



## Clinical trial results:

**A randomised, double-blind, placebo-controlled, parallel-group, multi-centre, phase 3 trial investigating the efficacy, safety, and tolerability of tralokinumab administered in combination with topical corticosteroids to adult subjects with severe atopic dermatitis who are not adequately controlled with or have contraindications to oral cyclosporine A**

### Summary

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2018-000747-76    |
| Trial protocol           | FR DE BE GB ES CZ |
| Global end of trial date | 28 September 2020 |

### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v1              |
| This version publication date  | 13 October 2021 |
| First version publication date | 13 October 2021 |

### Trial information

#### Trial identification

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | LP0162-1346 |
|-----------------------|-------------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03761537 |
| 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, 0045 44945888, disclosure@leo-pharma.com |
| Scientific contact           | Clinical Disclosure Specialist, Leo Pharma A/S, 0045 44945888, disclosure@leo-pharma.com |

Notes:

### Paediatric regulatory details

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

Notes:

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**Results analysis stage**

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|  |                   |
|--|-------------------|
| Analysis stage                                       | Final             |
| Date of interim/final analysis                       | 04 March 2021     |
| Is this the analysis of the primary completion data? | Yes               |
| Primary completion date                              | 21 April 2020     |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 28 September 2020 |
| Was the trial ended prematurely?                     | No                |

Notes:

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**General information about the trial**

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Main objective of the trial:

To demonstrate that tralokinumab in combination with topical corticosteroids (TCS) is superior to placebo in combination with TCS in treating severe Atopic Dermatitis (AD) in subjects who are not adequately controlled with or have contraindications to oral cyclosporine A (CSA).

Protection of trial subjects:

Subjects were asked to consent that their personal data were recorded, collected, processed and could be transferred to EU and non-EU countries in accordance with any national legislation regulating privacy and data protection

Background therapy:

All subjects were required to use an emollient twice daily (or more as needed) for at least 14 days before randomisation and to continue this treatment throughout the trial until the end of the safety follow-up period.

Evidence for comparator: -

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

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Poland: 77         |
| Country: Number of subjects enrolled | Spain: 49          |
| Country: Number of subjects enrolled | United Kingdom: 14 |
| Country: Number of subjects enrolled | Belgium: 52        |
| Country: Number of subjects enrolled | Czechia: 26        |
| Country: Number of subjects enrolled | France: 19         |
| Country: Number of subjects enrolled | Germany: 40        |
| Worldwide total number of subjects   | 277                |
| EEA total number of subjects         | 263                |

Notes:

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**Subjects enrolled per age group**

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|   |   |
|---|---|
| In utero                                  | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |

|  |     |
|--|-----|
| Newborns (0-27 days)                     | 0   |
| Infants and toddlers (28 days-23 months) | 0   |
| Children (2-11 years)                    | 0   |
| Adolescents (12-17 years)                | 0   |
| Adults (18-64 years)                     | 265 |
| From 65 to 84 years                      | 12  |
| 85 years and over                        | 0   |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

After the participant gave informed consent, they went through a 2- to 6-week screening period. Eligibility was assessed at the (first) screening visit and on Day 0 (hereinafter "baseline") prior to randomisation.

### Period 1

|                              |   |
|------------------------------|---|
| Period 1 title               | 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:

Subjects were randomised to treatment at Day 0 (Visit 3, baseline). This was a double-blinded trial where tralokinumab and placebo were visually distinct from each other and not matched for viscosity. They were therefore handled and administered by a qualified unblinded health care professional (trained site staff) 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>             | Tralokinumab + TCS |

Arm description:

Subjects in the treatment period (Week 0 to Week 26) treated with tralokinumab every second week (Q2W) and topical corticosteroid (TCS) as needed.

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

Dosage and administration details:

Subjects received a loading dose of 600 mg tralokinumab at Day 0 (Visit 3, baseline) followed by a dose of 300 mg tralokinumab every second week (Q2W) from Week 2. The last administration of IMP occurred at Week 24. The injections were administered in the subcutaneous tissue of the upper arm, anterior thigh, or abdomen.

|                  |               |
|------------------|---------------|
| <b>Arm title</b> | Placebo + TCS |
|------------------|---------------|

Arm description:

Subjects in the treatment period (Week 0 to Week 26) treated with placebo every second week (Q2W) and topical corticosteroid (TCS) as needed.

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

Dosage and administration details:

Subjects received a loading dose of placebo at Day 0 (Visit 3, baseline) followed by a dose of placebo every second week (Q2W) from Week 2. The last administration of IMP occurred at Week 24. The injections were administered in the subcutaneous tissue of the upper arm, anterior thigh, or abdomen.

| <b>Number of subjects in period 1</b> | Tralokinumab + TCS | Placebo + TCS |
|---------------------------------------|--------------------|---------------|
| Started                               | 140                | 137           |
| Completed                             | 125                | 120           |
| Not completed                         | 15                 | 17            |
| Permanently discontinued IMP          | 13                 | 17            |
| Subject not dosed                     | 2                  | -             |

## Period 2

|                              |                         |
|------------------------------|-------------------------|
| Period 2 title               | Safety follow-up period |
| Is this the baseline period? | No                      |
| Allocation method            | Not applicable          |
| Blinding used                | Not blinded             |

Blinding implementation details:

No treatment was administered to the subjects during the safety follow-up period and therefore no randomisation took place. However, double blinding was maintained throughout the period.

## Arms

|                              |                                |
|------------------------------|--------------------------------|
| Are arms mutually exclusive? | Yes                            |
| <b>Arm title</b>             | Safety follow-up, tralokinumab |

Arm description:

Subjects who spent any amount of time in the safety follow-up period, independently of the treatment(s) received before. No treatment was administered to the subjects during this period. Eligible subjects who completed treatment could transfer to a long-term extension trial (conducted under a separate protocol) at any time during the safety follow-up period.

|   |                           |
|---|---------------------------|
| Arm type  | No intervention           |
| No investigational medicinal product assigned in this arm |                           |
| <b>Arm title</b>  | Safety follow-up, placebo |

Arm description:

Subjects who spent any amount of time in the safety follow-up period, independently of the treatment(s) received before. No treatment was administered to the subjects during this period. Eligible subjects who completed treatment could transfer to a long-term extension trial (conducted under a separate protocol) at any time during the safety follow-up period

|   |                 |
|---|-----------------|
| Arm type  | No intervention |
| No investigational medicinal product assigned in this arm |                 |

| Number of subjects in period 2 <sup>[1]</sup> | Safety follow-up, tralokinumab | Safety follow-up, placebo |
|---|--------------------------------|---------------------------|
|   |                                |                           |
| Started                                       | 75                             | 83                        |
| Completed                                     | 9                              | 17                        |
| Not completed                                 | 66                             | 66                        |
| Withdrew from trial                           | 1                              | 6                         |
| COVID-19                                      | 1                              | 3                         |
| Other   | 1                              | 1                         |
| Lost to follow-up                             | -                              | 1                         |
| Transferred to other trial                    | 63                             | 55                        |

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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: A proportion of subjects completing the treatment period were immediately transferred to an extension trial (ECZTEND trial) and thus, did not attend the safety follow-up period.

## Baseline characteristics

### Reporting groups

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | Tralokinumab + TCS |
|-----------------------|--------------------|

Reporting group description:

Subjects in the treatment period (Week 0 to Week 26) treated with tralokinumab every second week (Q2W) and topical corticosteroid (TCS) as needed.

|                       |               |
|-----------------------|---------------|
| Reporting group title | Placebo + TCS |
|-----------------------|---------------|

Reporting group description:

Subjects in the treatment period (Week 0 to Week 26) treated with placebo every second week (Q2W) and topical corticosteroid (TCS) as needed.

| Reporting group values  | Tralokinumab + TCS | Placebo + TCS | Total |
|---|--------------------|---------------|-------|
| Number of subjects  | 140                | 137           | 277   |
| Age categorical   |                    |               |       |
| Units: Subjects   |                    |               |       |
| Adults (18-64 years)  | 134                | 131           | 265   |
| From 65-84 years  | 6                  | 6             | 12    |
| Age continuous  |                    |               |       |
| Units: years  |                    |               |       |
| median  | 33.08              | 34.0          |       |
| inter-quartile range (Q1-Q3)  | 25.5 to 47.0       | 26.0 to 45.0  | -     |
| Gender categorical  |                    |               |       |
| Units: Subjects   |                    |               |       |
| Female  | 58                 | 54            | 112   |
| Male  | 82                 | 83            | 165   |
| Ethnicity   |                    |               |       |
| Units: Subjects   |                    |               |       |
| Hispanic or Latino  | 6                  | 4             | 10    |
| Not hispanic or latino  | 134                | 133           | 267   |
| Unknown or not reported   | 0                  | 0             | 0     |
| Race  |                    |               |       |
| Units: Subjects   |                    |               |       |
| Asian   | 0                  | 1             | 1     |
| Native Hawaiian or other pacific islander   | 1                  | 0             | 1     |
| Black or african american   | 0                  | 1             | 1     |
| White   | 137                | 135           | 272   |
| Unknown or not reported   | 2                  | 0             | 2     |
| Age at onset of atopic dermatitis   |                    |               |       |
| Units: Years  |                    |               |       |
| median  | 2.5                | 3.0           |       |
| inter-quartile range (Q1-Q3)  | 1.0 to 12.5        | 1.0 to 17.0   | -     |
| Body surface area with atopic dermatitis  |                    |               |       |
| Units: Percentage affected  |                    |               |       |
| median  | 52.0               | 52.0          |       |
| inter-quartile range (Q1-Q3)  | 36.5 to 70.0       | 35.0 to 70.0  | -     |
| Eczema area and severity index (EASI)   |                    |               |       |
| Measure Description: EASI is used to evaluate the extent and severity of atopic dermatitis. It is a composite |                    |               |       |

|  |              |               |   |
|--|--------------|---------------|---|
| score ranging from 0 to 72 with a higher score indicating a more extensive and/or severe condition.  |              |               |   |
| Measure Analysis Population Description: The number of participants analysed is different from the number of participants randomised due to missing data. Tralokinumab + TCS = 138 participants; Placebo + TCS = 137 participants.   |              |               |   |
| Units: Units on a scale  |              |               |   |
| median   | 28.6         | 29.1          |   |
| inter-quartile range (Q1-Q3)   | 22.4 to 38.0 | 22.8 to 40.15 | - |
| Duration of atopic dermatitis  |              |               |   |
| Units: Years   |              |               |   |
| median   | 26.0         | 25.0          |   |
| inter-quartile range (Q1-Q3)   | 18.0 to 35.0 | 17.0 to 34.0  | - |
| Scoring of Atopic Dermatitis   |              |               |   |
| Measure Description: SCORAD is used to evaluate the extent and severity of atopic dermatitis as well as subjective symptoms. The score ranges from 0 to 103 with a higher score indicating a more extensive and/or severe condition.   |              |               |   |
| Measure Analysis Population Description: The number of participants analysed is different from the number of participants randomised due to missing data. Tralokinumab + TCS = 138 participants; Placebo + TCS = 137 participants.   |              |               |   |
| Units: Units on a scale  |              |               |   |
| median   | 69.2         | 68.9          |   |
| inter-quartile range (Q1-Q3)   | 61.5 to 76.5 | 61.2 to 81.0  | - |
| Dermatology Life Quality Index (DLQI)  |              |               |   |
| Measure Description: DLQI is used by the participant to evaluate the impact of their condition on 10 different aspects of health-related quality of life (HRQoL) over the last week. Each item is scored on a 4-point Likert scale ranging from 0 (not at all/not relevant) to 3 (very much). The total score which is the sum of the 10 items ranges from 0 to 30, with a higher score indicating a poorer HRQoL. |              |               |   |
| The number of participants analysed is different from the number of participants randomised due to missing data. Tralokinumab + TCS = 137 subjects; Placebo + TCS = 134 subjects   |              |               |   |
| Units: Units on a scale  |              |               |   |
| median   | 16           | 16            |   |
| inter-quartile range (Q1-Q3)   | 11 to 21     | 11 to 21      | - |
| Worst Daily Pruritis numeric rating scale (NRS), weekly average  |              |               |   |
| Measure Description: Worst Daily Pruritus NRS is used by the participant to evaluate their worst itch severity over the past 24 hours. The score ranges from 0 ('no itch') to 10 ('worst itch imaginable').  |              |               |   |
| Measure Analysis Population Description: The number of participants analysed is different from the number of participants randomised due to missing data. Tralokinumab + TCS = 137 subjects; Placebo + TCS = 136 subjects  |              |               |   |
| Units: Units on a scale  |              |               |   |
| median   | 7.43         | 7.50          |   |
| inter-quartile range (Q1-Q3)   | 6.43 to 8.29 | 6.59 to 8.37  | - |



## End points

### End points reporting groups

|  |                                |
|--|--------------------------------|
| Reporting group title  | Tralokinumab + TCS             |
| Reporting group description:<br>Subjects in the treatment period (Week 0 to Week 26) treated with tralokinumab every second week (Q2W) and topical corticosteroid (TCS) as needed.   |                                |
| Reporting group title  | Placebo + TCS                  |
| Reporting group description:<br>Subjects in the treatment period (Week 0 to Week 26) treated with placebo every second week (Q2W) and topical corticosteroid (TCS) as needed.  |                                |
| Reporting group title  | Safety follow-up, tralokinumab |
| Reporting group description:<br>Subjects who spent any amount of time in the safety follow-up period, independently of the treatment(s) received before. No treatment was administered to the subjects during this period. Eligible subjects who completed treatment could transfer to a long-term extension trial (conducted under a separate protocol) at any time during the safety follow-up period. |                                |
| Reporting group title  | Safety follow-up, placebo      |
| Reporting group description:<br>Subjects who spent any amount of time in the safety follow-up period, independently of the treatment(s) received before. No treatment was administered to the subjects during this period. Eligible subjects who completed treatment could transfer to a long-term extension trial (conducted under a separate protocol) at any time during the safety follow-up period  |                                |

### Primary: Subjects achieving at least 75% reduction in Eczema Area and Severity Index (EASI75) from Week 0 to Week 16

|  |   |
|--|---|
| End point title  | Subjects achieving at least 75% reduction in Eczema Area and Severity Index (EASI75) from Week 0 to Week 16 |
| End point description:<br>Subjects who achieved at least 75% reduction in EASI at Week 16 were defined as responders. EASI is used to evaluate the extent and severity of atopic dermatitis. It is a composite score ranging from 0 to 72 with a higher score indicating a more extensive and/or severe condition. Results of the primary analysis of the primary estimand are reported below. The other analyses supported these results. The analysis was based on the full analysis set (FAS). Of the 277 subjects randomised to treatment, 275 were treated. Therefore, the FAS consisted of 275 subjects. |   |
| End point type   | Primary   |
| End point timeframe:<br>Week 0 to Week 16  |   |

| End point values                | Tralokinumab + TCS | Placebo + TCS   |  |  |
|---------------------------------|--------------------|-----------------|--|--|
| Subject group type              | Reporting group    | Reporting group |  |  |
| Number of subjects analysed     | 138                | 137             |  |  |
| Units: Percentage of responders |                    |                 |  |  |
| number (not applicable)         | 64.2               | 50.5            |  |  |

## Statistical analyses

|  |                                    |
|--|------------------------------------|
| <b>Statistical analysis title</b>  | Tralokinumab+TCS vs placebo+TCS    |
| Statistical analysis description:  |                                    |
| Subjects who received rescue treatment or permanently discontinued IMP, without prior subject-onset of the COVID-19 pandemic (SOC19), were considered non-responders after the relevant event occurred. Any data from subjects who had SOC19 as their first prior intercurrent event (ICE) were multiple imputed (MI) assuming missing at random (MAR) following start of SOC19. Data missing prior to any ICE were handled as non-response, except data missing due to the pandemic, which was MI assuming MAR. |                                    |
| Comparison groups  | Tralokinumab + TCS v Placebo + TCS |
| Number of subjects included in analysis  | 275                                |
| Analysis specification   | Pre-specified                      |
| Analysis type  | superiority <sup>[1]</sup>         |
| P-value  | = 0.018 <sup>[2]</sup>             |
| Method   | Cochran-Mantel-Haenszel            |
| Parameter estimate   | Risk difference (RD)               |
| Point estimate   | 14.1                               |
| Confidence interval  |                                    |
| level  | 95 %                               |
| sides  | 2-sided                            |
| lower limit  | 2.5                                |
| upper limit  | 25.7                               |

Notes:

[1] - The null hypothesis of no difference in response rates between tralokinumab +TCS and placebo+TCS was tested against the 2-sided alternative that there was a difference.

[2] - The significance level is set to 0.05 (5%). The analysis was conducted using Cochran-Mantel-Haenszel test stratified by prior CSA use and baseline disease severity.

### Secondary: Reduction of Worst Daily Pruritus (NRS) (Weekly Average) of at Least 4 from Week 0 to Week 16

|  |   |
|--|---|
| End point title  | Reduction of Worst Daily Pruritus (NRS) (Weekly Average) of at Least 4 from Week 0 to Week 16 |
| End point description:   |   |
| Subjects will assess their worst itch severity over the past 24 hours using an 11-point NRS ('Worst Daily Pruritus NRS') with 0 indicating 'no itch' and 10 indicating 'worst itch imaginable'. Results of the primary analysis of the primary estimand are reported below. The other analyses supported these results. The analysis was based on subjects in the full analysis set with a Worst Daily Pruritus NRS (weekly average) of at least 4 at baseline (Week 0). Subjects meeting the endpoint were defined as responders. |   |
| End point type   | Secondary   |
| End point timeframe:   |   |
| Week 0 to Week 16  |   |

| End point values                | Tralokinumab + TCS | Placebo + TCS   |  |  |
|---------------------------------|--------------------|-----------------|--|--|
| Subject group type              | Reporting group    | Reporting group |  |  |
| Number of subjects analysed     | 134                | 135             |  |  |
| Units: Percentage of responders |                    |                 |  |  |
| number (not applicable)         | 45.5               | 35.6            |  |  |

### Statistical analyses

|  |                                    |
|--|------------------------------------|
| <b>Statistical analysis title</b>  | Tralokinumab+TCS vs placebo+TCS    |
| Statistical analysis description:  |                                    |
| Subjects who received rescue treatment or permanently discontinued IMP, without prior subject-onset of the COVID-19 pandemic (SOC19), were considered non-responders after the relevant event occurred. Any data from subjects who had SOC19 as their first prior intercurrent event (ICE) were multiple imputed (MI) assuming missing at random (MAR) following start of SOC19. Data missing prior to any ICE were handled as non-response, except data missing due to the pandemic, which was MI assuming MAR. |                                    |
| Comparison groups  | Tralokinumab + TCS v Placebo + TCS |
| Number of subjects included in analysis  | 269                                |
| Analysis specification   | Pre-specified                      |
| Analysis type  | superiority <sup>[3]</sup>         |
| P-value  | = 0.106 <sup>[4]</sup>             |
| Method   | Cochran-Mantel-Haenszel            |
| Parameter estimate   | Risk difference (RD)               |
| Point estimate   | 9.7                                |
| Confidence interval  |                                    |
| level  | 95 %                               |
| sides  | 2-sided                            |
| lower limit  | -2                                 |
| upper limit  | 21.4                               |

Notes:

[3] - The null hypothesis of no difference between Tralokinumab+TCS and placebo+TCS was tested at a 5% significance level against the 2-sided alternative that there was a difference.

[4] - The significance level is set to 0.05 (5%). The analysis was conducted using Cochran-Mantel-Haenszel test stratified by prior CSA use and baseline disease severity.

## Secondary: Change in Scoring Atopic Dermatitis (SCORAD) from Week 0 to Week 16

|                 |   |
|-----------------|---|
| End point title | Change in Scoring Atopic Dermatitis (SCORAD) from Week 0 to Week 16 |
|-----------------|---|

End point description:

SCORAD is used to evaluate the extent and severity of atopic dermatitis as well as subjective symptoms. The score ranges from 0 to 103 with a higher score indicating a more extensive and/or severe condition. Results of the primary analysis of the primary estimand are reported below. The other analyses supported these results. The analysis was based on the full analysis set.

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

End point timeframe:

Week 0 to Week 16

| End point values                 | Tralokinumab + TCS | Placebo + TCS   |  |  |
|----------------------------------|--------------------|-----------------|--|--|
| Subject group type               | Reporting group    | Reporting group |  |  |
| Number of subjects analysed      | 138                | 137             |  |  |
| Units: Units on a scale          |                    |                 |  |  |
| arithmetic mean (standard error) | -42.7 (± 1.6)      | -34.1 (± 1.6)   |  |  |

## Statistical analyses

|                                   |                                 |
|-----------------------------------|---------------------------------|
| <b>Statistical analysis title</b> | Tralokinumab+TCS vs placebo+TCS |
|-----------------------------------|---------------------------------|

**Statistical analysis description:**

Data collected after permanent discontinuation of IMP, after initiation of rescue treatment, or after subject-onset of the COVID-19 pandemic, were not included in the analysis.

|   |                                    |
|---|------------------------------------|
| Comparison groups                       | Tralokinumab + TCS v Placebo + TCS |
| Number of subjects included in analysis | 275                                |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           | superiority <sup>[5]</sup>         |
| P-value                                 | < 0.001 <sup>[6]</sup>             |
| Method                                  | Repeated measurements model        |
| Parameter estimate                      | Difference                         |
| Point estimate                          | -8.6                               |
| Confidence interval                     |                                    |
| level                                   | 95 %                               |
| sides                                   | 2-sided                            |
| lower limit                             | -13                                |
| upper limit                             | -4.2                               |

**Notes:**

[5] - The null hypothesis of no difference between Tralokinumab+TCS and placebo+TCS was tested at a 5% significance level against the 2-sided alternative that there was a difference.

[6] - The significance level is set to 0.05 (5%).

## Secondary: Change in Dermatology Life Quality Index (DLQI) score from Week 0 to Week 16

|                 |  |
|-----------------|--|
| End point title | Change in Dermatology Life Quality Index (DLQI) score from Week 0 to Week 16 |
|-----------------|--|

**End point description:**

DLQI is used by the subject to evaluate the impact of their condition on 10 different aspects of health-related quality of life (HRQoL) over the last week. Each item is scored on a 4-point Likert scale ranging from 0 (not at all/not relevant) to 3 (very much). The total score which is the sum of the 10 items ranges from 0 to 30, with a higher score indicating a poorer HRQoL. Results of the primary analysis of the primary estimand are reported below. The other analyses supported these results. The analysis was based on the full analysis set.

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

**End point timeframe:**

Week 0 to Week 16

| End point values                 | Tralokinumab + TCS | Placebo + TCS   |  |  |
|----------------------------------|--------------------|-----------------|--|--|
| Subject group type               | Reporting group    | Reporting group |  |  |
| Number of subjects analysed      | 137                | 134             |  |  |
| Units: Units on a scale          |                    |                 |  |  |
| arithmetic mean (standard error) | -11.2 (± 0.4)      | -9.6 (± 0.4)    |  |  |

## Statistical analyses

|                                   |                                 |
|-----------------------------------|---------------------------------|
| <b>Statistical analysis title</b> | Tralokinumab+TCS vs placebo+TCS |
|-----------------------------------|---------------------------------|

**Statistical analysis description:**

Data collected after permanent discontinuation of IMP, after initiation of rescue treatment, or after subject-onset of the COVID-19 pandemic were not included in the analysis.

|                   |                                    |
|-------------------|------------------------------------|
| Comparison groups | Tralokinumab + TCS v Placebo + TCS |
|-------------------|------------------------------------|

|   |                             |
|---|-----------------------------|
| Number of subjects included in analysis | 271                         |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | superiority <sup>[7]</sup>  |
| P-value                                 | = 0.009 <sup>[8]</sup>      |
| Method                                  | Repeated measurements model |
| Parameter estimate                      | Difference                  |
| Point estimate                          | -1.5                        |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -2.6                        |
| upper limit                             | -0.4                        |

Notes:

[7] - The null hypothesis of no difference between Tralokinumab+TCS and placebo+TCS was tested at a 5% significance level against the 2-sided alternative that there was a difference.

[8] - The significance level is set to 0.05 (5%).

### Secondary: 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:

IGA is used to evaluate the severity of atopic dermatitis. It is a 5-point score ranging from 0 (clear) to 4 (severe). Subjects who achieved IGA 0 or 1 at Week 16 were defined as responders. Results of the primary analysis of the primary estimand are reported below. The other analyses supported these results. The analysis was based on the full analysis set.

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

End point timeframe:

At Week 16

| End point values                | Tralokinumab + TCS | Placebo + TCS   |  |  |
|---------------------------------|--------------------|-----------------|--|--|
| Subject group type              | Reporting group    | Reporting group |  |  |
| Number of subjects analysed     | 138                | 137             |  |  |
| Units: Percentage of responders |                    |                 |  |  |
| number (not applicable)         | 40.9               | 26.0            |  |  |

### Statistical analyses

|                            |                                 |
|----------------------------|---------------------------------|
| Statistical analysis title | Tralokinumab+TCS vs placebo+TCS |
|----------------------------|---------------------------------|

Statistical analysis description:

Subjects who received rescue treatment or permanently discontinued IMP, without prior subject-onset of the COVID-19 pandemic (SOC19), were considered non-responders after the relevant event occurred. Any data from subjects who had SOC19 as their first prior intercurrent event (ICE) were multiple imputed (MI) assuming missing at random (MAR) following start of SOC19. Data missing prior to any ICE were handled as non-response, except data missing due to the pandemic, which was MI assuming MAR.

|                   |                                    |
|-------------------|------------------------------------|
| Comparison groups | Tralokinumab + TCS v Placebo + TCS |
|-------------------|------------------------------------|

|   |                            |
|---|----------------------------|
| Number of subjects included in analysis | 275                        |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | superiority <sup>[9]</sup> |
| P-value                                 | = 0.005 <sup>[10]</sup>    |
| Method                                  | Cochran-Mantel-Haenszel    |
| Parameter estimate                      | Risk difference (RD)       |
| Point estimate                          | 15.6                       |
| Confidence interval                     |                            |
| level                                   | 95 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | 4.8                        |
| upper limit                             | 26.3                       |

Notes:

[9] - The null hypothesis of no difference between Tralokinumab+TCS and placebo+TCS was tested at a 5% significance level against the 2-sided alternative that there was a difference.

[10] - The significance level is set to 0.05 (5%). The analysis was conducted using Cochran-Mantel-Haenszel test stratified by prior CSA use and baseline disease severity.

### Secondary: Subjects achieving at least 75% reduction in Eczema Area and Severity Index (EASI75) from Week 0 to Week 26

|                 |   |
|-----------------|---|
| End point title | Subjects achieving at least 75% reduction in Eczema Area and Severity Index (EASI75) from Week 0 to Week 26 |
|-----------------|---|

End point description:

EASI (Eczema Area and Severity Index) 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. Subjects who achieved at least 75% reduction in EASI at Week 26 were defined as responders. Results of the primary analysis of the primary estimand are reported below. The other analyses supported these results. The analysis was based on the full analysis set.

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

End point timeframe:

Week 0 to Week 26

| End point values                | Tralokinumab + TCS | Placebo + TCS   |  |  |
|---------------------------------|--------------------|-----------------|--|--|
| Subject group type              | Reporting group    | Reporting group |  |  |
| Number of subjects analysed     | 138                | 137             |  |  |
| Units: Percentage of responders |                    |                 |  |  |
| number (not applicable)         | 68.8               | 55.3            |  |  |

### Statistical analyses

|                            |                                 |
|----------------------------|---------------------------------|
| Statistical analysis title | Tralokinumab+TCS vs placebo+TCS |
|----------------------------|---------------------------------|

Statistical analysis description:

Subjects who received rescue treatment or permanently discontinued IMP, without prior subject-onset of the COVID-19 pandemic (SOC19), were considered non-responders after the relevant event occurred. Any data from subjects who had SOC19 as their first prior intercurrent event (ICE) were multiple imputed (MI) assuming missing at random (MAR) following start of SOC19. Data missing prior to any ICE were handled as non-response, except data missing due to the pandemic, which was MI assuming MAR.

|                   |                                    |
|-------------------|------------------------------------|
| Comparison groups | Tralokinumab + TCS v Placebo + TCS |
|-------------------|------------------------------------|

|   |                             |
|---|-----------------------------|
| Number of subjects included in analysis | 275                         |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | superiority <sup>[11]</sup> |
| P-value                                 | = 0.014 <sup>[12]</sup>     |
| Method                                  | Cochran-Mantel-Haenszel     |
| Parameter estimate                      | Risk difference (RD)        |
| Point estimate                          | 14.1                        |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 2.9                         |
| upper limit                             | 25.3                        |

Notes:

[11] - The null hypothesis of no difference between Tralokinumab+TCS and placebo+TCS was tested at a 5% significance level against the 2-sided alternative that there was a difference.

[12] - The significance level is set to 0.05 (5%). The analysis was conducted using Cochran-Mantel-Haenszel test stratified by prior CSA use and baseline disease severity.

### Secondary: Reduction of Worst Daily Pruritus NRS (Weekly Average) of at Least 4 from Week 0 to Week 26

|                 |   |
|-----------------|---|
| End point title | Reduction of Worst Daily Pruritus NRS (Weekly Average) of at Least 4 from Week 0 to Week 26 |
|-----------------|---|

End point description:

Subjects will assess their worst itch severity over the past 24 hours using an 11-point numeric rating scale ('Worst Daily Pruritus NRS') with 0 indicating 'no itch' and 10 indicating 'worst itch imaginable'. Subjects meeting the endpoint were defined as responders. Results of the primary analysis of the primary estimand are reported below. The other analyses supported these results. The analysis was based on subjects in the full analysis set with a Worst Daily Pruritus NRS (weekly average) of at least 4 at baseline (Week 0).

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

End point timeframe:

Week 0 to Week 26

| End point values                | Tralokinumab + TCS | Placebo + TCS   |  |  |
|---------------------------------|--------------------|-----------------|--|--|
| Subject group type              | Reporting group    | Reporting group |  |  |
| Number of subjects analysed     | 134                | 135             |  |  |
| Units: Percentage of responders |                    |                 |  |  |
| number (not applicable)         | 47.2               | 39.7            |  |  |

### Statistical analyses

|                            |                                 |
|----------------------------|---------------------------------|
| Statistical analysis title | Tralokinumab+TCS vs placebo+TCS |
|----------------------------|---------------------------------|

Statistical analysis description:

Subjects who received rescue treatment or permanently discontinued IMP, without prior subject-onset of the COVID-19 pandemic (SOC19), were considered non-responders after the relevant event occurred. Any data from subjects who had SOC19 as their first prior intercurrent event (ICE) were multiple imputed (MI) assuming missing at random (MAR) following start of SOC19. Data missing prior to any ICE were handled as non-response, except data missing due to the pandemic, which was MI assuming MAR.

|                   |                                    |
|-------------------|------------------------------------|
| Comparison groups | Tralokinumab + TCS v Placebo + TCS |
|-------------------|------------------------------------|

|   |                             |
|---|-----------------------------|
| Number of subjects included in analysis | 269                         |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | superiority <sup>[13]</sup> |
| P-value                                 | = 0.228 <sup>[14]</sup>     |
| Method                                  | Cochran-Mantel-Haenszel     |
| Parameter estimate                      | Risk difference (RD)        |
| Point estimate                          | 7.3                         |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -4.6                        |
| upper limit                             | 19.2                        |

Notes:

[13] - The null hypothesis of no difference between Tralokinumab+TCS and placebo+TCS was tested at a 5% significance level against the 2-sided alternative that there was a difference.

[14] - The significance level is set to 0.05 (5%). The analysis was conducted using Cochran-Mantel-Haenszel test stratified by prior CSA use and baseline disease severity.

## Secondary: Change in Scoring Atopic Dermatitis (SCORAD) from Week 0 to Week 26

|                 |   |
|-----------------|---|
| End point title | Change in Scoring Atopic Dermatitis (SCORAD) from Week 0 to Week 26 |
|-----------------|---|

End point description:

SCORAD is used to evaluate the extent and severity of atopic dermatitis as well as subjective symptoms. The score ranges from 0 to 103 with a higher score indicating a more extensive and/or severe condition. Results of the primary analysis of the primary estimand are reported below. The other analyses supported these results. The analysis was based on the full analysis set.

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

End point timeframe:

Week 0 to Week 26

| End point values                 | Tralokinumab + TCS | Placebo + TCS   |  |  |
|----------------------------------|--------------------|-----------------|--|--|
| Subject group type               | Reporting group    | Reporting group |  |  |
| Number of subjects analysed      | 138                | 137             |  |  |
| Units: Units on a scale          |                    |                 |  |  |
| arithmetic mean (standard error) | -46.3 (± 1.5)      | -37.3 (± 1.6)   |  |  |

## Statistical analyses

|                            |                                 |
|----------------------------|---------------------------------|
| Statistical analysis title | Tralokinumab+TCS vs placebo+TCS |
|----------------------------|---------------------------------|

Statistical analysis description:

Data collected after permanent discontinuation of IMP, after initiation of rescue treatment, or after subject-onset of the COVID-19 pandemic will not be included in the analysis.

|                   |                                    |
|-------------------|------------------------------------|
| Comparison groups | Tralokinumab + TCS v Placebo + TCS |
|-------------------|------------------------------------|



|   |                             |
|---|-----------------------------|
| Number of subjects included in analysis | 275                         |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | superiority <sup>[15]</sup> |
| P-value                                 | < 0.001 <sup>[16]</sup>     |
| Method                                  | Repeated measurements model |
| Parameter estimate                      | Difference                  |
| Point estimate                          | -8.9                        |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -13.2                       |
| upper limit                             | -4.6                        |

Notes:

[15] - The null hypothesis of no difference between Tralokinumab+TCS and placebo+TCS was tested at a 5% significance level against the 2-sided alternative that there was a difference.

[16] - The significance level is set to 0.05 (5%).

## Secondary: Change in Dermatology Life Quality Index (DLQI) score from Week 0 to Week 26

|                 |  |
|-----------------|--|
| End point title | Change in Dermatology Life Quality Index (DLQI) score from Week 0 to Week 26 |
|-----------------|--|

End point description:

DLQI 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 different aspects of their health-related quality of life (HRQoL) over the last week such as dermatology-related symptoms and feelings, daily activities, leisure, work or school, personal relationships, and the treatment. Each item is scored on a 4-point Likert scale (0 = not at all /not relevant; 1 = a little; 2 = 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 HRQoL. Results of the primary analysis of the primary estimand are reported below. The other analyses supported these results. The analysis was based on the full analysis set.

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

End point timeframe:

Week 0 to Week 26

| End point values                 | Tralokinumab + TCS | Placebo + TCS   |  |  |
|----------------------------------|--------------------|-----------------|--|--|
| Subject group type               | Reporting group    | Reporting group |  |  |
| Number of subjects analysed      | 137                | 134             |  |  |
| Units: Units on a scale          |                    |                 |  |  |
| arithmetic mean (standard error) | -11.5 (± 0.4)      | -9.9 (± 0.4)    |  |  |

## Statistical analyses

|                            |                                 |
|----------------------------|---------------------------------|
| Statistical analysis title | Tralokinumab+TCS vs placebo+TCS |
|----------------------------|---------------------------------|

Statistical analysis description:

Data collected after permanent discontinuation of IMP, after initiation of rescue treatment, or after subject-onset of the COVID-19 pandemic will not be included in the analysis.

|                   |                                    |
|-------------------|------------------------------------|
| Comparison groups | Tralokinumab + TCS v Placebo + TCS |
|-------------------|------------------------------------|

|   |                             |
|---|-----------------------------|
| Number of subjects included in analysis | 271                         |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | superiority <sup>[17]</sup> |
| P-value                                 | = 0.005 <sup>[18]</sup>     |
| Method                                  | Repeated measurements model |
| Parameter estimate                      | Difference                  |
| Point estimate                          | -1.6                        |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -2.7                        |
| upper limit                             | -0.5                        |

Notes:

[17] - The null hypothesis of no difference between Tralokinumab+TCS and placebo+TCS was tested at a 5% significance level against the 2-sided alternative that there was a difference.

[18] - The significance level is set to 0.05 (5%).

### Secondary: Subjects with Investigator's Global Assessment (IGA) score of 0 (clear) or 1 (almost clear) at Week 26

|                 |  |
|-----------------|--|
| End point title | Subjects with Investigator's Global Assessment (IGA) score of 0 (clear) or 1 (almost clear) at Week 26 |
|-----------------|--|

End point description:

IGA is used to evaluate the severity of atopic dermatitis. It is a 5-point score ranging from 0 (clear) to 4 (severe). Subjects who achieved IGA 0 or 1 at Week 26 were defined as responders. Results of the primary analysis of the primary estimand are reported below. The other analyses supported these results. The analysis was based on the full analysis set.

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

End point timeframe:

Week 26

| End point values                | Tralokinumab + TCS | Placebo + TCS   |  |  |
|---------------------------------|--------------------|-----------------|--|--|
| Subject group type              | Reporting group    | Reporting group |  |  |
| Number of subjects analysed     | 138                | 137             |  |  |
| Units: Percentage of responders |                    |                 |  |  |
| number (not applicable)         | 47.0               | 33.4            |  |  |

### Statistical analyses

|                            |                                 |
|----------------------------|---------------------------------|
| Statistical analysis title | Tralokinumab+TCS vs placebo+TCS |
|----------------------------|---------------------------------|

Statistical analysis description:

Subjects who received rescue treatment or permanently discontinued IMP, without prior subject-onset of the COVID-19 pandemic (SOC19), were considered non-responders after the relevant event occurred. Any data from subjects who had SOC19 as their first prior intercurrent event (ICE) were multiple imputed (MI) assuming missing at random (MAR) following start of SOC19. Data missing prior to any ICE were handled as non-response, except data missing due to the pandemic, which was MI assuming MAR.

|                   |                                    |
|-------------------|------------------------------------|
| Comparison groups | Tralokinumab + TCS v Placebo + TCS |
|-------------------|------------------------------------|

|   |                             |
|---|-----------------------------|
| Number of subjects included in analysis | 275                         |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | superiority <sup>[19]</sup> |
| P-value                                 | = 0.014 <sup>[20]</sup>     |
| Method                                  | Cochran-Mantel-Haenszel     |
| Parameter estimate                      | Risk difference (RD)        |
| Point estimate                          | 14.3                        |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 2.9                         |
| upper limit                             | 25.6                        |

Notes:

[19] - The null hypothesis of no difference between Tralokinumab+TCS and placebo+TCS was tested at a 5% significance level against the 2-sided alternative that there was a difference.

[20] - The significance level is set to 0.05 (5%). The analysis was conducted using Cochran-Mantel-Haenszel test stratified by prior CSA use and baseline disease severity.

### Secondary: Frequency of anti-drug antibodies (ADA)

|                        |   |
|------------------------|---|
| End point title        | Frequency of anti-drug antibodies (ADA) |
| End point description: |   |
|                        |   |
| End point type         | Secondary                               |
| End point timeframe:   |   |
| From Week 0 to Week 40 |   |

| End point values                | Tralokinumab + TCS | Placebo + TCS   |  |  |
|---------------------------------|--------------------|-----------------|--|--|
| Subject group type              | Reporting group    | Reporting group |  |  |
| Number of subjects analysed     | 138                | 137             |  |  |
| Units: Count of Participants    |                    |                 |  |  |
| Positive                        | 2                  | 3               |  |  |
| Negative                        | 134                | 133             |  |  |
| Perishing                       | 1                  | 1               |  |  |
| No post-baseline ADA assessment | 1                  | 0               |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

All adverse events were collected from the time of signed informed consent form to the end of the trial (safety follow-up visit at Week 40).

Adverse event reporting additional description:

The analysis was conducted based on the safety analysis set which consisted of subjects exposed to at least 1 dose of investigational medicinal product.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 20.0 |
|--------------------|------|

### Reporting groups

|                       |                                      |
|-----------------------|--------------------------------------|
| Reporting group title | Treatment period: Tralokinumab + TCS |
|-----------------------|--------------------------------------|

Reporting group description:

Subjects in the treatment period (Week 0 to Week 26) treated with tralokinumab every second week (Q2W) and topical corticosteroid (TCS) as needed. Subjects received a loading dose of 600 mg tralokinumab at Week 0 followed by a dose of 300 mg tralokinumab every second week (Q2W) from Week 2. The last administration of IMP occurred at Week 24.

|                       |                                 |
|-----------------------|---------------------------------|
| Reporting group title | Treatment period: Placebo + TCS |
|-----------------------|---------------------------------|

Reporting group description:

Subjects in the treatment period (Week 0 to Week 26) treated with placebo every second week (Q2W) and topical corticosteroid (TCS) as needed. Subjects were administered placebo at Week 0 followed by administration of placebo Q2W from Week 2. The last administration of IMP occurred at Week 24.

|                       |                                       |
|-----------------------|---------------------------------------|
| Reporting group title | Safety follow-up period: Tralokinumab |
|-----------------------|---------------------------------------|

Reporting group description:

Subjects who spent any amount of time in the safety follow-up period, independently of the treatment(s) received before. No treatment was administered to the subjects during this period. Eligible subjects who completed treatment could transfer to a long-term extension trial (conducted under a separate protocol) at any any time during the safety follow-up period.

|                       |                                  |
|-----------------------|----------------------------------|
| Reporting group title | Safety follow-up period: Placebo |
|-----------------------|----------------------------------|

Reporting group description: -

| Serious adverse events  | Treatment period:<br>Tralokinumab + TCS | Treatment period:<br>Placebo + TCS | Safety follow-up<br>period:<br>Tralokinumab |
|---|---|------------------------------------|---|
| Total subjects affected by serious adverse events                   |   |                                    |   |
| subjects affected / exposed   | 1 / 138 (0.72%)                         | 5 / 137 (3.65%)                    | 0 / 75 (0.00%)                              |
| number of deaths (all causes)                                       | 0                                       | 0                                  | 0   |
| number of deaths resulting from adverse events                      | 0                                       | 0                                  | 0   |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |   |                                    |   |
| Squamous cell carcinoma of skin                                     |   |                                    |   |
| subjects affected / exposed   | 0 / 138 (0.00%)                         | 1 / 137 (0.73%)                    | 0 / 75 (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                                       |
| Injury, poisoning and procedural                                    |   |                                    |   |

|   |                 |                 |                |
|---|-----------------|-----------------|----------------|
| complications                                   |                 |                 |                |
| Peripheral nerve injury                         |                 |                 |                |
| subjects affected / exposed                     | 0 / 138 (0.00%) | 1 / 137 (0.73%) | 0 / 75 (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          |
| Nervous system disorders                        |                 |                 |                |
| Cerebrovascular accident                        |                 |                 |                |
| subjects affected / exposed                     | 0 / 138 (0.00%) | 1 / 137 (0.73%) | 0 / 75 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0          |
| Seizure   |                 |                 |                |
| subjects affected / exposed                     | 0 / 138 (0.00%) | 1 / 137 (0.73%) | 0 / 75 (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 / 138 (0.00%) | 1 / 137 (0.73%) | 0 / 75 (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          |
| Respiratory, thoracic and mediastinal disorders |                 |                 |                |
| Asthma  |                 |                 |                |
| subjects affected / exposed                     | 0 / 138 (0.00%) | 1 / 137 (0.73%) | 0 / 75 (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          |
| Skin and subcutaneous tissue disorders          |                 |                 |                |
| Dermatitis atopic                               |                 |                 |                |
| subjects affected / exposed                     | 0 / 138 (0.00%) | 1 / 137 (0.73%) | 0 / 75 (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          |
| Psychiatric disorders                           |                 |                 |                |
| Depressed mood                                  |                 |                 |                |
| subjects affected / exposed                     | 0 / 138 (0.00%) | 1 / 137 (0.73%) | 0 / 75 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0          |
| Suicidal ideation                               |                 |                 |                |

|   |                 |                 |                |
|---|-----------------|-----------------|----------------|
| subjects affected / exposed                     | 0 / 138 (0.00%) | 1 / 137 (0.73%) | 0 / 75 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0          |
| <b>Infections and infestations</b>              |                 |                 |                |
| Appendicitis                                    |                 |                 |                |
| subjects affected / exposed                     | 1 / 138 (0.72%) | 0 / 137 (0.00%) | 0 / 75 (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          |
| Pyelonephritis                                  |                 |                 |                |
| subjects affected / exposed                     | 0 / 138 (0.00%) | 0 / 137 (0.00%) | 0 / 75 (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 period: Placebo |  |  |
| Total subjects affected by serious adverse events                   |                                  |  |  |
| subjects affected / exposed   | 1 / 83 (1.20%)                   |  |  |
| number of deaths (all causes)                                       | 0                                |  |  |
| number of deaths resulting from adverse events                      | 0                                |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                  |  |  |
| Squamous cell carcinoma of skin                                     |                                  |  |  |
| subjects affected / exposed   | 0 / 83 (0.00%)                   |  |  |
| occurrences causally related to treatment / all                     | 0 / 0                            |  |  |
| deaths causally related to treatment / all                          | 0 / 0                            |  |  |
| Injury, poisoning and procedural complications                      |                                  |  |  |
| Peripheral nerve injury   |                                  |  |  |
| subjects affected / exposed   | 0 / 83 (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 / 83 (0.00%)                   |  |  |
| occurrences causally related to treatment / all                     | 0 / 0                            |  |  |
| deaths causally related to treatment / all                          | 0 / 0                            |  |  |
| Seizure   |                                  |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 0 / 83 (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                     | 0 / 83 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Respiratory, thoracic and mediastinal disorders |                |  |  |
| Asthma  |                |  |  |
| subjects affected / exposed                     | 0 / 83 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Skin and subcutaneous tissue disorders          |                |  |  |
| Dermatitis atopic                               |                |  |  |
| subjects affected / exposed                     | 0 / 83 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Psychiatric disorders                           |                |  |  |
| Depressed mood                                  |                |  |  |
| subjects affected / exposed                     | 0 / 83 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Suicidal ideation                               |                |  |  |
| subjects affected / exposed                     | 0 / 83 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Infections and infestations                     |                |  |  |
| Appendicitis                                    |                |  |  |
| subjects affected / exposed                     | 0 / 83 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Pyelonephritis                                  |                |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 1 / 83 (1.20%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |

Frequency threshold for reporting non-serious adverse events: 0 %

| <b>Non-serious adverse events</b>                                   | Treatment period:<br>Tralokinumab + TCS | Treatment period:<br>Placebo + TCS | Safety follow-up<br>period:<br>Tralokinumab |
|---|---|------------------------------------|---|
| Total subjects affected by non-serious adverse events               |   |                                    |   |
| subjects affected / exposed   | 107 / 138 (77.54%)                      | 108 / 137 (78.83%)                 | 4 / 75 (5.33%)                              |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |   |                                    |   |
| Basal cell carcinoma  |   |                                    |   |
| subjects affected / exposed   | 0 / 138 (0.00%)                         | 0 / 137 (0.00%)                    | 0 / 75 (0.00%)                              |
| occurrences (all)   | 0                                       | 0                                  | 0   |
| Vascular disorders  |   |                                    |   |
| Hypertension  |   |                                    |   |
| subjects affected / exposed   | 3 / 138 (2.17%)                         | 7 / 137 (5.11%)                    | 0 / 75 (0.00%)                              |
| occurrences (all)   | 3                                       | 7                                  | 0   |
| General disorders and administration site conditions                |   |                                    |   |
| Fatigue   |   |                                    |   |
| subjects affected / exposed   | 4 / 138 (2.90%)                         | 3 / 137 (2.19%)                    | 0 / 75 (0.00%)                              |
| occurrences (all)   | 4                                       | 3                                  | 0   |
| Influenza like illness  |   |                                    |   |
| subjects affected / exposed   | 3 / 138 (2.17%)                         | 0 / 137 (0.00%)                    | 0 / 75 (0.00%)                              |
| occurrences (all)   | 3                                       | 0                                  | 0   |
| Injection site pain   |   |                                    |   |
| subjects affected / exposed   | 4 / 138 (2.90%)                         | 1 / 137 (0.73%)                    | 0 / 75 (0.00%)                              |
| occurrences (all)   | 5                                       | 3                                  | 0   |
| Respiratory, thoracic and mediastinal disorders                     |   |                                    |   |
| Asthma  |   |                                    |   |
| subjects affected / exposed   | 4 / 138 (2.90%)                         | 8 / 137 (5.84%)                    | 0 / 75 (0.00%)                              |
| occurrences (all)   | 5                                       | 9                                  | 0   |
| Cough   |   |                                    |   |
| subjects affected / exposed   | 4 / 138 (2.90%)                         | 7 / 137 (5.11%)                    | 0 / 75 (0.00%)                              |
| occurrences (all)   | 5                                       | 7                                  | 0   |



|   |  |  |   |
|---|--|--|---|
| Oropharyngeal pain<br>subjects affected / exposed<br>occurrences (all)  | 1 / 138 (0.72%)<br>1   | 8 / 137 (5.84%)<br>8   | 0 / 75 (0.00%)<br>0   |
| Injury, poisoning and procedural complications<br>Skin abrasion<br>subjects affected / exposed<br>occurrences (all)   | 3 / 138 (2.17%)<br>3   | 0 / 137 (0.00%)<br>0   | 0 / 75 (0.00%)<br>0   |
| Nervous system disorders<br>Headache<br>subjects affected / exposed<br>occurrences (all)  | 21 / 138 (15.22%)<br>25  | 13 / 137 (9.49%)<br>18   | 0 / 75 (0.00%)<br>0   |
| Eye disorders<br>Conjunctivitis allergic<br>subjects affected / exposed<br>occurrences (all)<br><br>Dry eye<br>subjects affected / exposed<br>occurrences (all)   | 6 / 138 (4.35%)<br>8<br><br>3 / 138 (2.17%)<br>3                             | 5 / 137 (3.65%)<br>5<br><br>1 / 137 (0.73%)<br>1                             | 0 / 75 (0.00%)<br>0<br><br>0 / 75 (0.00%)<br>0                            |
| Gastrointestinal disorders<br>Diarrhoea<br>subjects affected / exposed<br>occurrences (all)<br><br>Dyspepsia<br>subjects affected / exposed<br>occurrences (all)<br><br>Diverticulum intestinal<br>subjects affected / exposed<br>occurrences (all) | 1 / 138 (0.72%)<br>1<br><br>1 / 138 (0.72%)<br>1<br><br>0 / 138 (0.00%)<br>0 | 5 / 137 (3.65%)<br>8<br><br>3 / 137 (2.19%)<br>3<br><br>0 / 137 (0.00%)<br>0 | 0 / 75 (0.00%)<br>0<br><br>0 / 75 (0.00%)<br>0<br><br>0 / 75 (0.00%)<br>0 |
| Hepatobiliary disorders<br>Cholelithiasis<br>subjects affected / exposed<br>occurrences (all)   | 0 / 138 (0.00%)<br>0   | 0 / 137 (0.00%)<br>0   | 1 / 75 (1.33%)<br>1   |
| Skin and subcutaneous tissue disorders<br>Alopecia areata<br>subjects affected / exposed<br>occurrences (all)<br><br>Dermatitis atopic  | 0 / 138 (0.00%)<br>0<br><br>   | 3 / 137 (2.19%)<br>3<br><br>   | 0 / 75 (0.00%)<br>0<br><br>   |

|   |                       |                         |                     |
|---|-----------------------|-------------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)  | 7 / 138 (5.07%)<br>11 | 16 / 137 (11.68%)<br>26 | 0 / 75 (0.00%)<br>0 |
| Diffuse alopecia<br>subjects affected / exposed<br>occurrences (all)  | 3 / 138 (2.17%)<br>3  | 3 / 137 (2.19%)<br>3    | 0 / 75 (0.00%)<br>0 |
| Pruritus<br>subjects affected / exposed<br>occurrences (all)  | 6 / 138 (4.35%)<br>12 | 5 / 137 (3.65%)<br>6    | 0 / 75 (0.00%)<br>0 |
| Night sweats<br>subjects affected / exposed<br>occurrences (all)  | 0 / 138 (0.00%)<br>0  | 0 / 137 (0.00%)<br>0    | 0 / 75 (0.00%)<br>0 |
| Renal and urinary disorders<br>Renal cyst<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 138 (0.00%)<br>0  | 0 / 137 (0.00%)<br>0    | 0 / 75 (0.00%)<br>0 |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all) | 2 / 138 (1.45%)<br>2  | 3 / 137 (2.19%)<br>3    | 1 / 75 (1.33%)<br>1 |
| Back pain<br>subjects affected / exposed<br>occurrences (all)   | 6 / 138 (4.35%)<br>6  | 4 / 137 (2.92%)<br>4    | 0 / 75 (0.00%)<br>0 |
| Musculoskeletal pain<br>subjects affected / exposed<br>occurrences (all)  | 0 / 138 (0.00%)<br>0  | 3 / 137 (2.19%)<br>4    | 0 / 75 (0.00%)<br>0 |
| Myalgia<br>subjects affected / exposed<br>occurrences (all)   | 4 / 138 (2.90%)<br>5  | 2 / 137 (1.46%)<br>2    | 0 / 75 (0.00%)<br>0 |
| Infections and infestations<br>Bronchitis<br>subjects affected / exposed<br>occurrences (all)                     | 3 / 138 (2.17%)<br>4  | 3 / 137 (2.19%)<br>3    | 0 / 75 (0.00%)<br>0 |
| Conjunctivitis<br>subjects affected / exposed<br>occurrences (all)  | 6 / 138 (4.35%)<br>6  | 2 / 137 (1.46%)<br>3    | 0 / 75 (0.00%)<br>0 |
| Dermatitis infected   |                       |                         |                     |

|   |                  |                  |                |
|---|------------------|------------------|----------------|
| subjects affected / exposed             | 2 / 138 (1.45%)  | 5 / 137 (3.65%)  | 0 / 75 (0.00%) |
| occurrences (all)                       | 2                | 10               | 0              |
| Folliculitis                            |                  |                  |                |
| subjects affected / exposed             | 6 / 138 (4.35%)  | 3 / 137 (2.19%)  | 0 / 75 (0.00%) |
| occurrences (all)                       | 6                | 3                | 0              |
| Gastroenteritis                         |                  |                  |                |
| subjects affected / exposed             | 4 / 138 (2.90%)  | 3 / 137 (2.19%)  | 0 / 75 (0.00%) |
| occurrences (all)                       | 4                | 3                | 0              |
| Herpes simplex                          |                  |                  |                |
| subjects affected / exposed             | 1 / 138 (0.72%)  | 3 / 137 (2.19%)  | 0 / 75 (0.00%) |
| occurrences (all)                       | 1                | 4                | 0              |
| Influenza                               |                  |                  |                |
| subjects affected / exposed             | 3 / 138 (2.17%)  | 4 / 137 (2.92%)  | 0 / 75 (0.00%) |
| occurrences (all)                       | 3                | 4                | 0              |
| Nasopharyngitis                         |                  |                  |                |
| subjects affected / exposed             | 1 / 138 (0.72%)  | 6 / 137 (4.38%)  | 0 / 75 (0.00%) |
| occurrences (all)                       | 1                | 6                | 0              |
| Oral herpes                             |                  |                  |                |
| subjects affected / exposed             | 5 / 138 (3.62%)  | 6 / 137 (4.38%)  | 0 / 75 (0.00%) |
| occurrences (all)                       | 8                | 6                | 0              |
| Pharyngitis                             |                  |                  |                |
| subjects affected / exposed             | 4 / 138 (2.90%)  | 3 / 137 (2.19%)  | 0 / 75 (0.00%) |
| occurrences (all)                       | 4                | 3                | 0              |
| Rhinitis                                |                  |                  |                |
| subjects affected / exposed             | 5 / 138 (3.62%)  | 3 / 137 (2.19%)  | 0 / 75 (0.00%) |
| occurrences (all)                       | 6                | 3                | 0              |
| Sinusitis                               |                  |                  |                |
| subjects affected / exposed             | 3 / 138 (2.17%)  | 5 / 137 (3.65%)  | 0 / 75 (0.00%) |
| occurrences (all)                       | 4                | 5                | 0              |
| Tonsillitis                             |                  |                  |                |
| subjects affected / exposed             | 0 / 138 (0.00%)  | 3 / 137 (2.19%)  | 0 / 75 (0.00%) |
| occurrences (all)                       | 0                | 3                | 0              |
| Upper respiratory tract infection       |                  |                  |                |
| subjects affected / exposed             | 10 / 138 (7.25%) | 10 / 137 (7.30%) | 0 / 75 (0.00%) |
| occurrences (all)                       | 12               | 11               | 0              |
| Viral upper respiratory tract infection |                  |                  |                |

|                                   |                   |                   |                |
|-----------------------------------|-------------------|-------------------|----------------|
| subjects affected / exposed       | 37 / 138 (26.81%) | 35 / 137 (25.55%) | 2 / 75 (2.67%) |
| occurrences (all)                 | 53                | 46                | 2              |
| Lower respiratory tract infection |                   |                   |                |
| subjects affected / exposed       | 0 / 138 (0.00%)   | 2 / 137 (1.46%)   | 0 / 75 (0.00%) |
| occurrences (all)                 | 0                 | 2                 | 0              |
| Pyelonephritis                    |                   |                   |                |
| subjects affected / exposed       | 0 / 138 (0.00%)   | 0 / 137 (0.00%)   | 0 / 75 (0.00%) |
| occurrences (all)                 | 0                 | 0                 | 0              |
| Urinary tract infection           |                   |                   |                |
| subjects affected / exposed       | 0 / 138 (0.00%)   | 0 / 137 (0.00%)   | 0 / 75 (0.00%) |
| occurrences (all)                 | 0                 | 0                 | 0              |

|   |                                  |  |  |
|---|----------------------------------|--|--|
| <b>Non-serious adverse events</b>                                   | Safety follow-up period: Placebo |  |  |
| Total subjects affected by non-serious adverse events               |                                  |  |  |
| subjects affected / exposed   | 6 / 83 (7.23%)                   |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                  |  |  |
| Basal cell carcinoma  |                                  |  |  |
| subjects affected / exposed   | 1 / 83 (1.20%)                   |  |  |
| occurrences (all)   | 1                                |  |  |
| Vascular disorders  |                                  |  |  |
| Hypertension  |                                  |  |  |
| subjects affected / exposed   | 0 / 83 (0.00%)                   |  |  |
| occurrences (all)   | 0                                |  |  |
| General disorders and administration site conditions                |                                  |  |  |
| Fatigue   |                                  |  |  |
| subjects affected / exposed   | 0 / 83 (0.00%)                   |  |  |
| occurrences (all)   | 0                                |  |  |
| Influenza like illness  |                                  |  |  |
| subjects affected / exposed   | 0 / 83 (0.00%)                   |  |  |
| occurrences (all)   | 0                                |  |  |
| Injection site pain   |                                  |  |  |
| subjects affected / exposed   | 0 / 83 (0.00%)                   |  |  |
| occurrences (all)   | 0                                |  |  |
| Respiratory, thoracic and mediastinal disorders                     |                                  |  |  |

|  |                |  |  |
|--|----------------|--|--|
| Asthma   |                |  |  |
| subjects affected / exposed                    | 0 / 83 (0.00%) |  |  |
| occurrences (all)                              | 0              |  |  |
| Cough  |                |  |  |
| subjects affected / exposed                    | 0 / 83 (0.00%) |  |  |
| occurrences (all)                              | 0              |  |  |
| Oropharyngeal pain                             |                |  |  |
| subjects affected / exposed                    | 0 / 83 (0.00%) |  |  |
| occurrences (all)                              | 0              |  |  |
| Injury, poisoning and procedural complications |                |  |  |
| Skin abrasion                                  |                |  |  |
| subjects affected / exposed                    | 0 / 83 (0.00%) |  |  |
| occurrences (all)                              | 0              |  |  |
| Nervous system disorders                       |                |  |  |
| Headache                                       |                |  |  |
| subjects affected / exposed                    | 0 / 83 (0.00%) |  |  |
| occurrences (all)                              | 0              |  |  |
| Eye disorders                                  |                |  |  |
| Conjunctivitis allergic                        |                |  |  |
| subjects affected / exposed                    | 0 / 83 (0.00%) |  |  |
| occurrences (all)                              | 0              |  |  |
| Dry eye  |                |  |  |
| subjects affected / exposed                    | 1 / 83 (1.20%) |  |  |
| occurrences (all)                              | 1              |  |  |
| Gastrointestinal disorders                     |                |  |  |
| Diarrhoea                                      |                |  |  |
| subjects affected / exposed                    | 0 / 83 (0.00%) |  |  |
| occurrences (all)                              | 0              |  |  |
| Dyspepsia                                      |                |  |  |
| subjects affected / exposed                    | 0 / 83 (0.00%) |  |  |
| occurrences (all)                              | 0              |  |  |
| Diverticulum intestinal                        |                |  |  |
| subjects affected / exposed                    | 1 / 83 (1.20%) |  |  |
| occurrences (all)                              | 1              |  |  |
| Hepatobiliary disorders                        |                |  |  |

|  |                     |  |  |
|--|---------------------|--|--|
| Cholelithiasis<br>subjects affected / exposed<br>occurrences (all)       | 0 / 83 (0.00%)<br>0 |  |  |
| Skin and subcutaneous tissue disorders                                   |                     |  |  |
| Alopecia areata<br>subjects affected / exposed<br>occurrences (all)      | 0 / 83 (0.00%)<br>0 |  |  |
| Dermatitis atopic<br>subjects affected / exposed<br>occurrences (all)    | 2 / 83 (2.41%)<br>2 |  |  |
| Diffuse alopecia<br>subjects affected / exposed<br>occurrences (all)     | 0 / 83 (0.00%)<br>0 |  |  |
| Pruritus<br>subjects affected / exposed<br>occurrences (all)             | 0 / 83 (0.00%)<br>0 |  |  |
| Night sweats<br>subjects affected / exposed<br>occurrences (all)         | 1 / 83 (1.20%)<br>1 |  |  |
| Renal and urinary disorders  |                     |  |  |
| Renal cyst<br>subjects affected / exposed<br>occurrences (all)           | 1 / 83 (1.20%)<br>1 |  |  |
| Musculoskeletal and connective tissue disorders                          |                     |  |  |
| Arthralgia<br>subjects affected / exposed<br>occurrences (all)           | 0 / 83 (0.00%)<br>0 |  |  |
| Back pain<br>subjects affected / exposed<br>occurrences (all)            | 0 / 83 (0.00%)<br>0 |  |  |
| Musculoskeletal pain<br>subjects affected / exposed<br>occurrences (all) | 0 / 83 (0.00%)<br>0 |  |  |
| Myalgia<br>subjects affected / exposed<br>occurrences (all)              | 0 / 83 (0.00%)<br>0 |  |  |

|                             |                |  |  |
|-----------------------------|----------------|--|--|
| Infections and infestations |                |  |  |
| Bronchitis                  |                |  |  |
| subjects affected / exposed | 0 / 83 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Conjunctivitis              |                |  |  |
| subjects affected / exposed | 0 / 83 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Dermatitis infected         |                |  |  |
| subjects affected / exposed | 1 / 83 (1.20%) |  |  |
| occurrences (all)           | 1              |  |  |
| Folliculitis                |                |  |  |
| subjects affected / exposed | 0 / 83 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Gastroenteritis             |                |  |  |
| subjects affected / exposed | 0 / 83 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Herpes simplex              |                |  |  |
| subjects affected / exposed | 0 / 83 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Influenza                   |                |  |  |
| subjects affected / exposed | 0 / 83 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Nasopharyngitis             |                |  |  |
| subjects affected / exposed | 0 / 83 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Oral herpes                 |                |  |  |
| subjects affected / exposed | 0 / 83 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Pharyngitis                 |                |  |  |
| subjects affected / exposed | 0 / 83 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Rhinitis                    |                |  |  |
| subjects affected / exposed | 0 / 83 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Sinusitis                   |                |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed             | 0 / 83 (0.00%) |  |  |
| occurrences (all)                       | 0              |  |  |
| Tonsillitis                             |                |  |  |
| subjects affected / exposed             | 0 / 83 (0.00%) |  |  |
| occurrences (all)                       | 0              |  |  |
| Upper respiratory tract infection       |                |  |  |
| subjects affected / exposed             | 0 / 83 (0.00%) |  |  |
| occurrences (all)                       | 0              |  |  |
| Viral upper respiratory tract infection |                |  |  |
| subjects affected / exposed             | 1 / 83 (1.20%) |  |  |
| occurrences (all)                       | 1              |  |  |
| Lower respiratory tract infection       |                |  |  |
| subjects affected / exposed             | 1 / 83 (1.20%) |  |  |
| occurrences (all)                       | 1              |  |  |
| Pyelonephritis                          |                |  |  |
| subjects affected / exposed             | 1 / 83 (1.20%) |  |  |
| occurrences (all)                       | 1              |  |  |
| Urinary tract infection                 |                |  |  |
| subjects affected / exposed             | 1 / 83 (1.20%) |  |  |
| occurrences (all)                       | 1              |  |  |



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment   |
|------------------|---|
| 13 November 2018 | The main reason for the amendment was to introduce the possibility for eligible subjects in selected countries to participate in a long-term extension trial (conducted under a separate protocol [LP0162-1337, ECZTEND]) without completing the safety follow-up period in the present trial.      |
| 15 June 2020     | The main reason for the amendment was to modify the statistical analyses to account for an unusually high number of missing information due to COVID 19 pandemic in this trial. Statistical analysis was therefore revisited to ensure an unbiased evaluation of the treatment effect in the trial. |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported