50) at Week 16. |
| End point description:<br>The EASI is a validated measure used in clinical practice and clinical trials to assess the severity and extent of AD. The EASI is a composite index with scores ranging from 0 to 72, with higher values indicating more severe and/or more extensive condition. |   |
| End point type  | Secondary   |
| End point timeframe:<br>At Week 16  |   |

| End point values                        | Initial treatment period - Tralokinumab 300 mg Q2W | Initial treatment period - Tralokinumab 150 mg Q2W | Initial treatment period - Placebo Q2W |  |
|---|--|--|--|--|
| Subject group type                      | Reporting group                                    | Reporting group                                    | Reporting group                        |  |
| Number of subjects analysed             | 97   | 98   | 94                                     |  |
| Units: Number of subjects with response | 50   | 45   | 13                                     |  |

### Statistical analyses

|  |  |
|--|--|
| Statistical analysis title   | Tralokinumab 300 mg Q2W versus Placebo |
| Statistical analysis description:<br>Subjects who achieved at least 50% reduction in EASI at Week 16 were considered responders. Subjects with missing data or subjects who received rescue medication from Week 2 to Week 16 were considered non-responders. Analysis was performed using Cochran-Mantel-Haenszel test stratified by region and baseline disease severity. The null hypothesis of no difference in response rate between tralokinumab 300 mg Q2W and placebo was tested against the 2-sided alternative that there is a difference. |  |

|   |   |
|---|---|
| Comparison groups                       | Initial treatment period - Tralokinumab 300 mg Q2W v Initial treatment period - Placebo Q2W |
| Number of subjects included in analysis | 191   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | superiority <sup>[27]</sup>   |
| P-value                                 | < 0.001 <sup>[28]</sup>   |
| Method                                  | Cochran-Mantel-Haenszel   |
| Parameter estimate                      | Risk difference (RD)  |
| Point estimate                          | 38.5  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | 26.8  |
| upper limit                             | 50.2  |

Notes:

[27] - The statistical test was not controlled for multiplicity.

[28] - Based on the primary analysis of the primary estimand 'composite'.

|                                   |  |
|-----------------------------------|--|
| <b>Statistical analysis title</b> | Tralokinumab 150 mg Q2W versus Placebo |
|-----------------------------------|--|

Statistical analysis description:

Subjects who achieved at least 50% reduction in EASI at Week 16 were considered responders. Subjects with missing data or subjects who received rescue medication from Week 2 to Week 16 were considered non-responders. Analysis was performed using Cochran-Mantel-Haenszel test stratified by region and baseline disease severity. The null hypothesis of no difference in response rate between tralokinumab 150 mg Q2W and placebo was tested against the 2-sided alternative that there is a difference.

|   |   |
|---|---|
| Comparison groups                       | Initial treatment period - Tralokinumab 150 mg Q2W v Initial treatment period - Placebo Q2W |
| Number of subjects included in analysis | 192   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | superiority <sup>[29]</sup>   |
| P-value                                 | < 0.001 <sup>[30]</sup>   |
| Method                                  | Cochran-Mantel-Haenszel   |
| Parameter estimate                      | Risk difference (RD)  |
| Point estimate                          | 32.4  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | 20.6  |
| upper limit                             | 44.1  |

Notes:

[29] - The statistical test was not controlled for multiplicity.

[30] - Based on the primary analysis of the primary estimand 'composite'.

## **Secondary: Subjects With at Least 90% Reduction in Eczema Area and Severity Index (EASI90) at Week 16.**

|                 |   |
|-----------------|---|
| End point title | Subjects With at Least 90% Reduction in Eczema Area and Severity Index (EASI90) at Week 16. |
|-----------------|---|

End point description:

The EASI is a validated measure used in clinical practice and clinical trials to assess the severity and extent of AD. The EASI is a composite index with scores ranging from 0 to 72, with higher values indicating more severe and/or more extensive condition.

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

End point timeframe:

At Week 16



| <b>End point values</b>                 | Initial treatment period - Tralokinumab 300 mg Q2W | Initial treatment period - Tralokinumab 150 mg Q2W | Initial treatment period - Placebo Q2W |  |
|---|--|--|--|--|
| Subject group type                      | Reporting group                                    | Reporting group                                    | Reporting group                        |  |
| Number of subjects analysed             | 97   | 98   | 94                                     |  |
| Units: Number of subjects with response | 17   | 19   | 4                                      |  |

## Statistical analyses

| <b>Statistical analysis title</b>   | Tralokinumab 300 mg Q2W versus Placebo  |
|---|---|
| Statistical analysis description:   |   |
| Subjects who achieved at least 90% reduction in EASI at Week 16 were considered responders. Subjects with missing data or subjects who received rescue medication from Week 2 to Week 16 were considered non-responders. Analysis was performed using Cochran-Mantel-Haenszel test stratified by region and baseline disease severity. The null hypothesis of no difference in response rate between tralokinumab 300 mg Q2W and placebo was tested against the 2-sided alternative that there is a difference. |   |
| Comparison groups   | Initial treatment period - Tralokinumab 300 mg Q2W v Initial treatment period - Placebo Q2W |
| Number of subjects included in analysis   | 191   |
| Analysis specification  | Pre-specified   |
| Analysis type   | superiority <sup>[31]</sup>   |
| P-value   | = 0.002 <sup>[32]</sup>   |
| Method  | Cochran-Mantel-Haenszel   |
| Parameter estimate  | Risk difference (RD)  |
| Point estimate  | 13.7  |
| Confidence interval   |   |
| level   | 95 %  |
| sides   | 2-sided   |
| lower limit   | 5.2   |
| upper limit   | 22.2  |

Notes:

[31] - The statistical test was not controlled for multiplicity.

[32] - Based on the primary analysis of the primary estimand 'composite'.

| <b>Statistical analysis title</b>   | Tralokinumab 150 mg Q2W versus Placebo  |
|---|---|
| Statistical analysis description:   |   |
| Subjects who achieved at least 90% reduction in EASI at Week 16 were considered responders. Subjects with missing data or subjects who received rescue medication from Week 2 to Week 16 were considered non-responders. Analysis was performed using Cochran-Mantel-Haenszel test stratified by region and baseline disease severity. The null hypothesis of no difference in response rate between tralokinumab 150 mg Q2W and placebo was tested against the 2-sided alternative that there is a difference. |   |
| Comparison groups   | Initial treatment period - Tralokinumab 150 mg Q2W v Initial treatment period - Placebo Q2W |

|   |                             |
|---|-----------------------------|
| Number of subjects included in analysis | 192                         |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | superiority <sup>[33]</sup> |
| P-value                                 | < 0.001 <sup>[34]</sup>     |
| Method                                  | Cochran-Mantel-Haenszel     |
| Parameter estimate                      | Risk difference (RD)        |
| Point estimate                          | 15.3                        |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 6.5                         |
| upper limit                             | 24.1                        |

Notes:

[33] - The statistical test was not controlled for multiplicity.

[34] - Based on the primary analysis of the primary estimand 'composite'.

### Secondary: Change in Eczema Area and Severity Index (EASI) Score From Baseline to Week 16

|                 |  |
|-----------------|--|
| End point title | Change in Eczema Area and Severity Index (EASI) Score From Baseline to Week 16 |
|-----------------|--|

End point description:

The EASI is a validated measure used in clinical practice and clinical trials to assess the severity and extent of AD. The EASI is a composite index with scores ranging from 0 to 72, with higher values indicating more severe and/or more extensive condition.

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

End point timeframe:

From Week 0 to Week 16

| End point values                    | Initial treatment period - Tralokinumab 300 mg Q2W | Initial treatment period - Tralokinumab 150 mg Q2W | Initial treatment period - Placebo Q2W |  |
|-------------------------------------|--|--|--|--|
| Subject group type                  | Reporting group                                    | Reporting group                                    | Reporting group                        |  |
| Number of subjects analysed         | 97   | 98   | 94                                     |  |
| Units: Adjusted mean change         |  |  |  |  |
| least squares mean (standard error) | -18.1 (± 1.3)                                      | -18.1 (± 1.4)                                      | -8.7 (± 1.6)                           |  |

### Statistical analyses

|                            |  |
|----------------------------|--|
| Statistical analysis title | Tralokinumab 300 mg Q2W versus Placebo |
|----------------------------|--|

Statistical analysis description:

Repeated measurements model on post-baseline data. In case of no post-baseline assessments before initiation of rescue medication, the Week 2 change was imputed as 0. Data collected after permanent discontinuation of IMP or after use of rescue treatment from Week 2 to Week 16 were not included in the analysis.

|                   |   |
|-------------------|---|
| Comparison groups | Initial treatment period - Tralokinumab 300 mg Q2W v Initial treatment period - Placebo Q2W |
|-------------------|---|

|   |                                  |
|---|----------------------------------|
| Number of subjects included in analysis | 191                              |
| Analysis specification                  | Pre-specified                    |
| Analysis type                           | superiority <sup>[35]</sup>      |
| P-value                                 | < 0.001 <sup>[36]</sup>          |
| Method                                  | Repeated measurements model      |
| Parameter estimate                      | Difference of least square means |
| Point estimate                          | -9.4                             |
| Confidence interval                     |                                  |
| level                                   | 95 %                             |
| sides                                   | 2-sided                          |
| lower limit                             | -13.5                            |
| upper limit                             | -5.3                             |

Notes:

[35] - The statistical test was not controlled for multiplicity.

[36] - Based on the primary analysis of the primary estimand 'hypothetical'.

|                                   |  |
|-----------------------------------|--|
| <b>Statistical analysis title</b> | Tralokinumab 150 mg Q2W versus Placebo |
|-----------------------------------|--|

Statistical analysis description:

Repeated measurements model on post-baseline data. In case of no post-baseline assessments before initiation of rescue medication, the Week 2 change was imputed as 0. Data collected after permanent discontinuation of IMP or after use of rescue treatment from Week 2 to Week 16 were not included in the analysis.

|   |   |
|---|---|
| Comparison groups                       | Initial treatment period - Tralokinumab 150 mg Q2W v Initial treatment period - Placebo Q2W |
| Number of subjects included in analysis | 192   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | superiority <sup>[37]</sup>   |
| P-value                                 | < 0.001 <sup>[38]</sup>   |
| Method                                  | Repeated measurements model   |
| Parameter estimate                      | Difference of least square means  |
| Point estimate                          | -9.4  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -13.6   |
| upper limit                             | -5.3  |

Notes:

[37] - The statistical test was not controlled for multiplicity.

[38] - Based on the primary analysis of the primary estimand 'hypothetical'.

## **Secondary: Subjects With at Least 75% Reduction in Scoring Atopic Dermatitis (SCORAD75) at Week 16**

|                 |   |
|-----------------|---|
| End point title | Subjects With at Least 75% Reduction in Scoring Atopic Dermatitis (SCORAD75) at Week 16 |
|-----------------|---|

End point description:

The SCORAD is a validated tool to evaluate the extent and severity of atopic dermatitis lesions, along with subjective symptoms. The score ranges from 0 to 103, with a higher values indicating a more extensive and/or severe condition.

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

End point timeframe:

At Week 16

| <b>End point values</b>                 | Initial treatment period - Tralokinumab 300 mg Q2W | Initial treatment period - Tralokinumab 150 mg Q2W | Initial treatment period - Placebo Q2W |  |
|---|--|--|--|--|
| Subject group type                      | Reporting group                                    | Reporting group                                    | Reporting group                        |  |
| Number of subjects analysed             | 97   | 98   | 94                                     |  |
| Units: Number of subjects with response | 12   | 16   | 1                                      |  |

## Statistical analyses

| <b>Statistical analysis title</b> | Tralokinumab 300 mg Q2W versus Placebo |
|-----------------------------------|--|
|-----------------------------------|--|

Statistical analysis description:

Subjects who achieved at least 75% reduction in SCORAD at Week 16 were considered responders. Subjects with missing data or subjects who received rescue medication from Week 2 to Week 16 were considered non-responders. Analysis was performed using Cochran-Mantel-Haenszel test stratified by region and baseline disease severity. The null hypothesis of no difference in response rate between tralokinumab 300 mg Q2W and placebo was tested against the 2-sided alternative that there is a difference.

|   |   |
|---|---|
| Comparison groups                       | Initial treatment period - Tralokinumab 300 mg Q2W v Initial treatment period - Placebo Q2W |
| Number of subjects included in analysis | 191   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | superiority <sup>[39]</sup>   |
| P-value                                 | = 0.002 <sup>[40]</sup>   |
| Method                                  | Cochran-Mantel-Haenszel   |
| Parameter estimate                      | Risk difference (RD)  |
| Point estimate                          | 11.5  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | 4.5   |
| upper limit                             | 18.4  |

Notes:

[39] - The statistical test was not controlled for multiplicity.

[40] - Based on the primary analysis of the primary estimand 'composite'.

| <b>Statistical analysis title</b> | Tralokinumab 150 mg Q2W versus Placebo |
|-----------------------------------|--|
|-----------------------------------|--|

Statistical analysis description:

Subjects who achieved at least 75% reduction in SCORAD at Week 16 were considered responders. Subjects with missing data or subjects who received rescue medication from Week 2 to Week 16 were considered non-responders. Analysis was performed using Cochran-Mantel-Haenszel test stratified by region and baseline disease severity. The null hypothesis of no difference in response rate between tralokinumab 150 mg Q2W and placebo was tested against the 2-sided alternative that there is a difference.

|                   |   |
|-------------------|---|
| Comparison groups | Initial treatment period - Tralokinumab 150 mg Q2W v Initial treatment period - Placebo Q2W |
|-------------------|---|

|   |                             |
|---|-----------------------------|
| Number of subjects included in analysis | 192                         |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | superiority <sup>[41]</sup> |
| P-value                                 | < 0.001 <sup>[42]</sup>     |
| Method                                  | Cochran-Mantel-Haenszel     |
| Parameter estimate                      | Risk difference (RD)        |
| Point estimate                          | 15.6                        |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 7.8                         |
| upper limit                             | 23.3                        |

Notes:

[41] - The statistical test was not controlled for multiplicity.

[42] - Based on the primary analysis of the primary estimand 'composite'.

### Secondary: Subjects With at Least 50% Reduction in Scoring Atopic Dermatitis (SCORAD50) at Week 16

|                        |  |
|------------------------|--|
| End point title        | Subjects With at Least 50% Reduction in Scoring Atopic Dermatitis (SCORAD50) at Week 16  |
| End point description: | The SCORAD is a validated tool to evaluate the extent and severity of atopic dermatitis lesions, along with subjective symptoms. The score ranges from 0 to 103, with a higher values indicating a more extensive and/or severe condition. |
| End point type         | Secondary  |
| End point timeframe:   | At Week 16   |

| End point values                        | Initial treatment period - Tralokinumab 300 mg Q2W | Initial treatment period - Tralokinumab 150 mg Q2W | Initial treatment period - Placebo Q2W |  |
|---|--|--|--|--|
| Subject group type                      | Reporting group                                    | Reporting group                                    | Reporting group                        |  |
| Number of subjects analysed             | 97   | 98   | 94                                     |  |
| Units: Number of subjects with response | 30   | 30   | 5                                      |  |

### Statistical analyses

|                                   |   |
|-----------------------------------|---|
| Statistical analysis title        | Tralokinumab 300 mg Q2W versus Placebo  |
| Statistical analysis description: | Subjects who achieved at least 50% reduction in SCORAD at Week 16 were considered responders. Subjects with missing data or subjects who received rescue medication from Week 2 to Week 16 were considered non-responders. Analysis was performed using Cochran-Mantel-Haenszel test stratified by region and baseline disease severity. The null hypothesis of no difference in response rate between tralokinumab 300 mg Q2W and placebo was tested against the 2-sided alternative that there is a difference. |
| Comparison groups                 | Initial treatment period - Tralokinumab 300 mg Q2W v Initial treatment period - Placebo Q2W   |

|   |                             |
|---|-----------------------------|
| Number of subjects included in analysis | 191                         |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | superiority <sup>[43]</sup> |
| P-value                                 | < 0.001 <sup>[44]</sup>     |
| Method                                  | Cochran-Mantel-Haenszel     |
| Parameter estimate                      | Risk difference (RD)        |
| Point estimate                          | 26.2                        |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 16.1                        |
| upper limit                             | 36.3                        |

Notes:

[43] - The statistical test was not controlled for multiplicity.

[44] - Based on the primary analysis of the primary estimand 'composite'.

|                                   |  |
|-----------------------------------|--|
| <b>Statistical analysis title</b> | Tralokinumab 150 mg Q2W versus Placebo |
|-----------------------------------|--|

Statistical analysis description:

Subjects who achieved at least 50% reduction in SCORAD at Week 16 were considered responders. Subjects with missing data or subjects who received rescue medication from Week 2 to Week 16 were considered non-responders. Analysis was performed using Cochran-Mantel-Haenszel test stratified by region and baseline disease severity. The null hypothesis of no difference in response rate between tralokinumab 150 mg Q2W and placebo was tested against the 2-sided alternative that there is a difference.

|   |   |
|---|---|
| Comparison groups                       | Initial treatment period - Tralokinumab 150 mg Q2W v Initial treatment period - Placebo Q2W |
| Number of subjects included in analysis | 192   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | superiority <sup>[45]</sup>   |
| P-value                                 | < 0.001 <sup>[46]</sup>   |
| Method                                  | Cochran-Mantel-Haenszel   |
| Parameter estimate                      | Risk difference (RD)  |
| Point estimate                          | 25.5  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | 15.3  |
| upper limit                             | 35.7  |

Notes:

[45] - The statistical test was not controlled for multiplicity.

[46] - Based on the primary analysis of the primary estimand 'composite'.

### **Secondary: Change in Adolescent Worst Pruritus Numeric Rating Scale (NRS) (Weekly Average) From Baseline to Week 16**

|                 |  |
|-----------------|--|
| End point title | Change in Adolescent Worst Pruritus Numeric Rating Scale (NRS) (Weekly Average) From Baseline to Week 16 |
|-----------------|--|

End point description:

The Adolescent Worst Pruritus NRS is used by subjects to assess their worst itch over the past 24 hours using an 11-point NRS with 0 indicating 'no itch' and 10 indicating 'worst itch possible'.

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

End point timeframe:

From Week 0 to Week 16

| <b>End point values</b>             | Initial treatment period - Tralokinumab 300 mg Q2W | Initial treatment period - Tralokinumab 150 mg Q2W | Initial treatment period - Placebo Q2W |  |
|-------------------------------------|--|--|--|--|
| Subject group type                  | Reporting group                                    | Reporting group                                    | Reporting group                        |  |
| Number of subjects analysed         | 96 <sup>[47]</sup>                                 | 96 <sup>[48]</sup>                                 | 92 <sup>[49]</sup>                     |  |
| Units: Adjusted mean change         |  |  |  |  |
| least squares mean (standard error) | -3.0 (± 0.3)                                       | -2.7 (± 0.3)                                       | -1.5 (± 0.3)                           |  |

Notes:

[47] - Subjects in the full analysis set with non-missing baseline Adolescent Worst Pruritus NRS score.

[48] - Subjects in the full analysis set with non-missing baseline Adolescent Worst Pruritus NRS score.

[49] - Subjects in the full analysis set with non-missing baseline Adolescent Worst Pruritus NRS score.

## Statistical analyses

| <b>Statistical analysis title</b> | Tralokinumab 300 mg Q2W versus Placebo |
|-----------------------------------|--|
|-----------------------------------|--|

Statistical analysis description:

Repeated measurements model on post-baseline data. In case of no post-baseline assessments before initiation of rescue medication, the Week 2 change was imputed as 0. Data collected after permanent discontinuation of IMP or after use of rescue treatment from Week 2 to Week 16 were not included in the analysis.

|   |   |
|---|---|
| Comparison groups                       | Initial treatment period - Tralokinumab 300 mg Q2W v Initial treatment period - Placebo Q2W |
| Number of subjects included in analysis | 188   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | superiority <sup>[50]</sup>   |
| P-value                                 | < 0.001 <sup>[51]</sup>   |
| Method                                  | Repeated measurements model   |
| Parameter estimate                      | Difference of least square means  |
| Point estimate                          | -1.5  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -2.4  |
| upper limit                             | -0.6  |

Notes:

[50] - The statistical test was not controlled for multiplicity.

[51] - Based on the primary analysis of the primary estimand 'hypothetical'.

| <b>Statistical analysis title</b> | Tralokinumab 150 mg Q2W versus Placebo |
|-----------------------------------|--|
|-----------------------------------|--|

Statistical analysis description:

Repeated measurements model on post-baseline data. In case of no post-baseline assessments before initiation of rescue medication, the Week 2 change was imputed as 0. Data collected after permanent discontinuation of IMP or after use of rescue treatment from Week 2 to Week 16 were not included in the analysis.

|                   |   |
|-------------------|---|
| Comparison groups | Initial treatment period - Tralokinumab 150 mg Q2W v Initial treatment period - Placebo Q2W |
|-------------------|---|

|   |                                  |
|---|----------------------------------|
| Number of subjects included in analysis | 188                              |
| Analysis specification                  | Pre-specified                    |
| Analysis type                           | superiority <sup>[52]</sup>      |
| P-value                                 | = 0.007 <sup>[53]</sup>          |
| Method                                  | Repeated measurements model      |
| Parameter estimate                      | Difference of least square means |
| Point estimate                          | -1.2                             |
| Confidence interval                     |                                  |
| level                                   | 95 %                             |
| sides                                   | 2-sided                          |
| lower limit                             | -2.1                             |
| upper limit                             | -0.3                             |

Notes:

[52] - The statistical test was not controlled for multiplicity.

[53] - Based on the primary analysis of the primary estimand 'hypothetical'.

### Secondary: Subjects With Reduction of Adolescent Worst Pruritus Numeric Rating Scale (NRS) (Weekly Average) of at Least 3 From Baseline to Week 16

|                 |   |
|-----------------|---|
| End point title | Subjects With Reduction of Adolescent Worst Pruritus Numeric Rating Scale (NRS) (Weekly Average) of at Least 3 From Baseline to Week 16 |
|-----------------|---|

End point description:

The Adolescent Worst Pruritus NRS is used by subjects to assess their worst itch over the past 24 hours using an 11-point NRS with 0 indicating 'no itch' and 10 indicating 'worst itch possible'.

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

End point timeframe:

At Week 16

| End point values                        | Initial treatment period - Tralokinumab 300 mg Q2W | Initial treatment period - Tralokinumab 150 mg Q2W | Initial treatment period - Placebo Q2W |  |
|---|--|--|--|--|
| Subject group type                      | Reporting group                                    | Reporting group                                    | Reporting group                        |  |
| Number of subjects analysed             | 96 <sup>[54]</sup>                                 | 95 <sup>[55]</sup>                                 | 91 <sup>[56]</sup>                     |  |
| Units: Number of subjects with response | 28   | 29   | 8                                      |  |

Notes:

[54] - Subjects in the full analysis set with baseline Adolescent Worst Pruritus weekly average  $\geq 3$ .

[55] - Subjects in the full analysis set with baseline Adolescent Worst Pruritus weekly average  $\geq 3$ .

[56] - Subjects in the full analysis set with baseline Adolescent Worst Pruritus weekly average  $\geq 3$ .

### Statistical analyses

|                            |  |
|----------------------------|--|
| Statistical analysis title | Tralokinumab 300 mg Q2W versus Placebo |
|----------------------------|--|

Statistical analysis description:

Subjects with at least 3-point reduction in Adolescent Worst Pruritus NRS were considered responders. Subjects with missing data or who received rescue medication from Week 2 to Week 16 were considered non-responders. Analysis was performed using Cochran-Mantel-Haenszel test stratified by region and baseline disease severity. The null hypothesis of no difference in response rate between tralokinumab 150 mg Q2W and placebo was tested against the 2-sided alternative that there is a difference.

|                   |   |
|-------------------|---|
| Comparison groups | Initial treatment period - Tralokinumab 300 mg Q2W v Initial treatment period - Placebo Q2W |
|-------------------|---|



|   |                             |
|---|-----------------------------|
| Number of subjects included in analysis | 187                         |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | superiority <sup>[57]</sup> |
| P-value                                 | < 0.001 <sup>[58]</sup>     |
| Method                                  | Cochran-Mantel-Haenszel     |
| Parameter estimate                      | Risk difference (RD)        |
| Point estimate                          | 20.3                        |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 9.7                         |
| upper limit                             | 31                          |

Notes:

[57] - The statistical test was not controlled for multiplicity.

[58] - Based on the primary analysis of the primary estimand 'composite'.

|                                   |  |
|-----------------------------------|--|
| <b>Statistical analysis title</b> | Tralokinumab 150 mg Q2W versus Placebo |
|-----------------------------------|--|

Statistical analysis description:

Subjects with at least 3-point reduction in Adolescent Worst Pruritus NRS were considered responders. Subjects with missing data or who received rescue medication from Week 2 to Week 16 were considered non-responders. Analysis was performed using Cochran-Mantel-Haenszel test stratified by region and baseline disease severity. The null hypothesis of no difference in response rate between tralokinumab 150 mg Q2W and placebo was tested against the 2-sided alternative that there is a difference.

|   |   |
|---|---|
| Comparison groups                       | Initial treatment period - Tralokinumab 150 mg Q2W v Initial treatment period - Placebo Q2W |
| Number of subjects included in analysis | 186   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | superiority <sup>[59]</sup>   |
| P-value                                 | < 0.001 <sup>[60]</sup>   |
| Method                                  | Cochran-Mantel-Haenszel   |
| Parameter estimate                      | Risk difference (RD)  |
| Point estimate                          | 21.8  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | 10.9  |
| upper limit                             | 32.7  |

Notes:

[59] - The statistical test was not controlled for multiplicity.

[60] - Based on the primary analysis of the primary estimand 'composite'.

## Secondary: Change in Patient Oriented Eczema Measure (POEM) From Baseline to Week 16

|                 |   |
|-----------------|---|
| End point title | Change in Patient Oriented Eczema Measure (POEM) From Baseline to Week 16 |
|-----------------|---|

End point description:

The POEM is a validated questionnaire used to assess disease symptoms in atopic eczema patients in both clinical practice and clinical trials. The tool consists of 7 items each addressing a specific symptom (itching, sleep, bleeding, weeping, cracking, flaking, and dryness). Subjects will score how often they have experienced each symptom over the previous week on a 5-point categorical response scale (0 = 'no days'; 1 = '1 to 2 days'; 2 = '3 to 4 days'; 3 = '5 to 6 days'; 4 = 'every day'). The total score is the sum of the 7 items (range 0 to 28) and reflects disease-related morbidity; a high score is indicative of a worse disease severity.

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

End point timeframe:  
From Week 0 to Week 16

| End point values                    | Initial treatment period - Tralokinumab 300 mg Q2W | Initial treatment period - Tralokinumab 150 mg Q2W | Initial treatment period - Placebo Q2W |  |
|-------------------------------------|--|--|--|--|
| Subject group type                  | Reporting group                                    | Reporting group                                    | Reporting group                        |  |
| Number of subjects analysed         | 94 <sup>[61]</sup>                                 | 95 <sup>[62]</sup>                                 | 87 <sup>[63]</sup>                     |  |
| Units: Adjusted mean change         |  |  |  |  |
| least squares mean (standard error) | -8.4 (± 0.8)                                       | -7.8 (± 0.8)                                       | -2.4 (± 1.0)                           |  |

Notes:

[61] - Subjects in the full analysis set with non-missing baseline POEM score.

[62] - Subjects in the full analysis set with non-missing baseline POEM score.

[63] - Subjects in the full analysis set with non-missing baseline POEM score.

## Statistical analyses

| Statistical analysis title   | Tralokinumab 300 mg Q2W versus Placebo  |
|--|---|
| Statistical analysis description:<br>Repeated measurements model on post-baseline data. In case of no post-baseline assessments before initiation of rescue medication, the Week 2 change was imputed as 0. Data collected after permanent discontinuation of IMP or after use of rescue treatment from Week 2 to Week 16 were not included in the analysis. |   |
| Comparison groups  | Initial treatment period - Tralokinumab 300 mg Q2W v Initial treatment period - Placebo Q2W |
| Number of subjects included in analysis  | 181   |
| Analysis specification   | Pre-specified   |
| Analysis type  | superiority <sup>[64]</sup>   |
| P-value  | < 0.001 <sup>[65]</sup>   |
| Method   | Repeated measurements model   |
| Parameter estimate   | Difference of least square means  |
| Point estimate   | -6  |
| Confidence interval  |   |
| level  | 95 %  |
| sides  | 2-sided   |
| lower limit  | -8.4  |
| upper limit  | -3.6  |

Notes:

[64] - The statistical test was not controlled for multiplicity.

[65] - ents

Based on the primary analysis of the primary estimand 'hypothetical'.

| Statistical analysis title   | Tralokinumab 150 mg Q2W versus Placebo  |
|--|---|
| Statistical analysis description:<br>Repeated measurements model on post-baseline data. In case of no post-baseline assessments before initiation of rescue medication, the Week 2 change was imputed as 0. Data collected after permanent discontinuation of IMP or after use of rescue treatment from Week 2 to Week 16 were not included in the analysis. |   |
| Comparison groups  | Initial treatment period - Tralokinumab 150 mg Q2W v Initial treatment period - Placebo Q2W |

|   |                                  |
|---|----------------------------------|
| Number of subjects included in analysis | 182                              |
| Analysis specification                  | Pre-specified                    |
| Analysis type                           | superiority <sup>[66]</sup>      |
| P-value                                 | < 0.001 <sup>[67]</sup>          |
| Method                                  | Repeated measurements model      |
| Parameter estimate                      | Difference of least square means |
| Point estimate                          | -5.4                             |
| Confidence interval                     |                                  |
| level                                   | 95 %                             |
| sides                                   | 2-sided                          |
| lower limit                             | -7.9                             |
| upper limit                             | -3                               |

Notes:

[66] - The statistical test was not controlled for multiplicity.

[67] - Based on the primary analysis of the primary estimand 'hypothetical'.

### Secondary: Tralokinumab Serum Trough Concentration at Week 16

|                 |  |
|-----------------|--|
| End point title | Tralokinumab Serum Trough Concentration at Week 16 <sup>[68]</sup> |
|-----------------|--|

End point description:

Serum samples for determination of tralokinumab concentrations were analysed by a laboratory using a validated bioanalytical method.

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

End point timeframe:

At Week 16

Notes:

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

Justification: Tralokinumab serum trough concentration was not analysed for subjects who were not randomised to tralokinumab.

| End point values                                    | Initial treatment period - Tralokinumab 300 mg Q2W | Initial treatment period - Tralokinumab 150 mg Q2W |  |  |
|---|--|--|--|--|
| Subject group type                                  | Reporting group                                    | Reporting group                                    |  |  |
| Number of subjects analysed                         | 89   | 87   |  |  |
| Units: microgram/mL                                 |  |  |  |  |
| geometric mean (geometric coefficient of variation) | 129.1 (± 39.0)                                     | 69.0 (± 35.4)                                      |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Subjects With Investigator's Global Assessment (IGA) Score of 0 (Clear) or 1 (Almost Clear) at Week 52 Among Subjects With IGA Score of 0 or 1 at Week 16 After Initial Randomisation to Tralokinumab and Without Use of Rescue From Week 2 to Week 16

|                 |  |
|-----------------|--|
| End point title | Subjects With Investigator's Global Assessment (IGA) Score of 0 (Clear) or 1 (Almost Clear) at Week 52 Among Subjects With IGA Score of 0 or 1 at Week 16 After Initial Randomisation to |
|-----------------|--|

End point description:

The IGA is an instrument used in clinical trials to rate the severity of the subject's global AD and is based on a 5-point scale ranging from 0 (clear) to 4 (severe).

End point type Secondary

End point timeframe:

At Week 52

| End point values                        | Maintenance Treatment Period - Tralokinumab 300 mg Q2W | Maintenance Treatment Period - Tralokinumab 300 mg Q4W | Maintenance Treatment Period - Tralokinumab 150 mg Q2W | Maintenance Treatment Period - Tralokinumab 150 mg Q4W |
|---|--|--|--|--|
| Subject group type                      | Reporting group  | Reporting group  | Reporting group  | Reporting group  |
| Number of subjects analysed             | 11   | 13   | 12   | 14   |
| Units: Number of subjects with response | 4  | 7  | 6  | 7  |

Statistical analyses

No statistical analyses for this end point

**Secondary: Subjects With at Least 75% Reduction in Eczema Area and Severity Index (EASI75) at Week 52 Among Subjects With at Least 75% Reduction in EASI at Week 16 After Initial Randomisation to Tralokinumab and Without Use of Rescue From Week 2 to Week 16**

|                 |   |
|-----------------|---|
| End point title | Subjects With at Least 75% Reduction in Eczema Area and Severity Index (EASI75) at Week 52 Among Subjects With at Least 75% Reduction in EASI at Week 16 After Initial Randomisation to Tralokinumab and Without Use of Rescue From Week 2 to Week 16 |
|-----------------|---|

End point description:

The EASI is a validated measure used in clinical practice and clinical trials to assess the severity and extent of AD. The EASI is a composite index with scores ranging from 0 to 72, with higher values indicating more severe and/or more extensive condition.

End point type Secondary

End point timeframe:

At Week 52

| End point values                        | Maintenance Treatment Period - Tralokinumab 300 mg Q2W | Maintenance Treatment Period - Tralokinumab 300 mg Q4W | Maintenance Treatment Period - Tralokinumab 150 mg Q2W | Maintenance Treatment Period - Tralokinumab 150 mg Q4W |
|---|--|--|--|--|
| Subject group type                      | Reporting group  | Reporting group  | Reporting group  | Reporting group  |
| Number of subjects analysed             | 11   | 13   | 12   | 14   |
| Units: Number of subjects with response | 5  | 7  | 7  | 7  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Tralokinumab Serum Trough Concentration at Week 66

|                 |  |
|-----------------|--|
| End point title | Tralokinumab Serum Trough Concentration at Week 66 |
|-----------------|--|

End point description:

Serum samples for determination of tralokinumab concentrations were analysed by a laboratory using a validated bioanalytical method.

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

End point timeframe:

At Week 66

| End point values                                    | Open-label Treatment - Tralokinumab 300 mg Q2W + optional TCS | Maintenance Treatment Period - Tralokinumab 300 mg Q2W | Maintenance Treatment Period - Tralokinumab 300 mg Q4W | Maintenance Treatment Period - Tralokinumab 150 mg Q2W |
|---|---|--|--|--|
| Subject group type                                  | Reporting group   | Reporting group  | Reporting group  | Reporting group  |
| Number of subjects analysed                         | 119   | 1  | 5  | 4  |
| Units: microgram/mL                                 |   |  |  |  |
| geometric mean (geometric coefficient of variation) | 8.27 (± 9.49)   | 7.26 (± 0)   | 2.40 (± 1.76)  | 3.02 (± 3.27)  |

| End point values                                    | Maintenance Treatment Period - Tralokinumab 150 mg Q4W |  |  |  |
|---|--|--|--|--|
| Subject group type                                  | Reporting group  |  |  |  |
| Number of subjects analysed                         | 3  |  |  |  |
| Units: microgram/mL                                 |  |  |  |  |
| geometric mean (geometric coefficient of variation) | 3.60 (± 2.12)  |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Timeframe for AE

Adverse event reporting additional description:

AE additional description

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

### Dictionary used

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

|                    |    |
|--------------------|----|
| Dictionary version | 20 |
|--------------------|----|

### Reporting groups

|                       |   |
|-----------------------|---|
| Reporting group title | Initial Treatment Period - Tralokinumab 300 Q2W |
|-----------------------|---|

Reporting group description: -

|                       |   |
|-----------------------|---|
| Reporting group title | Initial Treatment Period - Tralokinumab 150 Q2W |
|-----------------------|---|

Reporting group description: -

|                       |                                    |
|-----------------------|------------------------------------|
| Reporting group title | Initial Treatment Period - Placebo |
|-----------------------|------------------------------------|

Reporting group description: -

|                       |   |
|-----------------------|---|
| Reporting group title | Maintenance Treatment Period - Tralokinumab 300 Q2W |
|-----------------------|---|

Reporting group description: -

|                       |   |
|-----------------------|---|
| Reporting group title | Maintenance Treatment Period - Tralokinumab 300 Q4W |
|-----------------------|---|

Reporting group description: -

|                       |   |
|-----------------------|---|
| Reporting group title | Maintenance Treatment Period - Tralokinumab 150 Q2W |
|-----------------------|---|

Reporting group description: -

|                       |   |
|-----------------------|---|
| Reporting group title | Maintenance Treatment Period - Tralokinumab 150 Q4W |
|-----------------------|---|

Reporting group description: -

|                       |  |
|-----------------------|--|
| Reporting group title | Maintenance Treatment Period - Placebo |
|-----------------------|--|

Reporting group description: -

|                       |  |
|-----------------------|--|
| Reporting group title | Open-label Treatment - Tralokinumab 300 Q2W + optional TCS |
|-----------------------|--|

Reporting group description: -

|                       |                  |
|-----------------------|------------------|
| Reporting group title | Safety Follow-up |
|-----------------------|------------------|

Reporting group description: -

| <b>Serious adverse events</b>                     | Initial Treatment Period - Tralokinumab 300 Q2W | Initial Treatment Period - Tralokinumab 150 Q2W | Initial Treatment Period - Placebo |
|---|---|---|------------------------------------|
| Total subjects affected by serious adverse events |   |   |                                    |
| subjects affected / exposed                       | 1 / 97 (1.03%)                                  | 3 / 98 (3.06%)                                  | 5 / 94 (5.32%)                     |
| number of deaths (all causes)                     | 0   | 0   | 0                                  |
| number of deaths resulting from adverse events    | 0   | 0   | 0                                  |
| Injury, poisoning and procedural complications    |   |   |                                    |
| Concussion  |   |   |                                    |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 97 (0.00%) | 0 / 98 (0.00%) | 0 / 94 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Intentional overdose                            |                |                |                |
| subjects affected / exposed                     | 0 / 97 (0.00%) | 0 / 98 (0.00%) | 0 / 94 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Radius fracture                                 |                |                |                |
| subjects affected / exposed                     | 1 / 97 (1.03%) | 0 / 98 (0.00%) | 0 / 94 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Nervous system disorders                        |                |                |                |
| Cerebrovascular accident                        |                |                |                |
| subjects affected / exposed                     | 0 / 97 (0.00%) | 1 / 98 (1.02%) | 0 / 94 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Immune system disorders                         |                |                |                |
| Anaphylactic reaction                           |                |                |                |
| subjects affected / exposed                     | 0 / 97 (0.00%) | 0 / 98 (0.00%) | 1 / 94 (1.06%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastrointestinal disorders                      |                |                |                |
| Gastritis                                       |                |                |                |
| subjects affected / exposed                     | 0 / 97 (0.00%) | 0 / 98 (0.00%) | 0 / 94 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Respiratory, thoracic and mediastinal disorders |                |                |                |
| Acute respiratory failure                       |                |                |                |
| subjects affected / exposed                     | 0 / 97 (0.00%) | 0 / 98 (0.00%) | 1 / 94 (1.06%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Asthma  |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 97 (0.00%) | 0 / 98 (0.00%) | 1 / 94 (1.06%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Skin and subcutaneous tissue disorders          |                |                |                |
| Dermatitis atopic                               |                |                |                |
| subjects affected / exposed                     | 0 / 97 (0.00%) | 1 / 98 (1.02%) | 1 / 94 (1.06%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Psychiatric disorders                           |                |                |                |
| Anorexia nervosa                                |                |                |                |
| subjects affected / exposed                     | 0 / 97 (0.00%) | 0 / 98 (0.00%) | 0 / 94 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Obsessive-compulsive disorder                   |                |                |                |
| subjects affected / exposed                     | 0 / 97 (0.00%) | 0 / 98 (0.00%) | 0 / 94 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Suicidal ideation                               |                |                |                |
| subjects affected / exposed                     | 0 / 97 (0.00%) | 0 / 98 (0.00%) | 0 / 94 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Renal and urinary disorders                     |                |                |                |
| Renal injury                                    |                |                |                |
| subjects affected / exposed                     | 0 / 97 (0.00%) | 0 / 98 (0.00%) | 0 / 94 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Infections and infestations                     |                |                |                |
| Appendicitis perforated                         |                |                |                |
| subjects affected / exposed                     | 0 / 97 (0.00%) | 0 / 98 (0.00%) | 0 / 94 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cellulitis                                      |                |                |                |



|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 97 (0.00%) | 1 / 98 (1.02%) | 0 / 94 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Infectious mononucleosis                        |                |                |                |
| subjects affected / exposed                     | 0 / 97 (0.00%) | 0 / 98 (0.00%) | 1 / 94 (1.06%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

| <b>Serious adverse events</b>                     | Maintenance Treatment Period - Tralokinumab 300 Q2W | Maintenance Treatment Period - Tralokinumab 300 Q4W | Maintenance Treatment Period - Tralokinumab 150 Q2W |
|---|---|---|---|
| Total subjects affected by serious adverse events |   |   |   |
| subjects affected / exposed                       | 0 / 11 (0.00%)                                      | 0 / 13 (0.00%)                                      | 0 / 12 (0.00%)                                      |
| number of deaths (all causes)                     | 0   | 0   | 0   |
| number of deaths resulting from adverse events    | 0   | 0   | 0   |
| Injury, poisoning and procedural complications    |   |   |   |
| Concussion  |   |   |   |
| subjects affected / exposed                       | 0 / 11 (0.00%)                                      | 0 / 13 (0.00%)                                      | 0 / 12 (0.00%)                                      |
| occurrences causally related to treatment / all   | 0 / 0   | 0 / 0   | 0 / 0   |
| deaths causally related to treatment / all        | 0 / 0   | 0 / 0   | 0 / 0   |
| Intentional overdose                              |   |   |   |
| subjects affected / exposed                       | 0 / 11 (0.00%)                                      | 0 / 13 (0.00%)                                      | 0 / 12 (0.00%)                                      |
| occurrences causally related to treatment / all   | 0 / 0   | 0 / 0   | 0 / 0   |
| deaths causally related to treatment / all        | 0 / 0   | 0 / 0   | 0 / 0   |
| Radius fracture                                   |   |   |   |
| subjects affected / exposed                       | 0 / 11 (0.00%)                                      | 0 / 13 (0.00%)                                      | 0 / 12 (0.00%)                                      |
| occurrences causally related to treatment / all   | 0 / 0   | 0 / 0   | 0 / 0   |
| deaths causally related to treatment / all        | 0 / 0   | 0 / 0   | 0 / 0   |
| Nervous system disorders                          |   |   |   |
| Cerebrovascular accident                          |   |   |   |
| subjects affected / exposed                       | 0 / 11 (0.00%)                                      | 0 / 13 (0.00%)                                      | 0 / 12 (0.00%)                                      |
| occurrences causally related to treatment / all   | 0 / 0   | 0 / 0   | 0 / 0   |
| deaths causally related to treatment / all        | 0 / 0   | 0 / 0   | 0 / 0   |
| Immune system disorders                           |   |   |   |
| Anaphylactic reaction                             |   |   |   |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 11 (0.00%) | 0 / 13 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastrointestinal disorders                      |                |                |                |
| Gastritis                                       |                |                |                |
| subjects affected / exposed                     | 0 / 11 (0.00%) | 0 / 13 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Respiratory, thoracic and mediastinal disorders |                |                |                |
| Acute respiratory failure                       |                |                |                |
| subjects affected / exposed                     | 0 / 11 (0.00%) | 0 / 13 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Asthma  |                |                |                |
| subjects affected / exposed                     | 0 / 11 (0.00%) | 0 / 13 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Skin and subcutaneous tissue disorders          |                |                |                |
| Dermatitis atopic                               |                |                |                |
| subjects affected / exposed                     | 0 / 11 (0.00%) | 0 / 13 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Psychiatric disorders                           |                |                |                |
| Anorexia nervosa                                |                |                |                |
| subjects affected / exposed                     | 0 / 11 (0.00%) | 0 / 13 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Obsessive-compulsive disorder                   |                |                |                |
| subjects affected / exposed                     | 0 / 11 (0.00%) | 0 / 13 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Suicidal ideation                               |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 11 (0.00%) | 0 / 13 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Renal and urinary disorders                     |                |                |                |
| Renal injury                                    |                |                |                |
| subjects affected / exposed                     | 0 / 11 (0.00%) | 0 / 13 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Infections and infestations                     |                |                |                |
| Appendicitis perforated                         |                |                |                |
| subjects affected / exposed                     | 0 / 11 (0.00%) | 0 / 13 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cellulitis                                      |                |                |                |
| subjects affected / exposed                     | 0 / 11 (0.00%) | 0 / 13 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Infectious mononucleosis                        |                |                |                |
| subjects affected / exposed                     | 0 / 11 (0.00%) | 0 / 13 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

| <b>Serious adverse events</b>                     | Maintenance Treatment Period - Tralokinumab 150 Q4W | Maintenance Treatment Period - Placebo | Open-label Treatment - Tralokinumab 300 Q2W + optional TCS |
|---|---|--|--|
| Total subjects affected by serious adverse events |   |  |  |
| subjects affected / exposed                       | 0 / 14 (0.00%)                                      | 0 / 6 (0.00%)                          | 7 / 234 (2.99%)  |
| number of deaths (all causes)                     | 0   | 0                                      | 0  |
| number of deaths resulting from adverse events    | 0   | 0                                      | 0  |
| Injury, poisoning and procedural complications    |   |  |  |
| Concussion  |   |  |  |
| subjects affected / exposed                       | 0 / 14 (0.00%)                                      | 0 / 6 (0.00%)                          | 1 / 234 (0.43%)  |
| occurrences causally related to treatment / all   | 0 / 0   | 0 / 0                                  | 0 / 1  |
| deaths causally related to treatment / all        | 0 / 0   | 0 / 0                                  | 0 / 0  |
| Intentional overdose                              |   |  |  |

|   |                |               |                 |
|---|----------------|---------------|-----------------|
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 6 (0.00%) | 0 / 234 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0           |
| Radius fracture                                 |                |               |                 |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 6 (0.00%) | 0 / 234 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0           |
| Nervous system disorders                        |                |               |                 |
| Cerebrovascular accident                        |                |               |                 |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 6 (0.00%) | 0 / 234 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0           |
| Immune system disorders                         |                |               |                 |
| Anaphylactic reaction                           |                |               |                 |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 6 (0.00%) | 1 / 234 (0.43%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0           |
| Gastrointestinal disorders                      |                |               |                 |
| Gastritis                                       |                |               |                 |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 6 (0.00%) | 1 / 234 (0.43%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0           |
| Respiratory, thoracic and mediastinal disorders |                |               |                 |
| Acute respiratory failure                       |                |               |                 |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 6 (0.00%) | 0 / 234 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0           |
| Asthma  |                |               |                 |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 6 (0.00%) | 0 / 234 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0           |
| Skin and subcutaneous tissue disorders          |                |               |                 |
| Dermatitis atopic                               |                |               |                 |

|   |                |               |                 |
|---|----------------|---------------|-----------------|
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 6 (0.00%) | 0 / 234 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0           |
| <b>Psychiatric disorders</b>                    |                |               |                 |
| Anorexia nervosa                                |                |               |                 |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 6 (0.00%) | 1 / 234 (0.43%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0           |
| Obsessive-compulsive disorder                   |                |               |                 |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 6 (0.00%) | 1 / 234 (0.43%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0           |
| Suicidal ideation                               |                |               |                 |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 6 (0.00%) | 1 / 234 (0.43%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0           |
| <b>Renal and urinary disorders</b>              |                |               |                 |
| Renal injury                                    |                |               |                 |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 6 (0.00%) | 0 / 234 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0           |
| <b>Infections and infestations</b>              |                |               |                 |
| Appendicitis perforated                         |                |               |                 |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 6 (0.00%) | 1 / 234 (0.43%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0           |
| Cellulitis                                      |                |               |                 |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 6 (0.00%) | 0 / 234 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0           |
| Infectious mononucleosis                        |                |               |                 |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 6 (0.00%) | 0 / 234 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0           |

| <b>Serious adverse events</b>                     | Safety Follow-up |  |  |
|---|------------------|--|--|
| Total subjects affected by serious adverse events |                  |  |  |
| subjects affected / exposed                       | 3 / 234 (1.28%)  |  |  |
| number of deaths (all causes)                     | 0                |  |  |
| number of deaths resulting from adverse events    | 0                |  |  |
| Injury, poisoning and procedural complications    |                  |  |  |
| Concussion  |                  |  |  |
| subjects affected / exposed                       | 0 / 234 (0.00%)  |  |  |
| occurrences causally related to treatment / all   | 0 / 0            |  |  |
| deaths causally related to treatment / all        | 0 / 0            |  |  |
| Intentional overdose                              |                  |  |  |
| subjects affected / exposed                       | 1 / 234 (0.43%)  |  |  |
| occurrences causally related to treatment / all   | 0 / 1            |  |  |
| deaths causally related to treatment / all        | 0 / 0            |  |  |
| Radius fracture                                   |                  |  |  |
| subjects affected / exposed                       | 0 / 234 (0.00%)  |  |  |
| occurrences causally related to treatment / all   | 0 / 0            |  |  |
| deaths causally related to treatment / all        | 0 / 0            |  |  |
| Nervous system disorders                          |                  |  |  |
| Cerebrovascular accident                          |                  |  |  |
| subjects affected / exposed                       | 0 / 234 (0.00%)  |  |  |
| occurrences causally related to treatment / all   | 0 / 0            |  |  |
| deaths causally related to treatment / all        | 0 / 0            |  |  |
| Immune system disorders                           |                  |  |  |
| Anaphylactic reaction                             |                  |  |  |
| subjects affected / exposed                       | 1 / 234 (0.43%)  |  |  |
| occurrences causally related to treatment / all   | 0 / 1            |  |  |
| deaths causally related to treatment / all        | 0 / 0            |  |  |
| Gastrointestinal disorders                        |                  |  |  |
| Gastritis   |                  |  |  |
| subjects affected / exposed                       | 0 / 234 (0.00%)  |  |  |
| occurrences causally related to treatment / all   | 0 / 0            |  |  |
| deaths causally related to treatment / all        | 0 / 0            |  |  |
| Respiratory, thoracic and mediastinal disorders   |                  |  |  |

|  |                 |  |  |
|--|-----------------|--|--|
| Acute respiratory failure<br>subjects affected / exposed                                   | 0 / 234 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all   | 0 / 0           |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0           |  |  |
| Asthma<br>subjects affected / exposed  | 0 / 234 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all   | 0 / 0           |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0           |  |  |
| Skin and subcutaneous tissue disorders<br>Dermatitis atopic<br>subjects affected / exposed | 0 / 234 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all   | 0 / 0           |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0           |  |  |
| Psychiatric disorders<br>Anorexia nervosa<br>subjects affected / exposed                   | 0 / 234 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all   | 0 / 0           |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0           |  |  |
| Obsessive-compulsive disorder<br>subjects affected / exposed                               | 0 / 234 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all   | 0 / 0           |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0           |  |  |
| Suicidal ideation<br>subjects affected / exposed   | 0 / 234 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all   | 0 / 0           |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0           |  |  |
| Renal and urinary disorders<br>Renal injury<br>subjects affected / exposed                 | 1 / 234 (0.43%) |  |  |
| occurrences causally related to<br>treatment / all   | 0 / 1           |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0           |  |  |
| Infections and infestations<br>Appendicitis perforated                                     |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 0 / 234 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Cellulitis                                      |                 |  |  |
| subjects affected / exposed                     | 0 / 234 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Infectious mononucleosis                        |                 |  |  |
| subjects affected / exposed                     | 0 / 234 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |

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

| <b>Non-serious adverse events</b>                     | Initial Treatment Period - Tralokinumab 300 Q2W | Initial Treatment Period - Tralokinumab 150 Q2W | Initial Treatment Period - Placebo |
|---|---|---|------------------------------------|
| Total subjects affected by non-serious adverse events |   |   |                                    |
| subjects affected / exposed                           | 44 / 97 (45.36%)                                | 47 / 98 (47.96%)                                | 36 / 94 (38.30%)                   |
| Injury, poisoning and procedural complications        |   |   |                                    |
| Inappropriate schedule of drug administration         |   |   |                                    |
| subjects affected / exposed                           | 0 / 97 (0.00%)                                  | 1 / 98 (1.02%)                                  | 0 / 94 (0.00%)                     |
| occurrences (all)                                     | 0   | 1   | 0                                  |
| Procedural anxiety                                    |   |   |                                    |
| subjects affected / exposed                           | 0 / 97 (0.00%)                                  | 0 / 98 (0.00%)                                  | 0 / 94 (0.00%)                     |
| occurrences (all)                                     | 0   | 0   | 0                                  |
| Wrong drug administered                               |   |   |                                    |
| subjects affected / exposed                           | 1 / 97 (1.03%)                                  | 0 / 98 (0.00%)                                  | 0 / 94 (0.00%)                     |
| occurrences (all)                                     | 1   | 0   | 0                                  |
| Nervous system disorders                              |   |   |                                    |
| Headache  |   |   |                                    |
| subjects affected / exposed                           | 6 / 97 (6.19%)                                  | 5 / 98 (5.10%)                                  | 3 / 94 (3.19%)                     |
| occurrences (all)                                     | 6   | 5   | 3                                  |
| Migraine  |   |   |                                    |



|   |                     |                     |                     |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)        | 0 / 97 (0.00%)<br>0 | 0 / 98 (0.00%)<br>0 | 1 / 94 (1.06%)<br>1 |
| General disorders and administration<br>site conditions |                     |                     |                     |
| Fatigue   |                     |                     |                     |
| subjects affected / exposed                             | 0 / 97 (0.00%)      | 4 / 98 (4.08%)      | 4 / 94 (4.26%)      |
| occurrences (all)                                       | 0                   | 4                   | 4                   |
| Injection site reaction                                 |                     |                     |                     |
| subjects affected / exposed                             | 2 / 97 (2.06%)      | 6 / 98 (6.12%)      | 0 / 94 (0.00%)      |
| occurrences (all)                                       | 3                   | 9                   | 0                   |
| Malaise   |                     |                     |                     |
| subjects affected / exposed                             | 0 / 97 (0.00%)      | 1 / 98 (1.02%)      | 0 / 94 (0.00%)      |
| occurrences (all)                                       | 0                   | 2                   | 0                   |
| Immune system disorders                                 |                     |                     |                     |
| Hypersensitivity  |                     |                     |                     |
| subjects affected / exposed                             | 0 / 97 (0.00%)      | 0 / 98 (0.00%)      | 0 / 94 (0.00%)      |
| occurrences (all)                                       | 0                   | 0                   | 0                   |
| Eye disorders   |                     |                     |                     |
| Cataract  |                     |                     |                     |
| subjects affected / exposed                             | 0 / 97 (0.00%)      | 0 / 98 (0.00%)      | 0 / 94 (0.00%)      |
| occurrences (all)                                       | 0                   | 0                   | 0                   |
| Conjunctivitis allergic                                 |                     |                     |                     |
| subjects affected / exposed                             | 2 / 97 (2.06%)      | 2 / 98 (2.04%)      | 2 / 94 (2.13%)      |
| occurrences (all)                                       | 2                   | 2                   | 3                   |
| Respiratory, thoracic and mediastinal<br>disorders      |                     |                     |                     |
| Oropharyngeal pain                                      |                     |                     |                     |
| subjects affected / exposed                             | 4 / 97 (4.12%)      | 1 / 98 (1.02%)      | 3 / 94 (3.19%)      |
| occurrences (all)                                       | 4                   | 2                   | 3                   |
| Rhinorrhoea   |                     |                     |                     |
| subjects affected / exposed                             | 1 / 97 (1.03%)      | 0 / 98 (0.00%)      | 1 / 94 (1.06%)      |
| occurrences (all)                                       | 1                   | 0                   | 1                   |
| Skin and subcutaneous tissue disorders                  |                     |                     |                     |
| Acne  |                     |                     |                     |
| subjects affected / exposed                             | 3 / 97 (3.09%)      | 0 / 98 (0.00%)      | 4 / 94 (4.26%)      |
| occurrences (all)                                       | 3                   | 0                   | 4                   |
| Dermatitis allergic                                     |                     |                     |                     |

|  |                     |                        |                        |
|--|---------------------|------------------------|------------------------|
| subjects affected / exposed<br>occurrences (all)   | 0 / 97 (0.00%)<br>0 | 0 / 98 (0.00%)<br>0    | 0 / 94 (0.00%)<br>0    |
| Dermatitis atopic<br>subjects affected / exposed<br>occurrences (all)  | 7 / 97 (7.22%)<br>7 | 12 / 98 (12.24%)<br>16 | 11 / 94 (11.70%)<br>15 |
| Dermatitis contact<br>subjects affected / exposed<br>occurrences (all)   | 0 / 97 (0.00%)<br>0 | 1 / 98 (1.02%)<br>1    | 0 / 94 (0.00%)<br>0    |
| Psychiatric disorders<br>Abnormal behaviour<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 97 (0.00%)<br>0 | 0 / 98 (0.00%)<br>0    | 0 / 94 (0.00%)<br>0    |
| Attention deficit/hyperactivity<br>disorder<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 97 (0.00%)<br>0 | 0 / 98 (0.00%)<br>0    | 0 / 94 (0.00%)<br>0    |
| Endocrine disorders<br>Adrenal insufficiency<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 97 (0.00%)<br>0 | 0 / 98 (0.00%)<br>0    | 0 / 94 (0.00%)<br>0    |
| Musculoskeletal and connective tissue<br>disorders<br>Bursitis<br>subjects affected / exposed<br>occurrences (all) | 0 / 97 (0.00%)<br>0 | 0 / 98 (0.00%)<br>0    | 0 / 94 (0.00%)<br>0    |
| Infections and infestations<br>Acute sinusitis<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 97 (0.00%)<br>0 | 0 / 98 (0.00%)<br>0    | 1 / 94 (1.06%)<br>1    |
| Bacterial vaginosis<br>subjects affected / exposed<br>occurrences (all)  | 0 / 97 (0.00%)<br>0 | 0 / 98 (0.00%)<br>0    | 0 / 94 (0.00%)<br>0    |
| Conjunctivitis<br>subjects affected / exposed<br>occurrences (all)   | 0 / 97 (0.00%)<br>0 | 2 / 98 (2.04%)<br>2    | 0 / 94 (0.00%)<br>0    |
| Furuncle<br>subjects affected / exposed<br>occurrences (all)   | 0 / 97 (0.00%)<br>0 | 0 / 98 (0.00%)<br>0    | 0 / 94 (0.00%)<br>0    |

|   |                  |                  |                |
|---|------------------|------------------|----------------|
| Herpes zoster                           |                  |                  |                |
| subjects affected / exposed             | 0 / 97 (0.00%)   | 1 / 98 (1.02%)   | 0 / 94 (0.00%) |
| occurrences (all)                       | 0                | 1                | 0              |
| Infectious mononucleosis                |                  |                  |                |
| subjects affected / exposed             | 0 / 97 (0.00%)   | 0 / 98 (0.00%)   | 0 / 94 (0.00%) |
| occurrences (all)                       | 0                | 0                | 0              |
| Influenza                               |                  |                  |                |
| subjects affected / exposed             | 2 / 97 (2.06%)   | 2 / 98 (2.04%)   | 1 / 94 (1.06%) |
| occurrences (all)                       | 2                | 2                | 1              |
| Oral herpes                             |                  |                  |                |
| subjects affected / exposed             | 0 / 97 (0.00%)   | 0 / 98 (0.00%)   | 1 / 94 (1.06%) |
| occurrences (all)                       | 0                | 0                | 1              |
| Pharyngitis                             |                  |                  |                |
| subjects affected / exposed             | 0 / 97 (0.00%)   | 2 / 98 (2.04%)   | 4 / 94 (4.26%) |
| occurrences (all)                       | 0                | 2                | 4              |
| Upper respiratory tract infection       |                  |                  |                |
| subjects affected / exposed             | 11 / 97 (11.34%) | 8 / 98 (8.16%)   | 4 / 94 (4.26%) |
| occurrences (all)                       | 11               | 10               | 5              |
| Viral upper respiratory tract infection |                  |                  |                |
| subjects affected / exposed             | 12 / 97 (12.37%) | 19 / 98 (19.39%) | 8 / 94 (8.51%) |
| occurrences (all)                       | 16               | 22               | 10             |

| <b>Non-serious adverse events</b>                     | Maintenance<br>Treatment Period -<br>Tralokinumab 300<br>Q2W | Maintenance<br>Treatment Period -<br>Tralokinumab 300<br>Q4W | Maintenance<br>Treatment Period -<br>Tralokinumab 150<br>Q2W |
|---|--|--|--|
| Total subjects affected by non-serious adverse events |  |  |  |
| subjects affected / exposed                           | 7 / 11 (63.64%)  | 6 / 13 (46.15%)  | 7 / 12 (58.33%)  |
| Injury, poisoning and procedural complications        |  |  |  |
| Inappropriate schedule of drug administration         |  |  |  |
| subjects affected / exposed                           | 0 / 11 (0.00%)   | 1 / 13 (7.69%)   | 0 / 12 (0.00%)   |
| occurrences (all)                                     | 0  | 1  | 0  |
| Procedural anxiety                                    |  |  |  |
| subjects affected / exposed                           | 1 / 11 (9.09%)   | 0 / 13 (0.00%)   | 0 / 12 (0.00%)   |
| occurrences (all)                                     | 1  | 0  | 0  |
| Wrong drug administered                               |  |  |  |

|   |                     |                     |                     |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)        | 0 / 11 (0.00%)<br>0 | 0 / 13 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |
| Nervous system disorders                                |                     |                     |                     |
| Headache  |                     |                     |                     |
| subjects affected / exposed                             | 0 / 11 (0.00%)      | 0 / 13 (0.00%)      | 0 / 12 (0.00%)      |
| occurrences (all)                                       | 0                   | 0                   | 0                   |
| Migraine  |                     |                     |                     |
| subjects affected / exposed                             | 0 / 11 (0.00%)      | 0 / 13 (0.00%)      | 0 / 12 (0.00%)      |
| occurrences (all)                                       | 0                   | 0                   | 0                   |
| General disorders and administration<br>site conditions |                     |                     |                     |
| Fatigue   |                     |                     |                     |
| subjects affected / exposed                             | 1 / 11 (9.09%)      | 0 / 13 (0.00%)      | 0 / 12 (0.00%)      |
| occurrences (all)                                       | 1                   | 0                   | 0                   |
| Injection site reaction                                 |                     |                     |                     |
| subjects affected / exposed                             | 0 / 11 (0.00%)      | 1 / 13 (7.69%)      | 0 / 12 (0.00%)      |
| occurrences (all)                                       | 0                   | 1                   | 0                   |
| Malaise   |                     |                     |                     |
| subjects affected / exposed                             | 0 / 11 (0.00%)      | 0 / 13 (0.00%)      | 1 / 12 (8.33%)      |
| occurrences (all)                                       | 0                   | 0                   | 6                   |
| Immune system disorders                                 |                     |                     |                     |
| Hypersensitivity  |                     |                     |                     |
| subjects affected / exposed                             | 1 / 11 (9.09%)      | 0 / 13 (0.00%)      | 0 / 12 (0.00%)      |
| occurrences (all)                                       | 1                   | 0                   | 0                   |
| Eye disorders   |                     |                     |                     |
| Cataract  |                     |                     |                     |
| subjects affected / exposed                             | 1 / 11 (9.09%)      | 0 / 13 (0.00%)      | 0 / 12 (0.00%)      |
| occurrences (all)                                       | 1                   | 0                   | 0                   |
| Conjunctivitis allergic                                 |                     |                     |                     |
| subjects affected / exposed                             | 0 / 11 (0.00%)      | 0 / 13 (0.00%)      | 1 / 12 (8.33%)      |
| occurrences (all)                                       | 0                   | 0                   | 1                   |
| Respiratory, thoracic and mediastinal<br>disorders      |                     |                     |                     |
| Oropharyngeal pain                                      |                     |                     |                     |
| subjects affected / exposed                             | 0 / 11 (0.00%)      | 1 / 13 (7.69%)      | 0 / 12 (0.00%)      |
| occurrences (all)                                       | 0                   | 1                   | 0                   |
| Rhinorrhoea   |                     |                     |                     |

|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 11 (0.00%)<br>0 | 1 / 13 (7.69%)<br>1 | 0 / 12 (0.00%)<br>0 |
| Skin and subcutaneous tissue disorders           |                     |                     |                     |
| Acne   |                     |                     |                     |
| subjects affected / exposed                      | 0 / 11 (0.00%)      | 0 / 13 (0.00%)      | 1 / 12 (8.33%)      |
| occurrences (all)                                | 0                   | 0                   | 1                   |
| Dermatitis allergic                              |                     |                     |                     |
| subjects affected / exposed                      | 0 / 11 (0.00%)      | 0 / 13 (0.00%)      | 1 / 12 (8.33%)      |
| occurrences (all)                                | 0                   | 0                   | 1                   |
| Dermatitis atopic                                |                     |                     |                     |
| subjects affected / exposed                      | 0 / 11 (0.00%)      | 0 / 13 (0.00%)      | 1 / 12 (8.33%)      |
| occurrences (all)                                | 0                   | 0                   | 1                   |
| Dermatitis contact                               |                     |                     |                     |
| subjects affected / exposed                      | 0 / 11 (0.00%)      | 0 / 13 (0.00%)      | 1 / 12 (8.33%)      |
| occurrences (all)                                | 0                   | 0                   | 1                   |
| Psychiatric disorders                            |                     |                     |                     |
| Abnormal behaviour                               |                     |                     |                     |
| subjects affected / exposed                      | 1 / 11 (9.09%)      | 0 / 13 (0.00%)      | 0 / 12 (0.00%)      |
| occurrences (all)                                | 1                   | 0                   | 0                   |
| Attention deficit/hyperactivity disorder         |                     |                     |                     |
| subjects affected / exposed                      | 0 / 11 (0.00%)      | 0 / 13 (0.00%)      | 0 / 12 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Endocrine disorders                              |                     |                     |                     |
| Adrenal insufficiency                            |                     |                     |                     |
| subjects affected / exposed                      | 1 / 11 (9.09%)      | 0 / 13 (0.00%)      | 0 / 12 (0.00%)      |
| occurrences (all)                                | 1                   | 0                   | 0                   |
| Musculoskeletal and connective tissue disorders  |                     |                     |                     |
| Bursitis   |                     |                     |                     |
| subjects affected / exposed                      | 0 / 11 (0.00%)      | 0 / 13 (0.00%)      | 0 / 12 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Infections and infestations                      |                     |                     |                     |
| Acute sinusitis                                  |                     |                     |                     |
| subjects affected / exposed                      | 0 / 11 (0.00%)      | 0 / 13 (0.00%)      | 1 / 12 (8.33%)      |
| occurrences (all)                                | 0                   | 0                   | 2                   |
| Bacterial vaginosis                              |                     |                     |                     |

|   |                 |                |                 |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed             | 0 / 11 (0.00%)  | 1 / 13 (7.69%) | 0 / 12 (0.00%)  |
| occurrences (all)                       | 0               | 1              | 0               |
| Conjunctivitis                          |                 |                |                 |
| subjects affected / exposed             | 0 / 11 (0.00%)  | 1 / 13 (7.69%) | 0 / 12 (0.00%)  |
| occurrences (all)                       | 0               | 1              | 0               |
| Furuncle                                |                 |                |                 |
| subjects affected / exposed             | 0 / 11 (0.00%)  | 0 / 13 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)                       | 0               | 0              | 0               |
| Herpes zoster                           |                 |                |                 |
| subjects affected / exposed             | 0 / 11 (0.00%)  | 0 / 13 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)                       | 0               | 0              | 0               |
| Infectious mononucleosis                |                 |                |                 |
| subjects affected / exposed             | 0 / 11 (0.00%)  | 0 / 13 (0.00%) | 1 / 12 (8.33%)  |
| occurrences (all)                       | 0               | 0              | 1               |
| Influenza                               |                 |                |                 |
| subjects affected / exposed             | 2 / 11 (18.18%) | 0 / 13 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)                       | 2               | 0              | 0               |
| Oral herpes                             |                 |                |                 |
| subjects affected / exposed             | 1 / 11 (9.09%)  | 0 / 13 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)                       | 1               | 0              | 0               |
| Pharyngitis                             |                 |                |                 |
| subjects affected / exposed             | 0 / 11 (0.00%)  | 0 / 13 (0.00%) | 3 / 12 (25.00%) |
| occurrences (all)                       | 0               | 0              | 4               |
| Upper respiratory tract infection       |                 |                |                 |
| subjects affected / exposed             | 2 / 11 (18.18%) | 0 / 13 (0.00%) | 1 / 12 (8.33%)  |
| occurrences (all)                       | 2               | 0              | 2               |
| Viral upper respiratory tract infection |                 |                |                 |
| subjects affected / exposed             | 2 / 11 (18.18%) | 1 / 13 (7.69%) | 1 / 12 (8.33%)  |
| occurrences (all)                       | 2               | 1              | 2               |

| <b>Non-serious adverse events</b>                        | Maintenance<br>Treatment Period -<br>Tralokinumab 150<br>Q4W | Maintenance<br>Treatment Period -<br>Placebo | Open-label<br>Treatment -<br>Tralokinumab 300<br>Q2W + optional TCS |
|--|--|--|---|
| Total subjects affected by non-serious<br>adverse events |  |  |   |
| subjects affected / exposed                              | 8 / 14 (57.14%)  | 4 / 6 (66.67%)                               | 100 / 234 (42.74%)  |
| Injury, poisoning and procedural<br>complications        |  |  |   |

|   |                     |                     |                        |
|---|---------------------|---------------------|------------------------|
| Inappropriate schedule of drug administration<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 14 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  | 2 / 234 (0.85%)<br>2   |
| Procedural anxiety<br>subjects affected / exposed<br>occurrences (all)  | 0 / 14 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  | 1 / 234 (0.43%)<br>1   |
| Wrong drug administered<br>subjects affected / exposed<br>occurrences (all)   | 0 / 14 (0.00%)<br>0 | 1 / 6 (16.67%)<br>1 | 0 / 234 (0.00%)<br>0   |
| Nervous system disorders<br>Headache<br>subjects affected / exposed<br>occurrences (all)                            | 0 / 14 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  | 12 / 234 (5.13%)<br>17 |
| Migraine<br>subjects affected / exposed<br>occurrences (all)  | 1 / 14 (7.14%)<br>1 | 0 / 6 (0.00%)<br>0  | 2 / 234 (0.85%)<br>2   |
| General disorders and administration site conditions<br>Fatigue<br>subjects affected / exposed<br>occurrences (all) | 0 / 14 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  | 0 / 234 (0.00%)<br>0   |
| Injection site reaction<br>subjects affected / exposed<br>occurrences (all)   | 0 / 14 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  | 10 / 234 (4.27%)<br>16 |
| Malaise<br>subjects affected / exposed<br>occurrences (all)   | 0 / 14 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  | 2 / 234 (0.85%)<br>12  |
| Immune system disorders<br>Hypersensitivity<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 14 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  | 1 / 234 (0.43%)<br>1   |
| Eye disorders<br>Cataract<br>subjects affected / exposed<br>occurrences (all)                                       | 0 / 14 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  | 0 / 234 (0.00%)<br>0   |
| Conjunctivitis allergic   |                     |                     |                        |

|  |                      |                     |                        |
|--|----------------------|---------------------|------------------------|
| subjects affected / exposed<br>occurrences (all)   | 1 / 14 (7.14%)<br>1  | 0 / 6 (0.00%)<br>0  | 4 / 234 (1.71%)<br>4   |
| Respiratory, thoracic and mediastinal disorders  |                      |                     |                        |
| Oropharyngeal pain<br>subjects affected / exposed<br>occurrences (all)                       | 1 / 14 (7.14%)<br>1  | 0 / 6 (0.00%)<br>0  | 4 / 234 (1.71%)<br>4   |
| Rhinorrhoea<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 14 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 2 / 234 (0.85%)<br>2   |
| Skin and subcutaneous tissue disorders   |                      |                     |                        |
| Acne<br>subjects affected / exposed<br>occurrences (all)                                     | 1 / 14 (7.14%)<br>1  | 0 / 6 (0.00%)<br>0  | 3 / 234 (1.28%)<br>3   |
| Dermatitis allergic<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 14 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 234 (0.00%)<br>0   |
| Dermatitis atopic<br>subjects affected / exposed<br>occurrences (all)                        | 2 / 14 (14.29%)<br>2 | 1 / 6 (16.67%)<br>1 | 19 / 234 (8.12%)<br>26 |
| Dermatitis contact<br>subjects affected / exposed<br>occurrences (all)                       | 0 / 14 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 1 / 234 (0.43%)<br>1   |
| Psychiatric disorders  |                      |                     |                        |
| Abnormal behaviour<br>subjects affected / exposed<br>occurrences (all)                       | 0 / 14 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 234 (0.00%)<br>0   |
| Attention deficit/hyperactivity disorder<br>subjects affected / exposed<br>occurrences (all) | 1 / 14 (7.14%)<br>1  | 0 / 6 (0.00%)<br>0  | 0 / 234 (0.00%)<br>0   |
| Endocrine disorders  |                      |                     |                        |
| Adrenal insufficiency<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 14 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 234 (0.00%)<br>0   |
| Musculoskeletal and connective tissue disorders  |                      |                     |                        |



|   |                |                |                   |
|---|----------------|----------------|-------------------|
| Bursitis                                |                |                |                   |
| subjects affected / exposed             | 1 / 14 (7.14%) | 0 / 6 (0.00%)  | 1 / 234 (0.43%)   |
| occurrences (all)                       | 1              | 0              | 1                 |
| Infections and infestations             |                |                |                   |
| Acute sinusitis                         |                |                |                   |
| subjects affected / exposed             | 0 / 14 (0.00%) | 0 / 6 (0.00%)  | 0 / 234 (0.00%)   |
| occurrences (all)                       | 0              | 0              | 0                 |
| Bacterial vaginosis                     |                |                |                   |
| subjects affected / exposed             | 0 / 14 (0.00%) | 0 / 6 (0.00%)  | 0 / 234 (0.00%)   |
| occurrences (all)                       | 0              | 0              | 0                 |
| Conjunctivitis                          |                |                |                   |
| subjects affected / exposed             | 0 / 14 (0.00%) | 0 / 6 (0.00%)  | 4 / 234 (1.71%)   |
| occurrences (all)                       | 0              | 0              | 6                 |
| Furuncle                                |                |                |                   |
| subjects affected / exposed             | 0 / 14 (0.00%) | 1 / 6 (16.67%) | 0 / 234 (0.00%)   |
| occurrences (all)                       | 0              | 1              | 0                 |
| Herpes zoster                           |                |                |                   |
| subjects affected / exposed             | 0 / 14 (0.00%) | 1 / 6 (16.67%) | 1 / 234 (0.43%)   |
| occurrences (all)                       | 0              | 1              | 1                 |
| Infectious mononucleosis                |                |                |                   |
| subjects affected / exposed             | 0 / 14 (0.00%) | 0 / 6 (0.00%)  | 0 / 234 (0.00%)   |
| occurrences (all)                       | 0              | 0              | 0                 |
| Influenza                               |                |                |                   |
| subjects affected / exposed             | 0 / 14 (0.00%) | 0 / 6 (0.00%)  | 3 / 234 (1.28%)   |
| occurrences (all)                       | 0              | 0              | 3                 |
| Oral herpes                             |                |                |                   |
| subjects affected / exposed             | 0 / 14 (0.00%) | 0 / 6 (0.00%)  | 6 / 234 (2.56%)   |
| occurrences (all)                       | 0              | 0              | 7                 |
| Pharyngitis                             |                |                |                   |
| subjects affected / exposed             | 0 / 14 (0.00%) | 0 / 6 (0.00%)  | 6 / 234 (2.56%)   |
| occurrences (all)                       | 0              | 0              | 6                 |
| Upper respiratory tract infection       |                |                |                   |
| subjects affected / exposed             | 1 / 14 (7.14%) | 0 / 6 (0.00%)  | 25 / 234 (10.68%) |
| occurrences (all)                       | 1              | 0              | 34                |
| Viral upper respiratory tract infection |                |                |                   |

|                             |                |               |                   |
|-----------------------------|----------------|---------------|-------------------|
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 6 (0.00%) | 44 / 234 (18.80%) |
| occurrences (all)           | 1              | 0             | 60                |

| <b>Non-serious adverse events</b>                     | Safety Follow-up |  |  |
|---|------------------|--|--|
| Total subjects affected by non-serious adverse events |                  |  |  |
| subjects affected / exposed                           | 16 / 234 (6.84%) |  |  |
| Injury, poisoning and procedural complications        |                  |  |  |
| Inappropriate schedule of drug administration         |                  |  |  |
| subjects affected / exposed                           | 0 / 234 (0.00%)  |  |  |
| occurrences (all)                                     | 0                |  |  |
| Procedural anxiety                                    |                  |  |  |
| subjects affected / exposed                           | 0 / 234 (0.00%)  |  |  |
| occurrences (all)                                     | 0                |  |  |
| Wrong drug administered                               |                  |  |  |
| subjects affected / exposed                           | 0 / 234 (0.00%)  |  |  |
| occurrences (all)                                     | 0                |  |  |
| Nervous system disorders                              |                  |  |  |
| Headache  |                  |  |  |
| subjects affected / exposed                           | 0 / 234 (0.00%)  |  |  |
| occurrences (all)                                     | 0                |  |  |
| Migraine  |                  |  |  |
| subjects affected / exposed                           | 0 / 234 (0.00%)  |  |  |
| occurrences (all)                                     | 0                |  |  |
| General disorders and administration site conditions  |                  |  |  |
| Fatigue   |                  |  |  |
| subjects affected / exposed                           | 0 / 234 (0.00%)  |  |  |
| occurrences (all)                                     | 0                |  |  |
| Injection site reaction                               |                  |  |  |
| subjects affected / exposed                           | 0 / 234 (0.00%)  |  |  |
| occurrences (all)                                     | 0                |  |  |
| Malaise   |                  |  |  |
| subjects affected / exposed                           | 0 / 234 (0.00%)  |  |  |
| occurrences (all)                                     | 0                |  |  |
| Immune system disorders                               |                  |  |  |
| Hypersensitivity                                      |                  |  |  |

|  |                      |  |  |
|--|----------------------|--|--|
| subjects affected / exposed<br>occurrences (all) | 0 / 234 (0.00%)<br>0 |  |  |
| Eye disorders                                    |                      |  |  |
| Cataract   |                      |  |  |
| subjects affected / exposed                      | 0 / 234 (0.00%)      |  |  |
| occurrences (all)                                | 0                    |  |  |
| Conjunctivitis allergic                          |                      |  |  |
| subjects affected / exposed                      | 0 / 234 (0.00%)      |  |  |
| occurrences (all)                                | 0                    |  |  |
| Respiratory, thoracic and mediastinal disorders  |                      |  |  |
| Oropharyngeal pain                               |                      |  |  |
| subjects affected / exposed                      | 0 / 234 (0.00%)      |  |  |
| occurrences (all)                                | 0                    |  |  |
| Rhinorrhoea                                      |                      |  |  |
| subjects affected / exposed                      | 0 / 234 (0.00%)      |  |  |
| occurrences (all)                                | 0                    |  |  |
| Skin and subcutaneous tissue disorders           |                      |  |  |
| Acne   |                      |  |  |
| subjects affected / exposed                      | 1 / 234 (0.43%)      |  |  |
| occurrences (all)                                | 1                    |  |  |
| Dermatitis allergic                              |                      |  |  |
| subjects affected / exposed                      | 0 / 234 (0.00%)      |  |  |
| occurrences (all)                                | 0                    |  |  |
| Dermatitis atopic                                |                      |  |  |
| subjects affected / exposed                      | 8 / 234 (3.42%)      |  |  |
| occurrences (all)                                | 9                    |  |  |
| Dermatitis contact                               |                      |  |  |
| subjects affected / exposed                      | 0 / 234 (0.00%)      |  |  |
| occurrences (all)                                | 0                    |  |  |
| Psychiatric disorders                            |                      |  |  |
| Abnormal behaviour                               |                      |  |  |
| subjects affected / exposed                      | 0 / 234 (0.00%)      |  |  |
| occurrences (all)                                | 0                    |  |  |
| Attention deficit/hyperactivity disorder         |                      |  |  |
| subjects affected / exposed                      | 0 / 234 (0.00%)      |  |  |
| occurrences (all)                                | 0                    |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| Endocrine disorders                             |                 |  |  |
| Adrenal insufficiency                           |                 |  |  |
| subjects affected / exposed                     | 0 / 234 (0.00%) |  |  |
| occurrences (all)                               | 0               |  |  |
| Musculoskeletal and connective tissue disorders |                 |  |  |
| Bursitis  |                 |  |  |
| subjects affected / exposed                     | 0 / 234 (0.00%) |  |  |
| occurrences (all)                               | 0               |  |  |
| Infections and infestations                     |                 |  |  |
| Acute sinusitis                                 |                 |  |  |
| subjects affected / exposed                     | 0 / 234 (0.00%) |  |  |
| occurrences (all)                               | 0               |  |  |
| Bacterial vaginosis                             |                 |  |  |
| subjects affected / exposed                     | 0 / 234 (0.00%) |  |  |
| occurrences (all)                               | 0               |  |  |
| Conjunctivitis                                  |                 |  |  |
| subjects affected / exposed                     | 2 / 234 (0.85%) |  |  |
| occurrences (all)                               | 2               |  |  |
| Furuncle  |                 |  |  |
| subjects affected / exposed                     | 0 / 234 (0.00%) |  |  |
| occurrences (all)                               | 0               |  |  |
| Herpes zoster                                   |                 |  |  |
| subjects affected / exposed                     | 0 / 234 (0.00%) |  |  |
| occurrences (all)                               | 0               |  |  |
| Infectious mononucleosis                        |                 |  |  |
| subjects affected / exposed                     | 0 / 234 (0.00%) |  |  |
| occurrences (all)                               | 0               |  |  |
| Influenza                                       |                 |  |  |
| subjects affected / exposed                     | 2 / 234 (0.85%) |  |  |
| occurrences (all)                               | 2               |  |  |
| Oral herpes                                     |                 |  |  |
| subjects affected / exposed                     | 0 / 234 (0.00%) |  |  |
| occurrences (all)                               | 0               |  |  |
| Pharyngitis                                     |                 |  |  |
| subjects affected / exposed                     | 1 / 234 (0.43%) |  |  |
| occurrences (all)                               | 1               |  |  |

|   |                      |  |  |
|---|----------------------|--|--|
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)       | 3 / 234 (1.28%)<br>3 |  |  |
| Viral upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 1 / 234 (0.43%)<br>2 |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment  |
|------------------|--|
| 12 June 2018     | The main reason for this amendment was extension of the post-IMP observation period at the first 3 visits in the initial treatment period and in the in open label treatment period from 30 minutes to 2 hours.  |
| 06 February 2020 | The main reason for this amendment was introduction of the possibility for eligible subjects in selected countries to continue in a long-term extension trial (ECZTEND). Subjects could enter ECZTEND from completion of the treatment period and up to 26 weeks from their last IMP injection in the present trial to the first IMP injection in ECZTEND. |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported