Clinical trial results:
A randomised, double-blind, placebo-controlled, phase 3 trial to evaluate the efficacy and safety of tralokinumab monotherapy in subjects with moderate to severe atopic dermatitis who are candidates for systemic therapy

Summary

EudraCT number	2016-004201-13
Trial protocol	DK GB PL IT
Global end of trial date	14 August 2019

Results information

Result version number	v1 (current)
This version publication date	23 August 2020
First version publication date	23 August 2020

Trial information

Trial identification

Sponsor protocol code	LP0162-1326

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03160885
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, LEO Pharma A/S, +45 44945888, disclosure@leo-pharma.com
Scientific contact	Clinical Disclosure Specialist, LEO Pharma A/S, LEO Pharma A/S, +45 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:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	20 February 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 August 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of tralokinumab compared with placebo in treating moderate-to-severe Atopic dermatitis.

Protection of trial subjects:

This clinical trial was conducted to conform to the principles of the Declaration of Helsinki as adopted by the 18th World Medical Association General Assembly, 1964, and subsequent amendments.
All subjects received written and verbal information concerning the clinical trial.
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.
Both during the initial treatment period and the maintenance treatment period, some subjects were randomised to placebo treatment. If medically necessary (i.e. to control intolerable atopic dermatitis [AD] symptoms), rescue treatment for AD could be provided to subjects throughout the trial, both during the initial treatment period and the maintenance treatment period, at the discretion of the investigator.
For the first 3 investigational medicinal product (IMP) dosing visits in both the initial treatment period (i.e. Weeks 0, 2, and 4) and in open-label treatment, subjects were monitored after IMP administration for immediate drug reactions for a minimum of 2 hours with vital signs taken every 30 minutes or until stable, whichever was later. Vital signs were documented in the electronic case report forms.
Appropriate drugs, such as epinephrine, antihistamines, corticosteroids, etc., and medical equipment to treat acute anaphylactic reactions were immediately available at trial sites, and trial personnel was trained to recognise and respond to anaphylaxis according to local guidelines.

Background therapy:

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

Evidence for comparator: -

Actual start date of recruitment	29 June 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 94
Country: Number of subjects enrolled	United Kingdom: 70
Country: Number of subjects enrolled	Denmark: 10
Country: Number of subjects enrolled	Italy: 41
Country: Number of subjects enrolled	United States: 171
Country: Number of subjects enrolled	Australia: 121

Country: Number of subjects enrolled	Korea, Republic of: 78
Country: Number of subjects enrolled	Canada: 190
Country: Number of subjects enrolled	Russian Federation: 19
Worldwide total number of subjects	794
EEA total number of subjects	215

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	757
From 65 to 84 years	36
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

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

Period 1

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

Blinding implementation details:

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Initial Treatment Period - Tralokinumab 300 mg Q2W

Arm description:

Week 0 to Week 16:

Tralokinumab 300 mg Q2W

Tralokinumab: Tralokinumab is a human recombinant monoclonal antibody of the IgG4 subclass that specifically binds to human IL-13 and blocks interaction with the IL-13 receptors. It is presented as a liquid formulation for SC administration

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

Dosage and administration details:

At Day 0, each subject received 4 SC injections (each 1.0 mL) of 150 mg tralokinumab to receive a total loading dose of 600 mg tralokinumab (4.0 mL). At subsequent visits (Q2W) each subject received 2 SC injections (each 1.0 mL) of 150 mg tralokinumab to receive a total dose of 300 mg tralokinumab.
IMP was administered by a qualified, unblinded HCP.
The injections were administered into the SC tissue of the upper arm, anterior thigh, or abdomen, separated by at least 3 cm.

Arm title	Initial Treatment Period - Placebo Q2W

Arm description:

Week 0 to Week 16:

Placebo Q2W

Placebo: Placebo contains the same excipients, in the same concentration, only lacking tralokinumab

Arm type	Placebo

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

Dosage and administration details:

At Day 0, each subject received 4 SC injections (each 1.0 mL) of placebo to receive a total loading dose (4.0 mL). At subsequent visits (Q2W) each subject received 2 SC injections (each 1.0 mL) of placebo IMP was administered by a qualified, unblinded HCP.
The injections were administered into the SC tissue of the upper arm, anterior thigh, or abdomen, separated by at least 3 cm.

Number of subjects in period 1	Initial Treatment Period - Tralokinumab 300 mg Q2W	Initial Treatment Period - Placebo Q2W
Started	593	201
Completed	558	179
Not completed	35	22
Discontinued IMP before Week 16	33	22
Not dosed	2	-

Period 2

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

Blinding implementation details:

Subjects who did not achieve a clinical response at Week 16 as well as subjects who did not maintain adequate clinical response during the maintenance treatment period were transferred to open-label tralokinumab 300 mg Q2W treatment with optional use of TCS up to Week 52.

Arms

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

Arm description:

Week 16 to Week 52:
Subjects receiving initial treatment with tralokinumab/placebo Q2W who did not achieve protocol-defined clinical response assigned to open-label treatment at Week 16 with tralokinumab 300 mg Q2W regimen + optional topical corticosteroids (TCS)
OR
Subjects receiving maintenance treatment with tralokinumab 300 mg Q2W/Q4W or placebo Q2W assigned to open-label treatment after Week 16 with tralokinumab 300 mg Q2W regimen + optional TCS if:
-IGA of at least 2 and not achieving EASI75 over at least a 4-week period (over 3 consecutive visits) for subjects with IGA=0 at Week 16;
OR
-IGA of at least 3 and not achieving EASI75 over at least a 4-week period (i.e. over 3 consecutive visits) for subjects with IGA=1 at Week 16;
OR
-Not achieving EASI75 over at least a 4-week period (over 3 consecutive visits) for subjects with IGA>1

at Week 16.

Arm type	Experimental
Investigational medicinal product name	Open-label Tralokinumab 300 mg Q2W + Optional TCS
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

At each visit, subject received 2 SC injections (each 1.0 mL) of 150 mg tralokinumab Q2W to receive a total dose of 300 mg.
IMP was administered by a qualified HCP.

Subjects had the option to self-administer tralokinumab – or have tralokinumab administered by a caregiver – in their home after
adequate training by site staff at the investigator's discretion.

The injections were administered into the SC tissue of the upper arm, anterior thigh, or abdomen, separated by at least 3 cm.

Number of subjects in period 2[1]	Open-label Treatment - Tralokinumab 300 mg Q2W + Optional TCS
Started	560
Completed	423
Not completed	137
Discontinued IMP	131
Completed Week 50	4
Not dosed	2

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: Open-label treatment phase was in parallel to the Maintenance treatment phase. Subjects from the initial treatment phase entered either into the Open-label treatment phase or Maintenance treatment phase.

Period 3

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

Blinding implementation details:

This was a double-blind trial in which tralokinumab and placebo were visually distinct from each other. The IMP was handled and administered by a qualified, unblinded HCP at the site who was not involved in the management of trial subjects and who did not perform any of the assessments.
Maintenance treatment phase was in parallel to the Open-label phase.

Arms

Are arms mutually exclusive?	Yes

Arm title	Maintenance Treatment Period - Tralokinumab 300 mg Q2W

Arm description:

Week 16 to Week 52:

Subjects achieving a clinical response at Week 16 and initially randomised to tralokinumab re-randomised to tralokinumab 300 mg Q2W maintenance dosing regimen

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

Dosage and administration details:

At each visit, subject received 2 SC injections (each 1.0 mL) of 150 mg tralokinumab Q2W to receive a total dose of 300 mg tralokinumab.
IMP was administered by a qualified, unblinded HCP.
The injections were administered into the SC tissue of the upper arm, anterior thigh, or abdomen, separated by at least 3 cm.

Arm title	Maintenance Treatment Period - Tralokinumab 300 mg Q4W

Arm description:

Week 16 to Week 52:

Subjects achieving a clinical response at Week 16 and initially randomised to tralokinumab re-randomised to tralokinumab 300 mg Q4W maintenance dosing regimen

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

Dosage and administration details:

At each visit, subject received alternating dose administrations: 2 SC injections (each 1.0 mL) of 150 mg tralokinumab to receive a total dose of 300 mg tralokinumab and 2 SC injections (each 1.0 mL) of placebo.
IMP was administered by a qualified, unblinded HCP.
The injections were administered into the SC tissue of the upper arm, anterior thigh, or abdomen, separated by at least 3 cm.

Arm title	Maintenance Treatment Period - Placebo Q2W

Arm description:

Week 16 to Week 52:

Subjects achieving a clinical response at Week 16 and initially randomised to tralokinumab re-randomised to placebo Q2W dosing regimen

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

Dosage and administration details:

At each visit, subject received 2 SC injections (each 1.0 mL) of placebo Q2W to receive a total dose of placebo.
IMP was administered by a qualified, unblinded HCP.
The injections were administered into the SC tissue of the upper arm, anterior thigh, or abdomen, separated by at least 3 cm.

Arm title	Maintenance Treatment Period -Placebo Q2W - Tralokinumab Naive

Arm description:

Week 16 to Week 52:

Subjects achieving a clinical response at Week 16 and initially randomised to placebo re-assigned to placebo Q2W.

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

Dosage and administration details:

At each visit, subject received 2 SC injections (each 1.0 mL) of placebo Q2W to receive a total dose of placebo.
IMP was administered by a qualified, unblinded HCP.
The injections were administered into the SC tissue of the upper arm, anterior thigh, or abdomen, separated by at least 3 cm.

Number of subjects in period 3[2]	Maintenance Treatment Period - Tralokinumab 300 mg Q2W	Maintenance Treatment Period - Tralokinumab 300 mg Q4W	Maintenance Treatment Period - Placebo Q2W
Started	91	90	46
Completed	52	50	15
Not completed	39	40	31
Discontinued IMP	9	13	5
Completed Week 50	1	-	-
Transfer to open-label treatment	29	26	26
Not dosed - transfer to open-label	-	1	-

Number of subjects in period 3[2]	Maintenance Treatment Period - Placebo Q2W - Tralokinumab Naive
Started	31
Completed	16
Not completed	15
Discontinued IMP	7
Completed Week 50	-
Transfer to open-label treatment	8
Not dosed - transfer to open-label	-

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Maintenance treatment phase was in parallel to the Open-label treatment phase. Subjects from the initial treatment phase entered either into the Open-label treatment phase or Maintenance treatment phase.

Baseline characteristics

Reporting groups	
Reporting group title	Initial Treatment Period - Tralokinumab 300 mg Q2W
Reporting group description: Week 0 to Week 16: Tralokinumab 300 mg Q2W Tralokinumab: Tralokinumab is a human recombinant monoclonal antibody of the IgG4 subclass that specifically binds to human IL-13 and blocks interaction with the IL-13 receptors. It is presented as a liquid formulation for SC administration	
Reporting group title	Initial Treatment Period - Placebo Q2W
Reporting group description: Week 0 to Week 16: Placebo Q2W Placebo: Placebo contains the same excipients, in the same concentration, only lacking tralokinumab	

Reporting group values	Initial Treatment Period - Tralokinumab 300 mg Q2W	Initial Treatment Period - Placebo Q2W	Total
Number of subjects	593	201	794
Age categorical Units: Subjects			
Adults (18-64 years)	563	194	757
From 65-84 years	29	7	36
85 years and over	1	0	1
Age continuous Units: years			
arithmetic mean	37.2	35.1	
standard deviation	± 14.7	± 14.0	-
Gender categorical Units: Subjects			
Female	234	87	321
Male	359	114	473
Race/Ethnicity Units: Subjects			
White	374	123	497
Black or African American	43	17	60
Asian	154	52	206
American Indian or Alaska native	2	0	2
Native Hawaiian or Other Pacific Islander	1	0	1
Other	19	9	28
Investigator's Global Assessment			
Measure Description: The Investigator's Global Assessment (IGA) is an instrument used in clinical trials to rate the severity of the subject's global atopic dermatitis and is based on a 5-point scale ranging from 0 (clear) to 4 (severe)			
Units: Subjects			
Clear	0	0	0
Almost clear	0	0	0

Mild	0	0	0
Moderate	305	100	405
Severe	286	101	387
Missing	2	0	2
Eczema Area and Severity Index			
Measure Description: The Eczema Area and Severity Index (EASI) is a validated measure used in clinical practice and clinical trials to assess the severity and extent of atopic dermatitis. The EASI is a composite index with scores ranging from 0 to 72, with higher values indicating more severe and/or more extensive condition. Measure Analysis Population Description: Number of subjects analysed = subjects with available data for the baseline parameter.			
Units: Units on scale			
arithmetic mean	32.1	32.6	
standard deviation	± 14.3	± 13.9	-
Scoring Atopic Dermatitis			
Measure Description: The Scoring Atopic Dermatitis (SCORAD) is a validated tool to evaluate the extent and severity of AD lesions, along with subjective symptoms. The maximum total score is 103, with higher values indicating more severe disease. Measure Analysis Population Description: Number of subjects analysed = subjects with available data for the baseline parameter.			
Units: Units on scale			
arithmetic mean	70.0	70.5	
standard deviation	± 13.4	± 12.2	-
Dermatology Life Quality Index			
The Dermatology Life Quality Index (DLQI) 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 over the last week such as dermatology-related symptoms and feelings, daily activities, leisure, work or school, personal relationships, and the treatment (1). 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 health-related quality of life.			
Units: Units on scale			
arithmetic mean	17.7	17.8	
standard deviation	± 7.1	± 7.3	-
Worst Daily Pruritus Numeric rating scale (weekly average)			
Measure Description: Subjects assess their worst itch severity over the past 24 hours using an 11-point NRS (Numeric rating scale; 'Worst Daily Pruritus NRS') with 0 indicating 'no itch' and 10 indicating 'worst itch imaginable'. Measure Analysis Population Description: Number of subjects analysed = subjects with available data for the baseline parameter.			
Units: Units on scale			
arithmetic mean	7.9	8.0	
standard deviation	± 1.5	± 1.4	-
Body surface area affected by AD			
Units: percent			
arithmetic mean	52.6	53.0	
standard deviation	± 25.6	± 25.0	-
Age of onset of atopic dermatitis (AD)			
Measure Analysis Population Description: Number of subjects analysed = subjects with available data for the baseline parameter.			
Units: Years			
median	2.0	2.0	
inter-quartile range (Q1-Q3)	1.0 to 12.0	1.0 to 9.0	-
Duration of atopic dermatitis (AD)			
Measure Analysis Population Description: Number of subjects analysed = subjects with available data for the baseline parameter.			
Units: Years			

arithmetic mean	28.3	27.5	
standard deviation	± 15.9	± 14.7	-

End points

End points reporting groups

Reporting group title	Initial Treatment Period - Tralokinumab 300 mg Q2W

Reporting group description:

Week 0 to Week 16:

Tralokinumab 300 mg Q2W

Tralokinumab: Tralokinumab is a human recombinant monoclonal antibody of the IgG4 subclass that specifically binds to human IL-13 and blocks interaction with the IL-13 receptors. It is presented as a liquid formulation for SC administration

Reporting group title	Initial Treatment Period - Placebo Q2W

Reporting group description:

Week 0 to Week 16:

Placebo Q2W

Placebo: Placebo contains the same excipients, in the same concentration, only lacking tralokinumab

Reporting group title	Open-label Treatment -Tralokinumab 300 mg Q2W + Optional TCS

Reporting group description:

Week 16 to Week 52:
Subjects receiving initial treatment with tralokinumab/placebo Q2W who did not achieve protocol-defined clinical response assigned to open-label treatment at Week 16 with tralokinumab 300 mg Q2W regimen + optional topical corticosteroids (TCS)
OR
Subjects receiving maintenance treatment with tralokinumab 300 mg Q2W/Q4W or placebo Q2W assigned to open-label treatment after Week 16 with tralokinumab 300 mg Q2W regimen + optional TCS if:
-IGA of at least 2 and not achieving EASI75 over at least a 4-week period (over 3 consecutive visits) for subjects with IGA=0 at Week 16;
OR
-IGA of at least 3 and not achieving EASI75 over at least a 4-week period (i.e. over 3 consecutive visits) for subjects with IGA=1 at Week 16;
OR
-Not achieving EASI75 over at least a 4-week period (over 3 consecutive visits) for subjects with IGA>1 at Week 16.

Reporting group title	Maintenance Treatment Period - Tralokinumab 300 mg Q2W

Reporting group description:

Week 16 to Week 52:

Subjects achieving a clinical response at Week 16 and initially randomised to tralokinumab re-randomised to tralokinumab 300 mg Q2W maintenance dosing regimen

Reporting group title	Maintenance Treatment Period - Tralokinumab 300 mg Q4W

Reporting group description:

Week 16 to Week 52:

Subjects achieving a clinical response at Week 16 and initially randomised to tralokinumab re-randomised to tralokinumab 300 mg Q4W maintenance dosing regimen

Reporting group title	Maintenance Treatment Period - Placebo Q2W

Reporting group description:

Week 16 to Week 52:

Subjects achieving a clinical response at Week 16 and initially randomised to tralokinumab re-randomised to placebo Q2W dosing regimen

Reporting group title	Maintenance Treatment Period -Placebo Q2W - Tralokinumab Naive

Reporting group description:

Week 16 to Week 52:

Subjects achieving a clinical response at Week 16 and initially randomised to placebo re-assigned to placebo Q2W.

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

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

End point description:

The IGA is an instrument used in clinical trials to rate the severity of the subject's global AD and is based on a 5-point scale ranging from 0 (clear) to 4 (severe).
The full analysis set (FAS: all subjects randomised to initial treatment who were exposed to IMP) was used for the primary analysis; 794 subjects were randomised to initial treatment and 792 received IMP, thus the FAS comprised 792 subjects.

End point type	Primary

End point timeframe:

At Week 16

End point values	Initial Treatment Period - Tralokinumab 300 mg Q2W	Initial Treatment Period - Placebo Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	591	201		
Units: Number of subjects	131	22		

Statistical analyses

Statistical analysis title	Tralokinumab 300 mg Q2W vs Placebo Q2W
Comparison groups	Initial Treatment Period - Tralokinumab 300 mg Q2W v Initial Treatment Period - Placebo Q2W
Number of subjects included in analysis	792
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	< 0.001 [2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	11.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.8
upper limit	16.4

Notes:

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

[2] - Based on primary analysis of primary estimand composite. Subjects with missing data or subjects who received rescue medication prior to Week 16 were considered non-responders.
Primary endpoints tested sequentially at a 5% significance level.

Primary: Subjects Achieving at Least 75% Reduction in Eczema Area and Severity Index [EASI].

End point title	Subjects Achieving at Least 75% Reduction in Eczema Area and Severity Index [EASI].

End point description:

The EASI is a validated measure used in clinical practice and clinical trials to assess the severity and extent of AD. The EASI is a composite index with scores ranging from 0 to 72, with higher values indicating more severe and/or more extensive condition. The FAS was used for the primary analysis; 794 subjects were randomised to initial treatment and 792 received IMP, thus the FAS comprised 792 subjects.

End point type	Primary

End point timeframe:

At Week 16

End point values	Initial Treatment Period - Tralokinumab 300 mg Q2W	Initial Treatment Period - Placebo Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	591	201		
Units: Number of subjects	196	23		

Statistical analyses

Statistical analysis title	Tralokinumab 300 mg Q2W vs Placebo Q2W
Comparison groups	Initial Treatment Period - Tralokinumab 300 mg Q2W v Initial Treatment Period - Placebo Q2W
Number of subjects included in analysis	792
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	< 0.001 [4]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	21.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	15.8
upper limit	27.3

Notes:

[3] - Analysis was performed using Cochran-Mantel-Haenszel test stratified by region and baseline disease severity.The null hypothesis of no difference in response rates between tralokinumab and placebo were tested against the 2-sided alternative that there is a difference.
[4] - Based on the primary analysis of primary estimand 'composite'. Subjects with missing data or subjects who received rescue medication prior to Week 16 were considered non-responders.

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

End point title	Change in Scoring Atopic Dermatitis (SCORAD) From Baseline to Week 16.

End point description:

The SCORAD is a validated tool to evaluate the extent and severity of AD lesions, along with subjective symptoms. The maximum total score is 103, with higher values indicating more severe disease.

End point type	Secondary

End point timeframe:

Week 0 to Week 16

End point values	Initial Treatment Period - Tralokinumab 300 mg Q2W	Initial Treatment Period - Placebo Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	591	201		
Units: Units on scale				
least squares mean (standard error)	-28.1 (± 0.92)	-14.0 (± 1.79)		

Statistical analyses

Statistical analysis title	Tralokinumab 300 mg Q2W vs Placebo Q2W

Statistical analysis description:

Data collected after permanent discontinuation of IMP or initiation of rescue medication not included.

Comparison groups	Initial Treatment Period - Tralokinumab 300 mg Q2W v Initial Treatment Period - Placebo Q2W
Number of subjects included in analysis	792
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	< 0.001 [6]
Method	Repeated measurements model
Parameter estimate	Difference of least square means
Point estimate	-14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18
upper limit	-10.1

Notes:

[5] - Multiplicity adjustment using the Holm method.

[6] - Based on the primary analysis of the primary estimand 'hypothetical'. Repeated measurements model on post-baseline data. In case of no post-baseline assessments before initiation of rescue medication, the Week 2 change was imputed as 0.

Secondary: Reduction of Worst Daily Pruritus Numeric Rating Scale (Weekly Average) of at Least 4 From Baseline to Week 16

End point title	Reduction of Worst Daily Pruritus Numeric Rating Scale (Weekly Average) of at Least 4 From Baseline to Week 16

End point description:

Subjects will assess their worst itch severity over the past 24 hours using an 11 point Numeric Rating Scale (NRS; 'Worst Daily Pruritus NRS') with 0 indicating 'no itch' and 10 indicating 'worst itch imaginable'.
Number of subjects analysed = subjects with baseline pruritus NRS weekly average ≥4.

End point type	Secondary

End point timeframe:

Week 0 to Week 16

End point values	Initial Treatment Period - Tralokinumab 300 mg Q2W	Initial Treatment Period - Placebo Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	575	200		
Units: Number of subjects	144	19		

Statistical analyses

Statistical analysis title	Tralokinumab 300 mg Q2W vs Placebo Q2W
Comparison groups	Initial Treatment Period - Tralokinumab 300 mg Q2W v Initial Treatment Period - Placebo Q2W
Number of subjects included in analysis	775
Analysis specification	Pre-specified
Analysis type	superiority[7]
P-value	< 0.001 [8]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	15.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.3
upper limit	20.9

Notes:

[7] - Multiplicity adjustment using Holm method.

[8] - Based on the primary analysis of the primary estimand 'Composite', subjects who received rescue medication prior to Week 16 or have missing data at Week 16 were considered as non-responders'.

Secondary: Change in Dermatology Life Quality Index (DLQI) Score From Baseline to Week 16.

End point title	Change in Dermatology Life Quality Index (DLQI) Score From Baseline to Week 16.

End point description:

The 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 quality of life (QoL) 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 QoL.

End point type	Secondary

End point timeframe:

Week 0 to Week 16

End point values	Initial Treatment Period - Tralokinumab 300 mg Q2W	Initial Treatment Period - Placebo Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	591	201		
Units: Units on scale				
least squares mean (standard error)	-8.8 (± 0.30)	-4.9 (± 0.60)		

Statistical analyses

Statistical analysis title	Tralokinumab 300 mg Q2W vs Placebo Q2W

Statistical analysis description:

Data collected after permanent discontinuation of IMP or initiation of rescue medication not included.

Comparison groups	Initial Treatment Period - Tralokinumab 300 mg Q2W v Initial Treatment Period - Placebo Q2W
Number of subjects included in analysis	792
Analysis specification	Pre-specified
Analysis type	superiority[9]
P-value	< 0.001 [10]
Method	Repeated measurements model
Parameter estimate	Difference of least square means
Point estimate	-3.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.2
upper limit	-2.6

Notes:

[9] - Multiplicity adjustment using Holm method.

[10] - Based on the primary analysis of the primary estimand 'hypothetical'. Repeated measurements model on post-baseline data. In case of no post-baseline assessments before initiation of rescue medication, the Week 2 change was imputed as 0.

Secondary: Subjects With Investigator's Global Assessment (IGA) Score of 0 (Clear) or 1 (Almost Clear) at Week 52 Among Subjects With IGA of 0/1 at Week 16

End point title	Subjects With Investigator's Global Assessment (IGA) Score of 0 (Clear) or 1 (Almost Clear) at Week 52 Among Subjects With IGA of 0/1 at Week 16

End point description:

The IGA is an instrument used in clinical trials to rate the severity of the subject's global AD and is

based on a 5-point scale ranging from 0 (clear) to 4 (severe).
Maintenance analysis set - Subjects who achieved IGA 0/1 at Week 16 after initial treatment with tralokinumab without use of rescue medication.

End point type	Secondary
End point timeframe:	
At Week 52	

End point values	Maintenance Treatment Period - Tralokinumab 300 mg Q2W	Maintenance Treatment Period - Tralokinumab 300 mg Q4W	Maintenance Treatment Period - Placebo Q2W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	49	28	
Units: Number of subjects	32	22	7	

Statistical analyses

Statistical analysis title	Tralokinumab 300 mg Q2W vs Placebo Q2W
Statistical analysis description:	
Testing according to the hierarchical testing procedure in the order: IGA 0/1 at Week 52 between Q2W vs Placebo, EASI75 at Week 52 between Q2W vs Placebo, IGA 0/1 at Week 52 between Q4W vs Placebo, and EASI75 at Week 52 between Q4W vs Placebo	
Comparison groups	Maintenance Treatment Period - Tralokinumab 300 mg Q2W v Maintenance Treatment Period - Placebo Q2W
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004 [11]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	34.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.4
upper limit	54.9

Notes:

[11] - Based on the primary analysis of the 'composite' estimand. Subjects who received rescue medication or were transferred to open-label treatment were considered non-responders.

Statistical analysis title	Tralokinumab 300 mg Q4W vs Placebo Q2W
Statistical analysis description:	
Testing according to the hierarchical testing procedure in the order: IGA 0/1 at Week 52 between Q2W vs Placebo, EASI75 at Week 52 between Q2W vs Placebo, IGA 0/1 at Week 52 between Q4W vs Placebo, and EASI75 at Week 52 between Q4W vs Placebo	
Comparison groups	Maintenance Treatment Period - Placebo Q2W v Maintenance

	Treatment Period - Tralokinumab 300 mg Q4W
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	superiority[12]
P-value	= 0.084 [13]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	19.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	40.9

Notes:

[12] - This test was not statistically significant and hence next maintenance endpoint in the sequential testing procedure was not evaluated
[13] - Based on the primary analysis of the 'composite' estimand. Subjects who received rescue medication or were transferred to open-label treatment were considered non-responders.
The P value was considered non-significant.

Secondary: Subjects With at Least 75% Reduction in Eczema Area and Severity Index [EASI] at Week 52 Among Subjects With EASI75 at Week 16

End point title	Subjects With at Least 75% Reduction in Eczema Area and Severity Index [EASI] at Week 52 Among Subjects With EASI75 at Week 16

End point description:

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

End point type	Secondary

End point timeframe:

At Week 52

End point values	Maintenance Treatment Period - Tralokinumab 300 mg Q2W	Maintenance Treatment Period - Tralokinumab 300 mg Q4W	Maintenance Treatment Period - Placebo Q2W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	77	74	42	
Units: Number of subjects	43	38	9	

Statistical analyses

Statistical analysis title	Tralokinumab 300 mg Q2W vs Placebo Q2W

Statistical analysis description:

Testing according to the hierarchical testing procedure in the order:
IGA 0/1 at Week 52 between Q2W vs Placebo,
EASI75 at Week 52 between Q2W vs Placebo,
IGA 0/1 at Week 52 between Q4W vs Placebo, and
EASI75 at Week 52 between Q4W vs Placebo

Comparison groups	Maintenance Treatment Period - Tralokinumab 300 mg Q2W v Maintenance Treatment Period - Placebo Q2W
Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	superiority[14]
P-value	< 0.001 [15]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	33.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	17.3
upper limit	50

Notes:

[14] - Testing according to the hierarchical testing procedure (only performed if the previous outcome measure was statistically significant).
[15] - Based on the primary analysis of the primary estimand 'composite'. Subjects who received rescue medication or were transferred to open-label treatment are considered non-responders.

Statistical analysis title	Tralokinumab 300 mg Q4W vs Placebo Q2W

Statistical analysis description:

Testing according to the hierarchical testing procedure in the order:
IGA 0/1 at Week 52 between Q2W vs Placebo,
EASI75 at Week 52 between Q2W vs Placebo,
IGA 0/1 at Week 52 between Q4W vs Placebo, and
EASI75 at Week 52 between Q4W vs Placebo

Comparison groups	Maintenance Treatment Period - Tralokinumab 300 mg Q4W v Maintenance Treatment Period - Placebo Q2W
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001 [16]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	30
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.7
upper limit	46.4

Notes:

[16] - Test not evaluated for statistical significance. Based on the primary analysis of the 'composite' estimand. Subjects who received rescue medication or were transferred to open-label treatment were considered non-responders.

Secondary: Safety and Tolerability: Adverse event (AE) /Serious adverse event (SAE) Frequency

End point title	Safety and Tolerability: Adverse event (AE) /Serious adverse event (SAE) Frequency

End point description:

Overall summary of AEs and SAEs during the Initial treatment period is presented. For list of AEs and SAEs by MedDRA system organ class (SOC) and preferred term (PT) during the entire trial period (including safety follow-up), see Adverse Events Overview section.

End point type	Secondary

End point timeframe:
Week 0 to Week 16

End point values	Initial Treatment Period - Tralokinumab 300 mg Q2W	Initial Treatment Period - Placebo Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	592	200		
Units: Number of subjects				
AE	364	132		
SAE	10	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of Anti-drug Antibodies

End point title	Frequency of Anti-drug Antibodies

End point description:
Anti-tralokinumab antibody levels were analysed using a validated bioanalytical method

End point type	Secondary

End point timeframe:
Week 0 to Week 16

End point values	Initial Treatment Period - Tralokinumab 300 mg Q2W	Initial Treatment Period - Placebo Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	592	200		
Units: Number of subjects				
Total positive	10	3		
Pre-existing	2	1		
Treatment emergent	8	2		
Perishing	6	2		
Negative	558	185		
No post-baseline ADA assessment	18	10		

Statistical analyses

No statistical analyses for this end point

Secondary: Subjects Achieving at Least 50% Reduction in Eczema Area and Severity Index [EASI] at Week 16

End point title	Subjects Achieving at Least 50% Reduction in Eczema Area and Severity Index [EASI] at Week 16

End point description:

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

End point type	Secondary

End point timeframe:

At Week 16

End point values	Initial Treatment Period - Tralokinumab 300 mg Q2W	Initial Treatment Period - Placebo Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	591	201		
Units: Number of subjects	295	41		

Statistical analyses

Statistical analysis title	Tralokinumab 300 mg Q2W vs Placebo Q2W

Statistical analysis description:

Based on the primary analysis of the primary estimand 'composite'. Subjects with missing data or subjects who received rescue medication prior to Week 16 were considered non-responders

Comparison groups	Initial Treatment Period - Tralokinumab 300 mg Q2W v Initial Treatment Period - Placebo Q2W
Number of subjects included in analysis	792
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [17]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	29.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	22.5
upper limit	36.1

Notes:

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

Secondary: Subjects Achieving at Least 90% Reduction in Eczema Area and Severity Index [EASI] at Week 16.

End point title	Subjects Achieving at Least 90% Reduction in Eczema Area and Severity Index [EASI] at Week 16.

End point description:

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

End point type	Secondary

End point timeframe:

At Week 16

End point values	Initial Treatment Period - Tralokinumab 300 mg Q2W	Initial Treatment Period - Placebo Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	591	201		
Units: Number of subjects	108	11		

Statistical analyses

Statistical analysis title	Tralokinumab 300 mg Q2W vs Placebo Q2W
Comparison groups	Initial Treatment Period - Placebo Q2W v Initial Treatment Period - Tralokinumab 300 mg Q2W
Number of subjects included in analysis	792
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [18]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	12.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.3
upper limit	17

Notes:

[18] - Based on the primary analysis of the primary estimand 'composite'. Subjects with missing data or subjects who received rescue medication prior to Week 16 were considered non-responders. The statistical test was not controlled for multiplicity.

Secondary: Change From Baseline to Week 16 in Eczema Area and Severity Index [EASI] Score

End point title	Change From Baseline to Week 16 in Eczema Area and Severity Index [EASI] Score

End point description:

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

End point type	Secondary

End point timeframe:

At Week 16

End point values	Initial Treatment Period - Tralokinumab 300 mg Q2W	Initial Treatment Period - Placebo Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	591	201		
Units: Units on scale				
least squares mean (confidence interval 95%)	-16.9 (-18.0 to -15.8)	-7.0 (-9.1 to -5.0)		

Statistical analyses

Statistical analysis title	Tralokinumab 300 mg Q2W vs Placebo Q2W

Statistical analysis description:

Data collected after permanent discontinuation of IMP or initiation of rescue medication not included. In case of no post-baseline assessments before initiation of rescue medication, the Week 2 change will be imputed as 0.

Comparison groups	Initial Treatment Period - Placebo Q2W v Initial Treatment Period - Tralokinumab 300 mg Q2W
Number of subjects included in analysis	792
Analysis specification	Pre-specified
Analysis type	superiority[19]
P-value	< 0.001 [20]
Method	Repeated measurements model
Parameter estimate	Difference of least square means
Point estimate	-9.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.2
upper limit	-7.5

Notes:

[19] - Data collected after permanent discontinuation of IMP or initiation of rescue medication not included. In case of no post-baseline assessments before initiation of rescue medication, the Week 2 change will be imputed as 0.

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

Secondary: Subjects Achieving at Least 75% Reduction in Scoring Atopic Dermatitis (SCORAD) at Week 16.

End point title	Subjects Achieving at Least 75% Reduction in Scoring Atopic Dermatitis (SCORAD) at Week 16.

End point description:

The SCORAD is a validated tool to evaluate the extent and severity of AD lesions, along with subjective symptoms. The maximum total score is 103, with higher values indicating more severe disease.

End point type	Secondary

End point timeframe:

At Week 16

End point values	Initial Treatment Period - Tralokinumab 300 mg Q2W	Initial Treatment Period - Placebo Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	591	201		
Units: Number of subjects	68	7		

Statistical analyses

Statistical analysis title	Tralokinumab 300 mg Q2W vs Placebo Q2W
Comparison groups	Initial Treatment Period - Tralokinumab 300 mg Q2W v Initial Treatment Period - Placebo Q2W
Number of subjects included in analysis	792
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [21]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	8
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.4
upper limit	11.6

Notes:

[21] - Based on the primary analysis of the 'composite' estimand. Subjects who received rescue medication prior to Week 16 or with missing data at Week 16 were considered non-responders. The statistical test was not controlled for multiplicity.

Secondary: Subjects Achieving at Least 50% Reduction in Scoring Atopic Dermatitis (SCORAD) at Week 16.

End point title	Subjects Achieving at Least 50% Reduction in Scoring Atopic Dermatitis (SCORAD) at Week 16.

End point description:

The SCORAD is a validated tool to evaluate the extent and severity of AD lesions, along with subjective symptoms. The maximum total score is 103, with higher values indicating more severe disease.

End point type	Secondary

End point timeframe:

At Week 16

End point values	Initial Treatment Period - Tralokinumab 300 mg Q2W	Initial Treatment Period - Placebo Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	591	201		
Units: Number of subjects	198	29		

Statistical analyses

Statistical analysis title	Tralokinumab 300 mg Q2W vs Placebo Q2W
Comparison groups	Initial Treatment Period - Tralokinumab 300 mg Q2W v Initial Treatment Period - Placebo Q2W
Number of subjects included in analysis	792
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [22]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	18.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	12.8
upper limit	25.1

Notes:

[22] - Based on the primary analysis of the 'composite' estimand. Subjects who received rescue medication prior to Week 16 or with missing data at Week 16 were considered non-responders. The statistical test was not controlled for multiplicity.

Secondary: Change From Baseline to Week 16 in Worst Daily Pruritus NRS (Weekly Average).

End point title	Change From Baseline to Week 16 in Worst Daily Pruritus NRS (Weekly Average).

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'

End point type	Secondary

End point timeframe:

At Week 16

End point values	Initial Treatment Period - Tralokinumab 300 mg Q2W	Initial Treatment Period - Placebo Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	584	200		
Units: Units on scale				
least squares mean (confidence interval	-2.9 (-3.1 to	-1.6 (-2.0 to		

95%)	-2.6)	-1.2)

Statistical analyses

Statistical analysis title	Tralokinumab 300 mg Q2W vs Placebo Q2W

Statistical analysis description:

Data collected after permanent discontinuation of IMP or initiation of rescue medication not included. In case of no post-baseline assessments before initiation of rescue medication, the Week 1 change will be imputed as 0.

Comparison groups	Initial Treatment Period - Tralokinumab 300 mg Q2W v Initial Treatment Period - Placebo Q2W
Number of subjects included in analysis	784
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [23]
Method	Repeated measurements model
Parameter estimate	Difference of least square means
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	-0.8

Notes:

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

Secondary: Reduction of Worst Daily Pruritus NRS (Weekly Average) ≥3 From Baseline to Week 16.

End point title	Reduction of Worst Daily Pruritus NRS (Weekly Average) ≥3 From Baseline 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'.
Number of subjects analysed = subjects with baseline Pruritus NRS weekly average of at least 3.

End point type	Secondary

End point timeframe:

Baseline to Week 16

End point values	Initial Treatment Period - Tralokinumab 300 mg Q2W	Initial Treatment Period - Placebo Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	583	200		
Units: Number of subjects	199	28		

Statistical analyses

Statistical analysis title	Tralokinumab 300 mg Q2W vs Placebo Q2W
Comparison groups	Initial Treatment Period - Placebo Q2W v Initial Treatment Period - Tralokinumab 300 mg Q2W
Number of subjects included in analysis	783
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [24]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference of least square means
Point estimate	20.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.9
upper limit	26.2

Notes:

[24] - Subjects who received rescue medication prior to Week 16 or have missing data at Week 16 were considered as non-responders. The statistical test was not controlled for multiplicity.

Secondary: Reduction From Baseline to Week 16 of Dermatology Life Quality Index (DLQI) of ≥4 Points Among Subjects With Baseline DLQI ≥4.

End point title	Reduction From Baseline to Week 16 of Dermatology Life Quality Index (DLQI) of ≥4 Points Among Subjects With Baseline DLQI ≥4.

End point description:

The 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 QoL 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 QoL.
Number of subjects analysed = subjects with baseline DLQI ≥4.

End point type	Secondary

End point timeframe:

Baseline to Week 16

End point values	Initial Treatment Period - Tralokinumab 300 mg Q2W	Initial Treatment Period - Placebo Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	577	198		
Units: Number of subjects	325	54		

Statistical analyses

Statistical analysis title	Tralokinumab 300 mg Q2W vs Placebo Q2W
Comparison groups	Initial Treatment Period - Tralokinumab 300 mg Q2W v Initial Treatment Period - Placebo Q2W
Number of subjects included in analysis	775
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [25]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	28.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	21.4
upper limit	36.3

Notes:

[25] - Subjects who received rescue medication prior to Week 16 or have missing data at Week 16 were considered as non-responders. The statistical test was not controlled for multiplicity.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Initial Treatment Period: Week 0 to Week 16;
Maintenance Treatment Period: Week 16 to Week 52;
Open-label Treatment: Week 16 to Week 52;
Safety follow-up Period (All treatment arms): Week 52 to Week 66

Adverse event reporting additional description:

After completion of the maintenance treatment period (or open-label treatment), all subjects, except for those who entered the open-label long-term extension trial, continued in a 14-week off-treatment follow-up period for the assessment of safety and ADA.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20

Reporting groups

Reporting group title	Initial Period - Tralokinumab Q2W
Reporting group description: -	
Reporting group title	Initial Period - Placebo Q2W
Reporting group description: -	
Reporting group title	Maintenance Period - Tralokinumab Q2W
Reporting group description: -	
Reporting group title	Maintenance Period - Tralokinumab Q4W
Reporting group description: -	
Reporting group title	Maintenance Period - Placebo Q2W
Reporting group description: -	
Reporting group title	Maintenance Period - Placebo Q2W - Tralokinumab Naive
Reporting group description: -	
Reporting group title	Open-label Period - Tralokinumab 300 mg Q2W + Optional TCS
Reporting group description: -	
Reporting group title	Safety Follow-up (All treatment arms)

Reporting group description:

Safety Follow-up (n=641, PYE=142.90) includes subjects from Initial, Maintenance and Open-label Periods:
Tralokinumab Q2W (n=83); Tralokinumab Q4W (n=50); Tralokinumab Q2W + optional TCS (n=454); Placebo (n=54)

Serious adverse events	Initial Period - Tralokinumab Q2W	Initial Period - Placebo Q2W	Maintenance Period - Tralokinumab Q2W
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 592 (1.69%)	5 / 200 (2.50%)	0 / 91 (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)			
Angiosarcoma			

subjects affected / exposed	1 / 592 (0.17%)	0 / 200 (0.00%)	0 / 91 (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
Papillary thyroid cancer			
subjects affected / exposed	0 / 592 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 592 (0.17%)	0 / 200 (0.00%)	0 / 91 (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
Surgical and medical procedures			
Ovarian cystectomy			
subjects affected / exposed	0 / 592 (0.00%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 592 (0.00%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 592 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Pulmonary embolism			
subjects affected / exposed	1 / 592 (0.17%)	0 / 200 (0.00%)	0 / 91 (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
Status asthmaticus			
subjects affected / exposed	1 / 592 (0.17%)	0 / 200 (0.00%)	0 / 91 (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

Psychiatric disorders			
Depression suicidal			
subjects affected / exposed	1 / 592 (0.17%)	0 / 200 (0.00%)	0 / 91 (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
Schizophrenia			
subjects affected / exposed	0 / 592 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Product issues			
Device dislocation			
subjects affected / exposed	0 / 592 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Injury, poisoning and procedural complications			
Facial bones fracture			
subjects affected / exposed	0 / 592 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Head injury			
subjects affected / exposed	0 / 592 (0.00%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intentional overdose			
subjects affected / exposed	1 / 592 (0.17%)	0 / 200 (0.00%)	0 / 91 (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
Radius fracture			
subjects affected / exposed	0 / 592 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Road traffic accident			

subjects affected / exposed	0 / 592 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Cardiac disorders			
Pericarditis			
subjects affected / exposed	0 / 592 (0.00%)	1 / 200 (0.50%)	0 / 91 (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			
Dizziness			
subjects affected / exposed	0 / 592 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Neurological symptom			
subjects affected / exposed	0 / 592 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Syncope			
subjects affected / exposed	0 / 592 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Blood and lymphatic system disorders			
Benign ethnic neutropenia			
subjects affected / exposed	0 / 592 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Eye disorders			
Cataract subcapsular			
subjects affected / exposed	0 / 592 (0.00%)	1 / 200 (0.50%)	0 / 91 (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
Retinal detachment			

subjects affected / exposed	0 / 592 (0.00%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 592 (0.00%)	1 / 200 (0.50%)	0 / 91 (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
Duodenal ulcer			
subjects affected / exposed	1 / 592 (0.17%)	0 / 200 (0.00%)	0 / 91 (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
Gastric perforation			
subjects affected / exposed	0 / 592 (0.00%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	1 / 592 (0.17%)	0 / 200 (0.00%)	0 / 91 (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
Erythema			
subjects affected / exposed	0 / 592 (0.00%)	1 / 200 (0.50%)	0 / 91 (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
Photosensitivity reaction			
subjects affected / exposed	0 / 592 (0.00%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Eczema herpeticum			
subjects affected / exposed	0 / 592 (0.00%)	0 / 200 (0.00%)	0 / 91 (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

Gastroenteritis viral			
subjects affected / exposed	1 / 592 (0.17%)	0 / 200 (0.00%)	0 / 91 (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
Keratitis viral			
subjects affected / exposed	0 / 592 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Pilonidal cyst			
subjects affected / exposed	0 / 592 (0.00%)	1 / 200 (0.50%)	0 / 91 (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
Pneumonia			
subjects affected / exposed	1 / 592 (0.17%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection			
subjects affected / exposed	0 / 592 (0.00%)	1 / 200 (0.50%)	0 / 91 (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
Staphylococcal abscess			
subjects affected / exposed	0 / 592 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 592 (0.00%)	0 / 200 (0.00%)	0 / 91 (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

Serious adverse events	Maintenance Period - Tralokinumab Q4W	Maintenance Period - Placebo Q2W	Maintenance Period - Placebo Q2W - Tralokinumab Naive
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 89 (3.37%)	0 / 46 (0.00%)	0 / 31 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from	0	0	0

adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Angiosarcoma			
subjects affected / exposed	0 / 89 (0.00%)	0 / 46 (0.00%)	0 / 31 (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
Papillary thyroid cancer			
subjects affected / exposed	1 / 89 (1.12%)	0 / 46 (0.00%)	0 / 31 (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
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 89 (0.00%)	0 / 46 (0.00%)	0 / 31 (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
Surgical and medical procedures			
Ovarian cystectomy			
subjects affected / exposed	0 / 89 (0.00%)	0 / 46 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 89 (0.00%)	0 / 46 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 89 (0.00%)	0 / 46 (0.00%)	0 / 31 (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
Pulmonary embolism			
subjects affected / exposed	0 / 89 (0.00%)	0 / 46 (0.00%)	0 / 31 (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
Status asthmaticus			

subjects affected / exposed	0 / 89 (0.00%)	0 / 46 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression suicidal			
subjects affected / exposed	0 / 89 (0.00%)	0 / 46 (0.00%)	0 / 31 (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
Schizophrenia			
subjects affected / exposed	1 / 89 (1.12%)	0 / 46 (0.00%)	0 / 31 (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
Product issues			
Device dislocation			
subjects affected / exposed	0 / 89 (0.00%)	0 / 46 (0.00%)	0 / 31 (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
Injury, poisoning and procedural complications			
Facial bones fracture			
subjects affected / exposed	0 / 89 (0.00%)	0 / 46 (0.00%)	0 / 31 (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
Head injury			
subjects affected / exposed	0 / 89 (0.00%)	0 / 46 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intentional overdose			
subjects affected / exposed	0 / 89 (0.00%)	0 / 46 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	0 / 89 (0.00%)	0 / 46 (0.00%)	0 / 31 (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

Road traffic accident			
subjects affected / exposed	0 / 89 (0.00%)	0 / 46 (0.00%)	0 / 31 (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
Cardiac disorders			
Pericarditis			
subjects affected / exposed	0 / 89 (0.00%)	0 / 46 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 89 (1.12%)	0 / 46 (0.00%)	0 / 31 (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
Neurological symptom			
subjects affected / exposed	0 / 89 (0.00%)	0 / 46 (0.00%)	0 / 31 (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
Syncope			
subjects affected / exposed	0 / 89 (0.00%)	0 / 46 (0.00%)	0 / 31 (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
Blood and lymphatic system disorders			
Benign ethnic neutropenia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 46 (0.00%)	0 / 31 (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
Eye disorders			
Cataract subcapsular			
subjects affected / exposed	0 / 89 (0.00%)	0 / 46 (0.00%)	0 / 31 (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
Retinal detachment			

subjects affected / exposed	0 / 89 (0.00%)	0 / 46 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 89 (0.00%)	0 / 46 (0.00%)	0 / 31 (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
Duodenal ulcer			
subjects affected / exposed	0 / 89 (0.00%)	0 / 46 (0.00%)	0 / 31 (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
Gastric perforation			
subjects affected / exposed	0 / 89 (0.00%)	0 / 46 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	0 / 89 (0.00%)	0 / 46 (0.00%)	0 / 31 (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
Erythema			
subjects affected / exposed	0 / 89 (0.00%)	0 / 46 (0.00%)	0 / 31 (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
Photosensitivity reaction			
subjects affected / exposed	0 / 89 (0.00%)	0 / 46 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Eczema herpeticum			
subjects affected / exposed	0 / 89 (0.00%)	0 / 46 (0.00%)	0 / 31 (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

Gastroenteritis viral			
subjects affected / exposed	0 / 89 (0.00%)	0 / 46 (0.00%)	0 / 31 (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
Keratitis viral			
subjects affected / exposed	0 / 89 (0.00%)	0 / 46 (0.00%)	0 / 31 (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
Pilonidal cyst			
subjects affected / exposed	0 / 89 (0.00%)	0 / 46 (0.00%)	0 / 31 (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
Pneumonia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 46 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection			
subjects affected / exposed	0 / 89 (0.00%)	0 / 46 (0.00%)	0 / 31 (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
Staphylococcal abscess			
subjects affected / exposed	0 / 89 (0.00%)	0 / 46 (0.00%)	0 / 31 (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
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 46 (0.00%)	0 / 31 (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

Serious adverse events	Open-label Period - Tralokinumab 300 mg Q2W + Optional TCS	Safety Follow-up (All treatment arms)	
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 558 (2.87%)	4 / 641 (0.62%)	
number of deaths (all causes)	0	0	

number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Angiosarcoma			
subjects affected / exposed	0 / 558 (0.00%)	0 / 641 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Papillary thyroid cancer			
subjects affected / exposed	0 / 558 (0.00%)	0 / 641 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 558 (0.00%)	0 / 641 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Ovarian cystectomy			
subjects affected / exposed	1 / 558 (0.18%)	0 / 641 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	2 / 558 (0.36%)	0 / 641 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 558 (0.18%)	0 / 641 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 558 (0.00%)	0 / 641 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status asthmaticus			

subjects affected / exposed	0 / 558 (0.00%)	1 / 641 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression suicidal			
subjects affected / exposed	0 / 558 (0.00%)	0 / 641 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Schizophrenia			
subjects affected / exposed	0 / 558 (0.00%)	0 / 641 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device dislocation			
subjects affected / exposed	1 / 558 (0.18%)	0 / 641 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Facial bones fracture			
subjects affected / exposed	1 / 558 (0.18%)	0 / 641 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	1 / 558 (0.18%)	0 / 641 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intentional overdose			
subjects affected / exposed	0 / 558 (0.00%)	0 / 641 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	1 / 558 (0.18%)	0 / 641 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Road traffic accident			
subjects affected / exposed	1 / 558 (0.18%)	0 / 641 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Pericarditis			
subjects affected / exposed	0 / 558 (0.00%)	0 / 641 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 558 (0.00%)	0 / 641 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurological symptom			
subjects affected / exposed	1 / 558 (0.18%)	0 / 641 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 558 (0.18%)	0 / 641 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Benign ethnic neutropenia			
subjects affected / exposed	1 / 558 (0.18%)	0 / 641 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract subcapsular			
subjects affected / exposed	0 / 558 (0.00%)	0 / 641 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal detachment			

subjects affected / exposed	1 / 558 (0.18%)	0 / 641 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 558 (0.00%)	0 / 641 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	0 / 558 (0.00%)	0 / 641 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric perforation			
subjects affected / exposed	0 / 558 (0.00%)	1 / 641 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	1 / 558 (0.18%)	0 / 641 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erythema			
subjects affected / exposed	0 / 558 (0.00%)	0 / 641 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Photosensitivity reaction			
subjects affected / exposed	1 / 558 (0.18%)	0 / 641 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Eczema herpeticum			
subjects affected / exposed	0 / 558 (0.00%)	1 / 641 (0.16%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastroenteritis viral			
subjects affected / exposed	0 / 558 (0.00%)	0 / 641 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Keratitis viral			
subjects affected / exposed	1 / 558 (0.18%)	0 / 641 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pilonidal cyst			
subjects affected / exposed	0 / 558 (0.00%)	0 / 641 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 558 (0.18%)	0 / 641 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin infection			
subjects affected / exposed	0 / 558 (0.00%)	0 / 641 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal abscess			
subjects affected / exposed	0 / 558 (0.00%)	1 / 641 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 558 (0.18%)	0 / 641 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Initial Period - Tralokinumab Q2W	Initial Period - Placebo Q2W	Maintenance Period - Tralokinumab Q2W
Total subjects affected by non-serious adverse events			
subjects affected / exposed	202 / 592 (34.12%)	89 / 200 (44.50%)	37 / 91 (40.66%)
Vascular disorders			
Hypertension			
subjects affected / exposed	8 / 592 (1.35%)	1 / 200 (0.50%)	1 / 91 (1.10%)
occurrences (all)	8	1	1
Eye disorders			
Dry eye			
subjects affected / exposed	3 / 592 (0.51%)	1 / 200 (0.50%)	1 / 91 (1.10%)
occurrences (all)	3	1	1
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	6 / 592 (1.01%)	5 / 200 (2.50%)	2 / 91 (2.20%)
occurrences (all)	13	5	2
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	97 / 592 (16.39%)	67 / 200 (33.50%)	13 / 91 (14.29%)
occurrences (all)	131	97	25
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	18 / 592 (3.04%)	3 / 200 (1.50%)	5 / 91 (5.49%)
occurrences (all)	21	3	8
Oral herpes			
subjects affected / exposed	3 / 592 (0.51%)	4 / 200 (2.00%)	1 / 91 (1.10%)
occurrences (all)	3	4	2
Skin infection			
subjects affected / exposed	12 / 592 (2.03%)	10 / 200 (5.00%)	2 / 91 (2.20%)
occurrences (all)	13	10	2
Upper respiratory tract infection			
subjects affected / exposed	59 / 592 (9.97%)	17 / 200 (8.50%)	14 / 91 (15.38%)
occurrences (all)	65	17	18
Viral upper respiratory tract infection			
subjects affected / exposed	49 / 592 (8.28%)	17 / 200 (8.50%)	9 / 91 (9.89%)
occurrences (all)	52	19	10

Non-serious adverse events	Maintenance Period - Tralokinumab Q4W	Maintenance Period - Placebo Q2W	Maintenance Period - Placebo Q2W -

			Tralokinumab Naive
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 89 (31.46%)	21 / 46 (45.65%)	9 / 31 (29.03%)
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 89 (1.12%)	3 / 46 (6.52%)	0 / 31 (0.00%)
occurrences (all)	1	3	0
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 89 (0.00%)	3 / 46 (6.52%)	0 / 31 (0.00%)
occurrences (all)	0	4	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	3 / 89 (3.37%)	3 / 46 (6.52%)	0 / 31 (0.00%)
occurrences (all)	4	4	0
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	14 / 89 (15.73%)	9 / 46 (19.57%)	2 / 31 (6.45%)
occurrences (all)	19	16	2
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	1 / 89 (1.12%)	2 / 46 (4.35%)	1 / 31 (3.23%)
occurrences (all)	1	2	1
Oral herpes			
subjects affected / exposed	0 / 89 (0.00%)	1 / 46 (2.17%)	2 / 31 (6.45%)
occurrences (all)	0	1	2
Skin infection			
subjects affected / exposed	0 / 89 (0.00%)	1 / 46 (2.17%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	9 / 89 (10.11%)	3 / 46 (6.52%)	2 / 31 (6.45%)
occurrences (all)	12	3	2
Viral upper respiratory tract infection			
subjects affected / exposed	6 / 89 (6.74%)	7 / 46 (15.22%)	4 / 31 (12.90%)
occurrences (all)	6	7	7

Non-serious adverse events	Open-label Period - Tralokinumab 300 mg Q2W + Optional	Safety Follow-up (All treatment arms)	

	TCS		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	226 / 558 (40.50%)	28 / 641 (4.37%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	6 / 558 (1.08%)	0 / 641 (0.00%)	
occurrences (all)	6	0	
Eye disorders			
Dry eye			
subjects affected / exposed	5 / 558 (0.90%)	1 / 641 (0.16%)	
occurrences (all)	5	1	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	8 / 558 (1.43%)	1 / 641 (0.16%)	
occurrences (all)	8	1	
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	114 / 558 (20.43%)	15 / 641 (2.34%)	
occurrences (all)	174	15	
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	22 / 558 (3.94%)	3 / 641 (0.47%)	
occurrences (all)	23	3	
Oral herpes			
subjects affected / exposed	7 / 558 (1.25%)	1 / 641 (0.16%)	
occurrences (all)	7	1	
Skin infection			
subjects affected / exposed	11 / 558 (1.97%)	0 / 641 (0.00%)	
occurrences (all)	13	0	
Upper respiratory tract infection			
subjects affected / exposed	65 / 558 (11.65%)	6 / 641 (0.94%)	
occurrences (all)	87	7	
Viral upper respiratory tract infection			
subjects affected / exposed	58 / 558 (10.39%)	1 / 641 (0.16%)	
occurrences (all)	83	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 June 2017	Changes requested from the Health Authorities in Europe after their review. Clarification regarding procedure for emergency unblinding of the individual subject's treatment. Clarification throughout the section that the unblinding CRO is to be used for emergency unblinding only. Clarification that the handling of urgent safety measures will be in accordance with local legislation.
28 August 2017	Changes requested from Health Authorities in Europe after review. Safety evaluation can be made based on data collected after IMP has been discontinued. The evaluation of anti-drug antibodies is considered to be most reliable when samples are taken in the absence of IMP. Addition of 2 blood samples at Week 4. Modification to criteria for transfer to open-label treatment. Clarification that use of background treatment (emollients) is at least twice daily or more, as needed. Specification that 2 screening visits will be combined for subjects who only require a 2-week wash-out. Specification that no toxicity long-term treatment with TCI. Modification to benefit/risk assessment: deletion of infusion reaction and addition of malignancies and interference with reproductive function. Receipt of dupilumab added to exclusion criteria. Clarification on which kind of previous anaphylaxis will lead to exclusion. Clarification that subjects who permanently discontinue IMP prior to Week 16 should also be assessed at the nominal Week 16 visit. Clarification that product complaints related to IMP or any device deficiency must also be reported as product complaints, critical complaints are subject to expedited reporting, AEs in connection with product complaints are to be reported as AE/SAEs as appropriate. Clarification that SCORAD component C (completed by subject) will be completed prior to any investigator assessments. Added clinical signs and morphological descriptors to IGA scale. Clarification of EASI severity score scale also includes half-points, where questionnaires are filed, units of the clinical laboratory assessments and storage of ADA samples. Basal cell carcinoma, localised squamous cell carcinoma of the skin and carcinoma in situ of the cervix will be reported on standard AE form. Conjunctivitis, keratoconjunctivitis, and keratitis added as AESIs. Number of treatment-emergent AEs and deaths added.

12 December 2017	Changes requested from the Health Authorities in the US after their review of the protocol. Modification of other endpoints. Maintenance endpoints were modified to evaluate the maintenance of effect achieved with tralokinumab by adding 'achieved without rescue medication'. Clarification that the follow-up period has a duration of 14 weeks since the maintenance period and the open-label arm both include the Week 52 visit. Clarification that transfer to open-label requires a persistent worsening of disease observed over 3 consecutive visits in the maintenance period. Clarification of how Worst Daily Pruritus NRS at baseline will be calculated. Clarification that female subjects of childbearing potential must have used a highly effective form of birth control for at least 1 month prior to baseline. Clarification that AE reporting starts at screening, not baseline. Specification that the per protocol analysis set will be used for analysis of the primary endpoints only. Pre-defined criteria leading to exclusion from the per protocol analysis set, rather than deferring until a blinded review of the data. Clarification that reasons for permanent discontinuation of IMP will be presented. Baseline disease severity added. Specifying methods of handling missing data. Description of statistical analyses of new endpoints. Clarification regarding data collected after permanent discontinuation of IMP or after initiation of rescue medication. Addition of sensitivity analysis for primary estimand for primary endpoints. Initiation of rescue medication is unlikely to be independent of the time to relapse, hence it is not considered appropriate to consider it a censoring event. Clarification that the log-rank test is considered a supplementary exploratory analysis. Clarification that only subjects who achieve response at Week 16 without rescue medication will be included in the analysis.
14 August 2018	Addition of anti-drug antibodies assay, clarification that eligible subjects who have completed treatment periods may continue into the long-term extension trial (separate protocol) without completing safety follow-up period, clarification on training on home-use, clarify that the use of topical treatments is permitted during the safety follow-up period, addition of TCI along with topical corticosteroids, clarifications on IMP management, correction of definition of extremes in the vertical visual analogue scale and clarification on AE start and collection dates.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported