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	v2 (current)
This version publication date	26 May 2023
First version publication date	13 October 2021
Version creation reason	• Correction of full data set Data added.

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:

Results analysis stage

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:

General information about the trial

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:

Population of trial subjects

Subjects enrolled per country

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

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)	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
Arm title	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.

Arm title	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.

Number of subjects in period 1	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
Arm title	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

Arm title	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[1]	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

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:	
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 title	Safety follow-up, 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 time during the safety follow-up period.	
Reporting group title	Safety follow-up, placebo
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 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:	
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:	
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

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[1]
P-value	= 0.018 [2]
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

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[3]
P-value	= 0.106 [4]
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

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, 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[5]
P-value	< 0.001 [6]
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

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 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[7]
P-value	= 0.009 [8]
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[9]
P-value	= 0.005 [10]
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[11]
P-value	= 0.014 [12]
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[13]
P-value	= 0.228 [14]
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[15]
P-value	< 0.001 [16]
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[17]
P-value	= 0.005 [18]
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[19]
P-value	= 0.014 [20]
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

Secondary: Number of adverse events from Week 0 to Week 40

End point title	Number of adverse events from Week 0 to Week 40

End point description:

All adverse events are presented below under Adverse Events.

End point type	Secondary

End point timeframe:

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: Number of adverse events	389	435		

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: Tralokinumab + TCS	Treatment period: Placebo + TCS	Safety follow-up period: 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
Infections and infestations			
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

Serious adverse events	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 %

Non-serious adverse events	Treatment period: Tralokinumab + TCS	Treatment period: Placebo + TCS	Safety follow-up period: 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			
subjects affected / exposed	1 / 138 (0.72%)	8 / 137 (5.84%)	0 / 75 (0.00%)
occurrences (all)	1	8	0
Injury, poisoning and procedural complications			
Skin abrasion			
subjects affected / exposed	3 / 138 (2.17%)	0 / 137 (0.00%)	0 / 75 (0.00%)
occurrences (all)	3	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	21 / 138 (15.22%)	13 / 137 (9.49%)	0 / 75 (0.00%)
occurrences (all)	25	18	0
Eye disorders			
Conjunctivitis allergic			
subjects affected / exposed	6 / 138 (4.35%)	5 / 137 (3.65%)	0 / 75 (0.00%)
occurrences (all)	8	5	0
Dry eye			
subjects affected / exposed	3 / 138 (2.17%)	1 / 137 (0.73%)	0 / 75 (0.00%)
occurrences (all)	3	1	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 138 (0.72%)	5 / 137 (3.65%)	0 / 75 (0.00%)
occurrences (all)	1	8	0
Dyspepsia			
subjects affected / exposed	1 / 138 (0.72%)	3 / 137 (2.19%)	0 / 75 (0.00%)
occurrences (all)	1	3	0
Diverticulum intestinal			
subjects affected / exposed	0 / 138 (0.00%)	0 / 137 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 138 (0.00%)	0 / 137 (0.00%)	1 / 75 (1.33%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Alopecia areata			
subjects affected / exposed	0 / 138 (0.00%)	3 / 137 (2.19%)	0 / 75 (0.00%)
occurrences (all)	0	3	0
Dermatitis atopic			

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

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

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

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported