Clinical trial results:
A Randomised, Double-Blind, Placebo-Controlled Phase 3 Clinical Trial to Assess the Efficacy and Safety of Lebrikizumab in Combination With Topical Corticosteroids in Adult and Adolescent Patients With Moderate-To-Severe Atopic Dermatitis That Are Not Adequately Controlled With Cyclosporine or For Whom Cyclosporine is Not Medically Advisable

Summary

EudraCT number	2021-002967-23
Trial protocol	DE FR ES PL BE IT NL AT
Global end of trial date	07 May 2024

Results information

Result version number	v1 (current)
This version publication date	16 May 2025
First version publication date	16 May 2025

Trial information

Trial identification

Sponsor protocol code	M-17923-30

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05149313
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Almirall S.A
Sponsor organisation address	Ronda General Mitre, 151, Barcelona, Spain, 08022
Public contact	Clinical Trials Information, Almirall, S.A., +34 932913545, gco@almirall.com
Scientific contact	Clinical Trials Information, Almirall, S.A., +34 932913545, gco@almirall.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	07 May 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 May 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of lebrikizumab compared with placebo in patients not adequately controlled with cyclosporine or for whom cyclosporine is not medically advisable up to Week 16.

Protection of trial subjects:

This study is conducted in accordance with the recommendations guiding physicians in biomedical research involving human patients adopted by the 18th World Medical Assembly of Helsinki (1964), as amended in Fortaleza, Brazil (2013), as well as in compliance with ICH GCP guidelines, and according to the appropriate regulatory requirements in the countries where the study is conducted.

Background therapy:

All subjects will receive background topical corticosteroids (TCS) therapy at a dosage that can be adapted based on the patient’s needs, for up to Week 16.

Evidence for comparator:

All eligible subjects must use concomitant TCS (mid-potency TCS and low-potency TCS) At baseline (Week 0, Visit 2) and until Week 16.

Actual start date of recruitment	30 September 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 10
Country: Number of subjects enrolled	Netherlands: 7
Country: Number of subjects enrolled	Poland: 159
Country: Number of subjects enrolled	Spain: 32
Country: Number of subjects enrolled	Austria: 2
Country: Number of subjects enrolled	Belgium: 4
Country: Number of subjects enrolled	France: 43
Country: Number of subjects enrolled	Germany: 69
Country: Number of subjects enrolled	Italy: 5
Worldwide total number of subjects	331
EEA total number of subjects	321

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)	39
Adults (18-64 years)	280
From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study was conducted at 54 sites in Austria, Belgium, France, Germany, Italy, Netherlands, Poland, Spain, and United Kingdom. Randomization was stratified by previous use of dupilumab, age (adolescent subjects aged >=12 to < 18 years comprises 11.8% of the population compared to adults aged >=18 years) and baseline disease severity (IGA 3 vs 4).

Pre-assignment

Screening details:

A total of 368 subjects were screened, of which 331 subjects were randomized into 2 treatment arms (Lebrikizumab and Placebo). The study has 2 treatment periods: a 16-week double-blind Induction Period and 36 week open-label Maintenance Period.

Period 1

Period 1 title	Double-blind Induction Period (16-weeks)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	Double-blind Induction Period: Lebrikizumab +TCS

Arm description:

Subjects received loading dose of lebrikizumab 500 milligrams (mg) subcutaneous (SC) injection at Day 1 (Baseline) and Week 2 followed by lebrikizumab 250 mg SC injection once every two weeks (Q2W) for up to 16 weeks concomitantly with topical corticosteroids (TCS) in the double-blind induction period.

Arm type	Experimental
Investigational medicinal product name	Lebrikizumab
Investigational medicinal product code	LY3650150
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received lebrikizumab SC injections Q2W for up to 16 weeks concomitantly with TCS.

Arm title	Double-blind Induction Period: Placebo +TCS

Arm description:

Subjects received lebrikizumab-matched placebo SC injection, Q2W for up to 16 weeks concomitantly with TCS in the double-blind induction period.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received lebrikizumab-matched placebo SC injection, Q2W for up to 16 weeks concomitantly with TCS.

Number of subjects in period 1	Double-blind Induction Period: Lebrikizumab +TCS	Double-blind Induction Period: Placebo +TCS
Started	220	111
Completed	212	100
Not completed	8	11
Consent withdrawn by subject	2	5
Physician decision	1	-
Adverse Event	2	2
Pregnancy	1	-
Unspecified	-	1
Lost to follow-up	2	3

Period 2

Period 2 title	Open-label Maintenance Period (36 Weeks)
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Open-label Maintenance Period: Lebrikizumab to Lebrikizumab

Arm description:

Subjects who received lebrikizumab 250 mg Q2W during the Double-blind Induction Period continued to receive lebrikizumab 250 mg, Q2W during the 36-week Maintenance Period.

Arm type	Experimental
Investigational medicinal product name	Lebrikizumab
Investigational medicinal product code	LY3650150
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received lebrikizumab 250 mg, Q2W up to Week 52.

Arm title	Open-label Maintenance Period: Placebo to Lebrikizumab

Arm description:

During Maintenance Period, subjects who received placebo Q2W during the Induction Period received loading doses of lebrikizumab (500 mg) at Weeks 16 and 18. From Week 20 onward, the subjects received 1 injection of lebrikizumab 250mg Q2W.

Arm type	Experimental
Investigational medicinal product name	Lebrikizumab
Investigational medicinal product code	LY3650150
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received lebrikizumab 500 mg at Week 16 and 18. From Week 20 onward, Subjects received

250 mg, Q2W.

Number of subjects in period 2	Open-label Maintenance Period: Lebrikizumab to Lebrikizumab	Open-label Maintenance Period: Placebo to Lebrikizumab
Started	212	100
Completed	180	87
Not completed	32	13
Consent withdrawn by subject	14	7
Adverse Event	7	1
Lost to follow-up	4	-
Lack of efficacy	6	5
Protocol deviation	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Double-blind Induction Period: Lebrikizumab +TCS
Reporting group description:	
Subjects received loading dose of lebrikizumab 500 milligrams (mg) subcutaneous (SC) injection at Day 1 (Baseline) and Week 2 followed by lebrikizumab 250 mg SC injection once every two weeks (Q2W) for up to 16 weeks concomitantly with topical corticosteroids (TCS) in the double-blind induction period.	
Reporting group title	Double-blind Induction Period: Placebo +TCS
Reporting group description:	
Subjects received lebrikizumab-matched placebo SC injection, Q2W for up to 16 weeks concomitantly with TCS in the double-blind induction period.	

Reporting group values	Double-blind Induction Period: Lebrikizumab +TCS	Double-blind Induction Period: Placebo +TCS	Total
Number of subjects	220	111	331
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	33.7	34.1	
standard deviation	± 14.85	± 15.24	-
Gender categorical Units: Subjects			
Female	100	56	156
Male	120	55	175
Ethnicity Units: Subjects			
Hispanic or Latino	14	14	28
Not Hispanic or Latino	197	93	290
Unknown or Not Reported	9	4	13
Race Units: Subjects			
American Indian or Alaska Native	1	0	1
Asian	1	3	4
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	5	0	5
White	206	104	310
More than one race	0	2	2
Unknown or Not Reported	7	2	9

End points

End points reporting groups

Reporting group title	Double-blind Induction Period: Lebrikizumab +TCS
Reporting group description:	
Subjects received loading dose of lebrikizumab 500 milligrams (mg) subcutaneous (SC) injection at Day 1 (Baseline) and Week 2 followed by lebrikizumab 250 mg SC injection once every two weeks (Q2W) for up to 16 weeks concomitantly with topical corticosteroids (TCS) in the double-blind induction period.	
Reporting group title	Double-blind Induction Period: Placebo +TCS
Reporting group description:	
Subjects received lebrikizumab-matched placebo SC injection, Q2W for up to 16 weeks concomitantly with TCS in the double-blind induction period.	
Reporting group title	Open-label Maintenance Period: Lebrikizumab to Lebrikizumab
Reporting group description:	
Subjects who received lebrikizumab 250 mg Q2W during the Double-blind Induction Period continued to receive lebrikizumab 250 mg, Q2W during the 36-week Maintenance Period.	
Reporting group title	Open-label Maintenance Period: Placebo to Lebrikizumab
Reporting group description:	
During Maintenance Period, subjects who received placebo Q2W during the Induction Period received loading doses of lebrikizumab (500 mg) at Weeks 16 and 18. From Week 20 onward, the subjects received 1 injection of lebrikizumab 250mg Q2W.	

Primary: Double-blind Induction Period: Percentage of Subjects Who Achieved Eczema Area and Severity Index (EASI) 75 (>=75% Reduction From Baseline in EASI Score) at Week 16

End point title	Double-blind Induction Period: Percentage of Subjects Who Achieved Eczema Area and Severity Index (EASI) 75 (>=75% Reduction From Baseline in EASI Score) at Week 16
End point description:	
The EASI score is used to measure the severity and extent of atopic dermatitis (AD) and measures erythema, infiltration, excoriation and lichenification on 4 anatomic regions of the body: head, trunk, upper limbs, and lower limbs. The severity of the clinical signs of AD for each of 4 body regions was scored on a 4-point scale: 0=absent, 1=mild, 2=moderate and 3=severe. The area of AD involvement on each of the 4 anatomic regions was assessed as a percentage by body area: 0=no eruption, 1=1% to 9%, 2=10% to 29%, 3=30% to 49%, 4=50% to 60%, 5=70% to 80% and 6=90% to 100%. The composite index with total score ranged from 0 to 72, where higher scores indicates more severe and or extensive disease. FAS included all randomized subjects and were analyzed under the treatment group as randomized.	
End point type	Primary
End point timeframe:	
At Week 16	

End point values	Double-blind Induction Period: Lebrikizumab +TCS	Double-blind Induction Period: Placebo +TCS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	220	111		
Units: Percentage of subjects				
number (not applicable)	68.4	40.8		

Statistical analyses

Statistical analysis title	Lebrikizumab +TCS vs Placebo +TCS
Comparison groups	Double-blind Induction Period: Lebrikizumab +TCS v Double-blind Induction Period: Placebo +TCS
Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentages
Point estimate	27.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	15.63
upper limit	40.14

Secondary: Double-blind Induction Period: Percentage of Subjects Who Achieved Investigator Global Assessment (IGA) Score of 0 or 1 and 2-point Improvement at Week 16

End point title	Double-blind Induction Period: Percentage of Subjects Who Achieved Investigator Global Assessment (IGA) Score of 0 or 1 and 2-point Improvement at Week 16

End point description:

The IGA is an instrument used to globally rate the severity of the subjects AD. It is based on a 5-point scale ranging from 0 (clear), 1 (almost clear), 2 (mild), 3 (moderate) and 4 (severe), and a score is selected using descriptors that best describe the overall appearance of the lesions at a given time point. The score is based on an overall assessment of the degree of erythema, papulation/induration, oozing/crusting (minimal, palpable induration and significant induration). Therapeutic response is an IGA score of 0 (clear) or 1 (almost clear). FAS included all randomized subjects and were analyzed under the treatment group as randomized.

End point type	Secondary

End point timeframe:

At Week 16

End point values	Double-blind Induction Period: Lebrikizumab +TCS	Double-blind Induction Period: Placebo +TCS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	220	111		
Units: Percentage of subjects				

number (not applicable)	42.0	24.5		

Statistical analyses

Statistical analysis title	Lebrikizumab +TCS vs Placebo +TCS
Comparison groups	Double-blind Induction Period: Lebrikizumab +TCS v Double-blind Induction Period: Placebo +TCS
Number of subjects included in analysis	331
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0052
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentages
Point estimate	17.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.03
upper limit	28.57

Secondary: Double-blind Induction Period: Percentage of Subjects Who Achieved a 4-point Improvement in Pruritus Numeric Rating Score (NRS) at Week 16

End point title	Double-blind Induction Period: Percentage of Subjects Who Achieved a 4-point Improvement in Pruritus Numeric Rating Score (NRS) at Week 16

End point description:

The Pruritus NRS is an 11-point scale used by subjects to rate their worst pruritus (itch) severity over the past 24 hours, with 0 indicating "No itch," and 10 indicating "Worst itch imaginable. Higher score indicates more severity. FAS included all randomized subjects with the Baseline score >=4. Here, "subjects analysed" signifies subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

At Week 16

End point values	Double-blind Induction Period: Lebrikizumab +TCS	Double-blind Induction Period: Placebo +TCS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	199	102		
Units: Percentage of subjects				
number (not applicable)	49.9	29.7		

Statistical analyses

Statistical analysis title	Lebrikizumab +TCS vs Placebo +TCS
Comparison groups	Double-blind Induction Period: Lebrikizumab +TCS v Double-blind Induction Period: Placebo +TCS
Number of subjects included in analysis	301
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0114
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentages
Point estimate	18.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.47
upper limit	30.83

Secondary: Double-blind Induction Period: Percentage of Subjects Who Achieved EASI 75 (>=75% Reduction From Baseline in EASI Score) at Weeks 2, 4, 8, and 12

End point title	Double-blind Induction Period: Percentage of Subjects Who Achieved EASI 75 (>=75% Reduction From Baseline in EASI Score) at Weeks 2, 4, 8, and 12

End point description:

The EASI score is used to measure the severity and extent of atopic dermatitis (AD) and measures erythema, infiltration, excoriation and lichenification on 4 anatomic regions of the body: head, trunk, upper limbs, and lower limbs. The severity of the clinical signs of AD for each of 4 body regions was scored on a 4-point scale: 0=absent, 1=mild, 2=moderate and 3=severe. The area of AD involvement on each of the 4 anatomic regions was assessed as a percentage by body area: 0=no eruption, 1=1% to 9%, 2=10% to 29%, 3=30% to 49%, 4=50% to 60%, 5=70% to 80% and 6=90% to 100%. The composite index with total score ranged from 0 to 72, where higher scores indicates more severe and or extensive disease. Percentage of subjects who achieved EASI 75 (>=75% reduction from baseline in EASI score) at Weeks 2, 4, 8, and 12 were reported. FAS included all randomized subjects and were analyzed under the treatment group as randomized.

End point type	Secondary

End point timeframe:

At Weeks 2, 4, 8, and12

End point values	Double-blind Induction Period: Lebrikizumab +TCS	Double-blind Induction Period: Placebo +TCS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	220	111		
Units: Percentage of subjects				
number (not applicable)				
At Week 2	9.7	6.3		
At Week 4	28.3	19.2		
At Week 8	54.9	31.5		
At Week 12	64.9	41.1		

Statistical analyses

No statistical analyses for this end point

Secondary: Double-blind Induction Period: Percentage of Subjects Who Achieved EASI 90 (>=90% Reduction From Baseline in EASI Score) at Weeks 2, 4, 8, 12 and 16

End point title	Double-blind Induction Period: Percentage of Subjects Who Achieved EASI 90 (>=90% Reduction From Baseline in EASI Score) at Weeks 2, 4, 8, 12 and 16

End point description:

The EASI score is used to measure the severity and extent of AD and measures erythema, infiltration, excoriation and lichenification on 4 anatomic regions of the body: head, trunk, upper limbs, and lower limbs. The severity of the clinical signs of AD for each of 4 body regions was scored on a 4-point scale: 0=absent, 1=mild, 2=moderate and 3=severe. The area of AD involvement on each of the 4 anatomic regions was assessed as a percentage by body area: 0=no eruption, 1=1% to 9%, 2=10% to 29%, 3=30% to 49%, 4=50% to 60%, 5=70% to 80% and 6=90% to 100%. The composite index with total score ranged from 0 to 72, where higher scores indicates more severe and or extensive disease. FAS included all randomized subjects and were analyzed under the treatment group as randomized.

End point type	Secondary

End point timeframe:

At Weeks 2, 4, 8, 12 and 16

End point values	Double-blind Induction Period: Lebrikizumab +TCS	Double-blind Induction Period: Placebo +TCS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	220	111		
Units: Percentage of subjects				
number (not applicable)				
At Week 2	1.5	0.9		
At Week 4	15.8	6.4		
At Week 8	28.9	10.6		
At Week 12	42.1	21.0		
At Week 16	42.9	20.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Double-blind Induction Period: Percentage of Subjects Who Achieved EASI 50 (>=50% Reduction From Baseline in EASI Score) at Weeks 2, 4, 8, 12 and 16

End point title	Double-blind Induction Period: Percentage of Subjects Who Achieved EASI 50 (>=50% Reduction From Baseline in EASI Score) at Weeks 2, 4, 8, 12 and 16

End point description:

The EASI score is used to measure the severity and extent of AD and measures erythema, infiltration, excoriation and lichenification on 4 anatomic regions of the body: head, trunk, upper limbs, and lower limbs. The severity of the clinical signs of AD for each of 4 body regions was scored on a 4-point scale: 0=absent, 1=mild, 2=moderate and 3=severe. The area of AD involvement on each of the 4 anatomic regions was assessed as a percentage by body area: 0=no eruption, 1=1% to 9%, 2=10% to 29%, 3=30% to 49%, 4=50% to 60%, 5=70% to 80% and 6=90% to 100%. The composite index with total score ranged from 0 to 72, where higher scores indicates more severe and or extensive disease. FAS included all randomized subjects and were analyzed under the treatment group as randomized.

End point type	Secondary

End point timeframe:

At Weeks 2, 4, 8, 12 and 16

End point values	Double-blind Induction Period: Lebrikizumab +TCS	Double-blind Induction Period: Placebo +TCS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	220	111		
Units: Percentage of subjects				
number (not applicable)				
At Week 2	30.8	23.4		
At Week 4	58.9	46.0		
At Week 8	75.2	59.3		
At Week 12	80.3	68.0		
At Week 16	82.6	65.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Double-blind Induction Period: Percentage of Subjects Who Achieved a 4-point Improvement in Dermatology Life Quality Index (DLQI) at Weeks 2, 4, 8, 12

and 16

End point title	Double-blind Induction Period: Percentage of Subjects Who Achieved a 4-point Improvement in Dermatology Life Quality Index (DLQI) at Weeks 2, 4, 8, 12 and 16

End point description:

The DLQI is a 10-item validated questionnaire completed by the subject or caregiver used to assess the impact of skin disease on the participant's quality of life (QoL during the previous week. The 10 questions cover the following topics: symptoms, embarrassment, shopping and home care, clothes, social and leisure, sport, work or study, close relationships, sex, and treatment. Each question was scored on a 4-point scale (ranged from 0 to 3) where, 0 = not at all, 1= a little, 2= a lot, 3= very much, giving a total score ranging from 0 (not at all) to 30 (very much). A high score is indicative of a poor QoL. FAS included all randomized subjects with Baseline DLQI score of >=4. Here" number of subjects analysed" signified subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

At Weeks 2, 4, 8, 12 and 16

End point values	Double-blind Induction Period: Lebrikizumab +TCS	Double-blind Induction Period: Placebo +TCS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	180	90		
Units: Percentage of subjects				
number (not applicable)				
At Week 2	52.8	57.1		
At Week 4	66.1	61.9		
At Week 8	70.5	56.1		
At Week 12	73.1	59.6		
At Week 16	78.0	69.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Double-blind Induction Period: Percentage of Subjects Who Achieved a 4-point Improvement in Children's Dermatology Life Quality Index (CDLQI) at Weeks 2, 4, 8, 12 and 16

End point title	Double-blind Induction Period: Percentage of Subjects Who Achieved a 4-point Improvement in Children's Dermatology Life Quality Index (CDLQI) at Weeks 2, 4, 8, 12 and 16

End point description:

The CDLQI is validated from adolescents younger than age of 16 years, which is based on a set of 10 questions different from those of the DLQI to measure the impact of AD disease on QoL in children during the previous week. Each question is scored as follows: 0=not at all or unanswered, 1 = only a little, 2 = quite a lot and 3 = very much. Question 7 has an added possible response, which was scored as 3. CDLQI equals the sum of the score of each question, ranged from 0 (no impact of skin disease on QoL) to 30 (maximum impact on QoL). Higher scores indicate higher impact on QoL. FAS included all randomized subjects with Baseline Score >= 4. Here" number of subjects analysed" signified subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

At Weeks 2, 4, 8, 12 and 16

End point values	Double-blind Induction Period: Lebrikizumab +TCS	Double-blind Induction Period: Placebo +TCS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	8		
Units: Percentage of subjects				
number (not applicable)				
At Week 2	90.9	100		
At Week 4	68.2	62.5		
At Week 8	90.9	100		
At Week 12	95.5	100		
At Week 16	93.1	100		

Statistical analyses

No statistical analyses for this end point

Secondary: Double-blind Induction Period: Percentage of Subjects Who Achieved a 4- Point Improvement in Skin Pain NRS at Week 16

End point title	Double-blind Induction Period: Percentage of Subjects Who Achieved a 4- Point Improvement in Skin Pain NRS at Week 16

End point description:

The Skin Pain NRS is an 11-point scale completed by subjects to rate their worst skin pain (example, discomfort or soreness) severity over the past 24 hours, with 0 (indicating "No pain") and 10 (indicating "Worst pain imaginable). Higher scores indicated worse pain. FAS included all randomized subjects with Baseline Score >= 4. Here” number of subjects analysed" signified subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

At Week 16

End point values	Double-blind Induction Period: Lebrikizumab +TCS	Double-blind Induction Period: Placebo +TCS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	88		
Units: Percentage of Subjects				
number (not applicable)	51.6	27.5		

Statistical analyses

No statistical analyses for this end point

Secondary: Double-blind Induction Period: Change From Baseline in Body Surface Area (BSA) at Weeks 2, 4, 8, 12 and 16

End point title	Double-blind Induction Period: Change From Baseline in Body Surface Area (BSA) at Weeks 2, 4, 8, 12 and 16

End point description:

The BSA assessment estimates the extent of disease or skin involvement with respect to AD and is expressed as a percentage of total body surface. BSA was determined by the Investigator or designee using the subject palm = 1% BSA rule. The subject's palm is measured from the wrist to the proximal interphalangeal and thumb. This higher the BSA %, the more active atopic dermatitis is present. Percent of BSA for a body region = total number of palms in a body region * % surface area equivalent to 1 palm. Overall percent BSA for an individual is arithmetic mean of % BSA of all 4 body regions and ranges from 0% to 100% with higher values representing greater severity of AD and negative change from baseline indicate no severity. FAS included all randomized subjects and were analyzed under the treatment group as randomized. Here" number of subjects analysed" signified subjects who were evaluable for this endpoint and "n=number analysed" signifies who were evaluable at specified timepoints.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, 8, 12 and 16

End point values	Double-blind Induction Period: Lebrikizumab +TCS	Double-blind Induction Period: Placebo +TCS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	217	111		
Units: Percentage of body surface area				
arithmetic mean (standard deviation)				
Change at Week 2 (n= 216, 111)	-11.4 (± 15.33)	-10.6 (± 12.04)		
Change at Week 4 (n= 217, 107)	-19.5 (± 19.22)	-15.3 (± 13.77)		
Change at Week 8 (n= 211, 102)	-27.3 (± 20.60)	-19.2 (± 17.12)		
Change at Week 12 (n= 205, 99)	-30.6 (± 21.25)	-22.5 (± 17.06)		
Change at Week 16 (n= 209, 99)	-32.5 (± 21.44)	-22.1 (± 18.57)		

Statistical analyses

No statistical analyses for this end point

Secondary: Double-blind Induction Period: Change From Baseline in Scoring Atopic Dermatitis (SCORAD) at Weeks 8 and 16

End point title	Double-blind Induction Period: Change From Baseline in Scoring Atopic Dermatitis (SCORAD) at Weeks 8 and 16

End point description:

SCORAD is a validated clinical tool for assessing the extent and intensity of AD. There are 3 components: A) Surface involvement is assessed as proportion of involved surface area segment by segment by applying the rule of 9s and reported as the sum of all areas, with a score ranging from 0-100. B) Intensity part of the SCORAD consists of 6 items: erythema, oedema, oozing/crusting, excoriation, lichenification, and dryness. Each item graded as: none (0), mild (1), moderate (2), or severe (3). C) Subjective assessment of itch and of sleeplessness is recorded for each symptom using a visual analogue scale (VAS), where 0=no itch (or no sleeplessness) and 10= worst imaginable itch (or sleeplessness), with max score of 20. Formula: A/5+7B/2+C, A: extent (0-100), B: intensity (0-18), C: subjective symptoms (0-20). SCORAD total score ranged from 0 (no disease)- 103 (severe disease). Higher values represent worse outcome and negative change from baseline indicate improvement. FAS population.

End point type	Secondary

End point timeframe:

Baseline, Weeks 8 and 16

End point values	Double-blind Induction Period: Lebrikizumab +TCS	Double-blind Induction Period: Placebo +TCS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	199	94		
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Change at Week 8 (n= 198, 94)	-32.1 (± 17.90)	-20.0 (± 18.04)		
Change at Week 16 (n= 199, 89)	-36.8 (± 20.40)	-23.7 (± 21.25)		

Statistical analyses

No statistical analyses for this end point

Secondary: Double-blind Induction Period: Change From Baseline in Pruritus NRS by Week up to Week 16

End point title	Double-blind Induction Period: Change From Baseline in Pruritus NRS by Week up to Week 16

End point description:

The Pruritus NRS is an 11-point scale used by subjects to rate their worst pruritus (itch) severity over the past 24 hours, with 0 indicating "No itch," and 10 indicating "Worst itch imaginable." Higher scores indicated greater severity and negative change from baseline indicate no severity. FAS included all randomized subjects and were analyzed under the treatment group as randomized. Here” number of subjects analysed" signified subjects who were evaluable for this endpoint and "n=number analysed" signifies subjects who were evaluable at specified timepoints.

End point type	Secondary

End point timeframe:
Baseline, Weeks 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16

End point values	Double-blind Induction Period: Lebrikizumab +TCS	Double-blind Induction Period: Placebo +TCS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	214	108		
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Change at Week 2 (n= 206, 105)	-1.543 (± 1.6304)	-1.113 (± 1.7468)		
Change at Week 3 (n= 213, 108)	-2.199 (± 2.0960)	-1.420 (± 2.1401)		
Change at Week 4 (n= 214, 107)	-2.351 (± 2.2558)	-1.450 (± 2.3924)		
Change at Week 5 (n=211, 101)	-2.771 (± 2.4152)	-1.485 (± 2.4553)		
Change at Week 6 (n=207, 101)	-3.053 (± 2.3975)	-1.711 (± 2.5330)		
Change at Week 7 (n=203, 101)	-3.204 (± 2.4643)	-1.823 (± 2.5263)		
Change at Week 8 (n=212, 99)	-3.080 (± 2.4552)	-1.856 (± 2.5670)		
Change at Week 9 (n= 205, 100)	-3.283 (± 2.5105)	-1.861 (± 2.5872)		
Change at Week 10 (n=205, 98)	-3.245 (± 2.6101)	-1.529 (± 2.7489)		
Change at Week 11 (n= 201, 96)	-3.285 (± 2.5484)	-1.776 (± 2.7302)		
Change at Week 12 (n=206, 97)	-3.388 (± 2.6195)	-1.853 (± 2.3583)		
Change at Week 13 (n=196, 97)	-3.326 (± 2.6697)	-2.053 (± 2.5284)		
Change at Week 14 (n= 203, 96)	-3.313 (± 2.6843)	-1.948 (± 2.4181)		
Change at Week 15 (n=202, 96)	-3.366 (± 2.5291)	-1.938 (± 2.5245)		
Change at Week 16 (n=203, 92)	-3.476 (± 2.5453)	-2.183 (± 2.4246)		

Statistical analyses

No statistical analyses for this end point

Secondary: Double-blind Induction Period: Change From Baseline in the Sleep Loss at Week 16 Using Patient-related Outcome (PRO) by Week up to Week 16

End point title	Double-blind Induction Period: Change From Baseline in the Sleep Loss at Week 16 Using Patient-related Outcome (PRO) by Week up to Week 16

End point description:

Sleep loss was assessed by all subjects using a PRO instrument. Subjects (and if applicable, with help of parents/caregiver if required) rate their sleep on a 5-point Likert scale (with scores ranging from 0 [not at all] to 4 [unable to sleep at all]). Higher scores indicated a greater impact and worse outcome; therefore, negative change from baseline indicate less impact. FAS included all randomized subjects and were analyzed under the treatment group as randomized. Here" number of subjects analysed" signified subjects who were evaluable for this endpoint and "n=number analysed" signifies subjects who were evaluable at specified timepoints.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16

End point values	Double-blind Induction Period: Lebrikizumab +TCS	Double-blind Induction Period: Placebo +TCS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	214	108		
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Change at Week 2 (n=206, 105)	-0.603 (± 0.6985)	-0.493 (± 0.8407)		
Change at Week 3 (n=213, 108)	-0.816 (± 0.8809)	-0.673 (± 1.0262)		
Change at Week 4 (n=214, 107)	-0.875 (± 0.9387)	-0.577 (± 1.0885)		
Change at Week 5 (n=210, 101)	-0.942 (± 0.9646)	-0.607 (± 1.1342)		
Change at Week 6 (n=207,101)	-0.998 (± 0.9088)	-0.613 (± 1.0641)		
Change at Week 7 (n=203, 101)	-1.038 (± 0.9388)	-0.661 (± 1.1119)		
Change at Week 8 (n=212, 99)	-0.974 (± 0.9941)	-0.708 (± 1.1500)		
Change at Week 9 (n=205, 100)	-1.052 (± 0.9352)	-0.668 (± 1.0604)		
Change at Week 10 (n=205, 98)	-1.091 (± 0.9624)	-0.560 (± 1.1349)		
Change at Week 11 (n=201, 96)	-1.040 (± 0.9966)	-0.676 (± 1.0938)		
Change at Week 12 (n=206, 97)	-1.123 (± 1.0281)	-0.721 (± 1.0768)		
Change at Week 13 (n=196, 97)	-1.069 (± 0.9776)	-0.797 (± 1.1037)		
Change at Week 14 (n=203, 96)	-1.072 (± 1.0446)	-0.809 (± 1.0751)		
Change at Week 15 (n=202, 96)	-1.096 (± 0.9819)	-0.756 (± 1.0891)		
Change at Week 16 (n=203, 92)	-1.201 (± 0.9775)	-0.857 (± 1.0615)		

Statistical analyses

No statistical analyses for this end point

Secondary: Double-blind Induction Period: Change From Baseline in Patient-Oriented Eczema Measure (POEM) Total Score at Weeks 4, 8, 12 and 16

End point title	Double-blind Induction Period: Change From Baseline in Patient-Oriented Eczema Measure (POEM) Total Score at Weeks 4, 8, 12 and 16

End point description:

The POEM is a 7-item, validated questionnaire completed by the subject (and, if applicable, with help of parents/caregiver if required) to assess disease symptoms. Subjects are asked to respond to questions on skin dryness, itching, flaking, cracking, sleep loss, bleeding, and weeping. All answers carry equal weight, with a total possible score ranging from 0 to 28 (answers scored as: No days = 0; 1 to 2 days = 1; 3 to 4 days = 2; 5 to 6 days = 3; every day = 4. Higher scores indicated more severe disease and poor quality of life (QoL); therefore, negative change from baseline indicate improvement in QoL. Here" number of subjects analysed" signified subjects who were evaluable for this endpoint and "n=number analysed" signifies subjects who were evaluable at specified timepoints.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 12 and 16

End point values	Double-blind Induction Period: Lebrikizumab +TCS	Double-blind Induction Period: Placebo +TCS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	201	98		
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Change at Week 4 (n=201, 98)	-8.4 (± 6.82)	-4.7 (± 6.42)		
Change at Week 8 (n=199, 91)	-10.9 (± 7.45)	-5.2 (± 6.65)		
Change at Week 12 (n=197, 87)	-11.3 (± 8.08)	-5.1 (± 7.25)		
Change at Week 16 (n=196, 87)	-11.9 (± 8.01)	-5.8 (± 7.18)		

Statistical analyses

No statistical analyses for this end point

Secondary: Double-blind Induction Period: Change From Baseline in Dermatology Life Quality Index (DLQI) Total Score at Weeks 2. 4, 8, 12 and 16

End point title	Double-blind Induction Period: Change From Baseline in Dermatology Life Quality Index (DLQI) Total Score at Weeks 2. 4, 8, 12 and 16

End point description:

The DLQI is a 10-item validated questionnaire completed by the subject or caregiver used to assess the impact of skin disease on the participant's QoL during the previous week. The 10 questions cover the following topics: symptoms, embarrassment, shopping and home care, clothes, social and leisure, sport, work or study, close relationships, sex, and treatment. Each question was scored on a 4-point scale (ranged from 0 to 3) where, 0 = not at all, 1= a little, 2= a lot, 3= very much, giving a total score ranging from 0 (not at all) to 30 (very much). A high score is indicative of a poor QoL and negative change from baseline indicate improvement in QoL. FAS included all randomized subjects and were analyzed under the treatment group as randomized. Here" number of subjects analysed" signified subjects who were evaluable for this endpoint and "n=number analysed" signifies subjects who were

evaluable at specified timepoints.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2. 4, 8, 12 and 16

End point values	Double-blind Induction Period: Lebrikizumab +TCS	Double-blind Induction Period: Placebo +TCS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	185	91		
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Change at Week 2 (n=185, 91)	-4.6 (± 5.54)	-4.5 (± 6.00)		
Change at Week 4 (n=178, 90)	-7.1 (± 6.54)	-5.4 (± 6.86)		
Change at Week 8 (n=177, 83)	-8.3 (± 7.03)	-5.7 (± 7.89)		
Change at Week 12 (n=176, 79)	-8.7 (± 7.38)	-5.9 (± 7.90)		
Change at Week 16 (n=175, 79)	-9.5 (± 7.40)	-8.1 (± 7.62)		

Statistical analyses

No statistical analyses for this end point

Secondary: Double-blind Induction Period: Change From Baseline in Children's Dermatology Life Quality Index (CDLQI) at Week 2. 4, 8, 12 and 16

End point title	Double-blind Induction Period: Change From Baseline in Children's Dermatology Life Quality Index (CDLQI) at Week 2. 4, 8, 12 and 16

End point description:

The CDLQI is validated from adolescents younger than age of 16 years, which is based on a set of 10 questions different from those of the DLQI to measure the impact of AD disease on QoL in children during the previous week. Each question is scored as follows: 0=not at all or unanswered, 1 = only a little, 2 = quite a lot and 3 = very much. Question 7 has an added possible response, which was scored as 3. CDLQI equals the sum of the score of each question, ranged from 0 (no impact of skin disease on QoL) to 30 (maximum impact on QoL). Higher scores indicate higher impact on QoL and negative change from baseline indicate low impact on QoL. FAS included all randomized subjects and were analysed under the treatment group as randomized. Here” number of subjects analysed" signified subjects who were evaluable for this endpoint and "n=number analysed" signifies subjects who were evaluable at specified timepoints.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, 8, 12 and 16

End point values	Double-blind Induction Period: Lebrikizumab +TCS	Double-blind Induction Period: Placebo +TCS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	8		
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Change at Week 2 (n=23, 8)	-2.9 (± 3.41)	-3.6 (± 3.25)		
Change at Week 4 (n=23, 8)	-5.1 (± 4.76)	-4.3 (± 4.65)		
Change at Week 8 (n=23, 8)	-6.6 (± 6.69)	-6.9 (± 4.82)		
Change at Week 12 (n=21, 8)	-7.7 (± 7.60)	-7.4 (± 6.30)		
Change at Week 16 (n=21, 8)	-7.7 (± 6.91)	-6.8 (± 5.73)		

Statistical analyses

No statistical analyses for this end point

Secondary: Double-blind Induction Period: Change From Baseline in Skin Pain NRS by Week up to Week 16

End point title	Double-blind Induction Period: Change From Baseline in Skin Pain NRS by Week up to Week 16

End point description:

The Skin Pain NRS is an 11-point scale completed by subjects to rate their worst skin pain (example, discomfort or soreness) severity over the past 24 hours, with 0 (indicating "No pain") to 10 (indicating "Worst pain imaginable). Higher scores indicated worse pain and negative change from baseline indicate no pain. FAS included all randomized subjects and were analysed under the treatment group as randomized. Here" number of subjects analysed" signified subjects who were evaluable for this endpoint and "n=number analysed" signifies subjects who were evaluable at specified timepoints.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16

End point values	Double-blind Induction Period: Lebrikizumab +TCS	Double-blind Induction Period: Placebo +TCS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	214	108		
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Change at Week 2 (n=206, 105)	-1.546 (± 1.7978)	-0.905 (± 1.9170)		
Change at Week 3 (n=213, 108)	-2.152 (± 2.1719)	-1.316 (± 2.2680)		
Change at Week 4 (n=214, 107)	-2.308 (± 2.2457)	-1.271 (± 2.4880)		
Change at Week 5 (n=211, 101)	-2.589 (± 2.3577)	-1.333 (± 2.4462)		

Change at Week 6 (n=207, 101)	-2.862 (± 2.4428)	-1.309 (± 2.5079)		
Change at Week 7 (n=203, 101)	-2.886 (± 2.4473)	-1.656 (± 2.4816)		
Change at Week 8 (n=212, 99)	-2.872 (± 2.4975)	-1.711 (± 2.7208)		
Change at Week 9 (n=205, 100)	-3.017 (± 2.4897)	-1.598 (± 2.5693)		
Change at Week 10 (n=205, 98)	-3.017 (± 2.6017)	-1.382 (± 2.7463)		
Change at Week 11 (n=201, 96)	-3.116 (± 2.6230)	-1.572 (± 2.6465)		
Change at Week 12 (n=206, 97)	-3.115 (± 2.6181)	-1.520 (± 2.5976)		
Change at Week 13 (n=196, 97)	-3.140 (± 2.5568)	-1.788 (± 2.4726)		
Change at Week 14 (n=203, 96)	-3.035 (± 2.6733)	-1.683 (± 2.4462)		
Change at Week 15 (n=203, 96)	-3.138 (± 2.6062)	-1.781 (± 2.6443)		
Change at Week 16 (n=203, 92)	-3.302 (± 2.5844)	-1.831 (± 2.5766)		

Statistical analyses

No statistical analyses for this end point

Secondary: Double-blind Induction Period: Proportion of Topical Corticosteroids (TCS) Medication Free Days

End point title	Double-blind Induction Period: Proportion of Topical Corticosteroids (TCS) Medication Free Days

End point description:

TCS free days proportion = Number of days subject did not take TCS medication / Number of days from Baseline to Week 16 Date or early discontinuation. FAS included all randomized subjects and were analysed under the treatment group as randomized.

End point type	Secondary

End point timeframe:

Baseline up to Week 16

End point values	Double-blind Induction Period: Lebrikizumab +TCS	Double-blind Induction Period: Placebo +TCS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	220	111		
Units: Proportion of Days				
arithmetic mean (standard deviation)	0.224 (± 0.3491)	0.151 (± 0.3032)		

Statistical analyses

No statistical analyses for this end point

Secondary: Double-blind Induction Period: Median Time (Days) to TCS-Free Use

End point title	Double-blind Induction Period: Median Time (Days) to TCS-Free Use

End point description:

Days from first study drug injection to the day subject stopped using all TCS. FAS included all randomized subjects and were analysed under the treatment group as randomized. Here, '99999' represents median and full range was not estimated due to insufficient number of events.

End point type	Secondary

End point timeframe:

Baseline up to Week 16

End point values	Double-blind Induction Period: Lebrikizumab +TCS	Double-blind Induction Period: Placebo +TCS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	220	111		
Units: Days				
median (full range (min-max))	99999 (99999 to 99999)	99999 (99999 to 99999)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Double-blind Induction Period: Day 1 to Week 16; Open-label Maintenance Period: Week 16 to Week 52	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups	
Reporting group title	Double-blind Induction Period: Lebrikizumab +TCS
Reporting group description:	
Subjects received loading dose of lebrikizumab 500 mg SC injection at Day 1 (Baseline) and Week 2 followed by lebrikizumab 250 mg SC injection once Q2W for up to 16 weeks concomitantly with TCS in the double-blind induction period.	
Reporting group title	Double-blind Induction Period: Placebo +TCS
Reporting group description:	
Subjects received lebrikizumab-matched placebo SC injection, Q2W for up to 16 weeks concomitantly with TCS in the double-blind induction period.	
Reporting group title	Open-label Maintenance Period: Lebrikizumab to Lebrikizumab
Reporting group description:	
Subjects who received lebrikizumab 250 mg Q2W during the Double-blind Induction Period continued to receive lebrikizumab 250 mg, Q2W during the 36-week Maintenance Period.	
Reporting group title	Open-label Maintenance Period: Placebo to Lebrikizumab
Reporting group description:	
During Maintenance Period, subjects who received placebo Q2W during the Induction Period received loading doses of lebrikizumab (500 mg) at Weeks 16 and 18. From Week 20 onward, the subjects received 1 injection of lebrikizumab 250mg Q2W.	

Serious adverse events	Double-blind Induction Period: Lebrikizumab +TCS	Double-blind Induction Period: Placebo +TCS	Open-label Maintenance Period: Lebrikizumab to Lebrikizumab
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 220 (1.36%)	1 / 111 (0.90%)	12 / 212 (5.66%)
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)			
Cutaneous T-cell lymphoma			
subjects affected / exposed	0 / 220 (0.00%)	0 / 111 (0.00%)	0 / 212 (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
Fibroadenoma of breast			

subjects affected / exposed	0 / 220 (0.00%)	0 / 111 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Uterine polyp			
subjects affected / exposed	0 / 220 (0.00%)	0 / 111 (0.00%)	0 / 212 (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 / 220 (0.00%)	0 / 111 (0.00%)	2 / 212 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	0 / 220 (0.00%)	0 / 111 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 220 (0.00%)	0 / 111 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Alcohol abuse			
subjects affected / exposed	0 / 220 (0.00%)	0 / 111 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delirium			
subjects affected / exposed	0 / 220 (0.00%)	0 / 111 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femoral neck fracture			

subjects affected / exposed	0 / 220 (0.00%)	0 / 111 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 220 (0.00%)	0 / 111 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	0 / 220 (0.00%)	0 / 111 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Multiple sclerosis			
subjects affected / exposed	1 / 220 (0.45%)	0 / 111 (0.00%)	0 / 212 (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
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 220 (0.00%)	0 / 111 (0.00%)	0 / 212 (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 / 220 (0.00%)	1 / 111 (0.90%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	0 / 220 (0.00%)	0 / 111 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Autoimmune thyroiditis			

subjects affected / exposed	0 / 220 (0.00%)	0 / 111 (0.00%)	0 / 212 (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
Musculoskeletal and connective tissue disorders			
Fracture pain			
subjects affected / exposed	0 / 220 (0.00%)	0 / 111 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 111 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	1 / 220 (0.45%)	0 / 111 (0.00%)	0 / 212 (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
Influenza			
subjects affected / exposed	1 / 220 (0.45%)	0 / 111 (0.00%)	0 / 212 (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
Lower respiratory tract infection			
subjects affected / exposed	0 / 220 (0.00%)	0 / 111 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 220 (0.00%)	0 / 111 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 220 (0.00%)	0 / 111 (0.00%)	2 / 212 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Open-label Maintenance Period: Placebo to Lebrikizumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 100 (4.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cutaneous T-cell lymphoma			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fibroadenoma of breast			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Uterine polyp			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cough			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Psychiatric disorders			
Alcohol abuse			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Delirium			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Femur fracture			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Radius fracture			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Multiple sclerosis			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Dermatitis atopic			

subjects affected / exposed	0 / 100 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Autoimmune thyroiditis			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Fracture pain			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infection			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Influenza			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lower respiratory tract infection			

subjects affected / exposed	0 / 100 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection				
subjects affected / exposed	0 / 100 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Diabetes mellitus				
subjects affected / exposed	0 / 100 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

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

Non-serious adverse events	Double-blind Induction Period: Lebrikizumab +TCS	Double-blind Induction Period: Placebo +TCS	Open-label Maintenance Period: Lebrikizumab to Lebrikizumab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	84 / 220 (38.18%)	31 / 111 (27.93%)	108 / 212 (50.94%)
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 220 (2.73%)	6 / 111 (5.41%)	0 / 212 (0.00%)
occurrences (all)	10	10	0
Eye disorders			
Conjunctivitis allergic			
subjects affected / exposed	18 / 220 (8.18%)	3 / 111 (2.70%)	18 / 212 (8.49%)
occurrences (all)	19	4	19
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	0 / 220 (0.00%)	0 / 111 (0.00%)	12 / 212 (5.66%)
occurrences (all)	0	0	14
Infections and infestations			
COVID-19			
subjects affected / exposed	8 / 220 (3.64%)	7 / 111 (6.31%)	13 / 212 (6.13%)
occurrences (all)	8	7	13
Conjunctivitis			

subjects affected / exposed	25 / 220 (11.36%)	2 / 111 (1.80%)	25 / 212 (11.79%)
occurrences (all)	27	2	30
Nasopharyngitis			
subjects affected / exposed	28 / 220 (12.73%)	14 / 111 (12.61%)	52 / 212 (24.53%)
occurrences (all)	33	18	73
Oral herpes			
subjects affected / exposed	11 / 220 (5.00%)	3 / 111 (2.70%)	0 / 212 (0.00%)
occurrences (all)	15	3	0
Upper respiratory tract infection			
subjects affected / exposed	8 / 220 (3.64%)	7 / 111 (6.31%)	17 / 212 (8.02%)
occurrences (all)	8	7	21

Non-serious adverse events	Open-label Maintenance Period: Placebo to Lebrikizumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	48 / 100 (48.00%)		
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences (all)	0		
Eye disorders			
Conjunctivitis allergic			
subjects affected / exposed	11 / 100 (11.00%)		
occurrences (all)	14		
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	2 / 100 (2.00%)		
occurrences (all)	4		
Infections and infestations			
COVID-19			
subjects affected / exposed	4 / 100 (4.00%)		
occurrences (all)	4		
Conjunctivitis			
subjects affected / exposed	11 / 100 (11.00%)		
occurrences (all)	11		
Nasopharyngitis			

subjects affected / exposed	16 / 100 (16.00%)		
occurrences (all)	21		
Oral herpes			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	6 / 100 (6.00%)		
occurrences (all)	10		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 December 2021	Global Amendment 1: - This amendment provides an updated trial design of the 36-week open-label Maintenance Period with, lebrikizumab 250mg Q2W. Updated the statistical analysis plan accordingly. Removed every 4 weeks regimen and related details. - Added blood sample for the biomarkers assessment at Week 16. - Added genomic biomarker assessment at Baseline. - Added Treatment Satisfaction Questionnaire for Medication-9 items assessments at Baseline during the Induction Period. - Post-last dose follow-up period reviewed and increased from 12 to 18 weeks. Added urine pregnancy test follow-up every 4 weeks after last dose. - Updated number of trial centres and countries. - Added upadacitinib and tralokinumab to sentence about newly approved treatments in background section.
10 August 2022	Global Amendment 2: - Change of focus for primary analysis to Overall Population (instead of Dupilumab Naïve). - Estimand framework amended to match that of Phase III Lebrikizumab study. - Odds ratio added to CMH analyses.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported