



Clinical trial results:

A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL TO EVALUATE THE EFFICACY AND SAFETY OF LEBRIKIZUMAB IN PATIENTS WITH MODERATE-TO-SEVERE ATOPIC DERMATITIS

Summary

EudraCT number	2019-002933-12
Trial protocol	DE BG IT
Global end of trial date	

Results information

Result version number	v1
This version publication date	27 July 2022
First version publication date	27 July 2022

Trial information

Trial identification

Sponsor protocol code	J2T-DM-KGAC
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04178967
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 17802

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, IN, United States, 46285
Public contact	Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 877CTLilly,
Scientific contact	Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 8772854559,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-002536-PIP01-18
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	Interim
Date of interim/final analysis	12 July 2021
Is this the analysis of the primary completion data?	No
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

This is a randomized, double-blind, placebo-controlled, parallel-group study which is 52 weeks in duration. The study is designed to confirm the safety and efficacy of lebrikizumab as monotherapy for treatment of moderate-to-severe atopic dermatitis utilizing a 16-week induction treatment period and a 36-week long-term maintenance treatment period.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 October 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 58
Country: Number of subjects enrolled	Singapore: 19
Country: Number of subjects enrolled	United States: 185
Country: Number of subjects enrolled	Taiwan: 60
Country: Number of subjects enrolled	Ukraine: 11
Country: Number of subjects enrolled	Mexico: 9
Country: Number of subjects enrolled	Bulgaria: 22
Country: Number of subjects enrolled	Germany: 81
Worldwide total number of subjects	445
EEA total number of subjects	103

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)	50
Adults (18-64 years)	362
From 65 to 84 years	33
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

No Text Available

Pre-assignment

Screening details:

Reported are results for the Induction Period (Baseline to Week16), results for Maintenance Period (Week 16 to Week 52) will be posted after study completion. One investigational site with eighteen participants was excluded from analysis due to Good Clinical Practice (GCP) issues.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Induction Period (Baseline-Week 16):

Two subcutaneous (SC) injections of Placebo as a loading dose at Baseline and Week 2 followed by a single injection every 2 weeks (Q2W) from Week 4 until Week 14.

Maintenance Period (Week 16-Week 52):

Two placebo SC injections as loading dose on Week 16 and Week 18. One placebo SC injection Q2W until Week 50.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received subcutaneous Injection of Placebo.

Arm title	Lebrikizumab Q2W
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Arm description:

Induction Period (Baseline-Week 16):

500 milligram (mg) Lebrikizumab (2 x 250 mg) SC injections as a loading dose at Baseline and Week 2 visits followed by a single 250 mg Lebrikizumab injection Q2W from Week 4 until Week 14.

Maintenance Period (Week 16-Week 52):

One 250 mg Lebrikizumab SC injection and one placebo SC injection as maintenance loading dose on Week 16 and Week 18.

One 250 mg Lebrikizumab SC injection Q2W until Week 50.

Arm type	Experimental
Investigational medicinal product name	Lebrikizumab
Investigational medicinal product code	
Other name	LY3650150, DRM06
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received 250 mg of Lebrikizumab administered as subcutaneous injection.

Number of subjects in period 1	Placebo	Lebrikizumab Q2W
Started	150	295
Received at Least One Dose of Study Drug	149	295
Completed	133	273
Not completed	17	22
Consent withdrawn by subject	8	7
Adverse event, non-fatal	4	6
Due to Epidemic/Pandemic	-	1
Lost to follow-up	2	-
Lack of efficacy	3	1
Protocol deviation	-	7

Baseline characteristics

Reporting groups

Reporting group title	Placebo
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Reporting group description:

Induction Period (Baseline-Week 16):

Two subcutaneous (SC) injections of Placebo as a loading dose at Baseline and Week 2 followed by a single injection every 2 weeks (Q2W) from Week 4 until Week 14.

Maintenance Period (Week 16-Week 52):

Two placebo SC injections as loading dose on Week 16 and Week 18. One placebo SC injection Q2W until Week 50.

Reporting group title	Lebrikizumab Q2W
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Reporting group description:

Induction Period (Baseline-Week 16):

500 milligram (mg) Lebrikizumab (2 x 250 mg) SC injections as a loading dose at Baseline and Week 2 visits followed by a single 250 mg Lebrikizumab injection Q2W from Week 4 until Week 14.

Maintenance Period (Week 16-Week 52):

One 250 mg Lebrikizumab SC injection and one placebo SC injection as maintenance loading dose on Week 16 and Week 18.

One 250 mg Lebrikizumab SC injection Q2W until Week 50.

Reporting group values	Placebo	Lebrikizumab Q2W	Total
Number of subjects	150	295	445
Age categorical			
Units: Subjects			
<=18 years	17	33	50
Between 18 and 65 years	123	239	362
>=65 years	10	23	33
Age continuous			
Units: years			
arithmetic mean	35.6	36.5	
standard deviation	± 17.15	± 16.64	-
Gender categorical			
Units: Subjects			
Female	79	147	226
Male	71	148	219
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	2	3	5
Asian	44	78	122
Native Hawaiian or Other Pacific Islander	1	2	3
Black or African American	10	26	36
White	89	181	270
More than one race	3	4	7
Unknown or Not Reported	1	1	2
Region of Enrollment			
Units: Subjects			
Canada	16	42	58
Singapore	8	11	19
United States	64	121	185

Taiwan	21	39	60
Ukraine	3	8	11
Mexico	3	6	9
Bulgaria	7	15	22
Germany	28	53	81

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Induction Period (Baseline-Week 16): Two subcutaneous (SC) injections of Placebo as a loading dose at Baseline and Week 2 followed by a single injection every 2 weeks (Q2W) from Week 4 until Week 14.	
Maintenance Period (Week 16-Week 52): Two placebo SC injections as loading dose on Week 16 and Week 18. One placebo SC injection Q2W until Week 50.	
Reporting group title	Lebrikizumab Q2W
Reporting group description:	
Induction Period (Baseline-Week 16): 500 milligram (mg) Lebrikizumab (2 x 250 mg) SC injections as a loading dose at Baseline and Week 2 visits followed by a single 250 mg Lebrikizumab injection Q2W from Week 4 until Week 14.	
Maintenance Period (Week 16-Week 52): One 250 mg Lebrikizumab SC injection and one placebo SC injection as maintenance loading dose on Week 16 and Week 18. One 250 mg Lebrikizumab SC injection Q2W until Week 50.	

Primary: Percentage of Participants With an Investigator Global Assessment (IGA) Score of 0 or 1 and a Reduction ≥ 2 Points From Baseline to Week 16

End point title	Percentage of Participants With an Investigator Global Assessment (IGA) Score of 0 or 1 and a Reduction ≥ 2 Points From Baseline to Week 16
End point description: The IGA measures the investigator's global assessment of the participant's overall severity of their AD, based on a static, numeric 5-point scale from 0 (clear skin) to 4 (severe disease). The score is based on an overall assessment of the degree of erythema, papulation/induration, oozing/crusting, and lichenification.	
Analysis Population Description (APD): All randomized participants, even if the participant does not take the assigned treatment, does not receive the correct treatment, or otherwise does not follow the protocol. One investigational site with eighteen participants was excluded from analysis due to Good Clinical Practice (GCP) issues. Markov Chain Monte Carlo Multiple Imputation (MCMC-MI) was used to handle missing data.	
End point type	Primary
End point timeframe: Baseline to Week 16	

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	146	281		
Units: percentage of participants				
number (confidence interval 95%)	10.9 (5.7 to 16.1)	33.1 (27.4 to 38.8)		

Statistical analyses

Statistical analysis title	IGA Score of 0 or 1
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	427
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.000004
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	21.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.1
upper limit	29.4

Primary: Percentage of Participants Achieving Eczema Area And Severity Index (EASI-75) (≥75% Reduction in EASI Score) From Baseline to Week 16

End point title	Percentage of Participants Achieving Eczema Area And Severity Index (EASI-75) (≥75% Reduction in EASI Score) From Baseline to Week 16
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End point description:

The EASI assesses objective physician estimates of 2 dimensions of atopic dermatitis - disease extent and clinical signs affected: 0 = 0%; 1 = 1-9%; 2 = 10-29%; 3 = 30-49%; 4 = 50-69%; 5 = 70-89%; 6 = 90-100% and the severity of 4 clinical signs: (1) erythema, (2) edema/papulation, (3) excoriation, and (4) lichenification each on a scale of 0 to 3 (0 = none, absent; 1 = mild; 2 = moderate; 3 = severe) at 4 body sites (head/neck, trunk, upper limbs, and lower limbs). Half scores are allowed between severities 1, 2, and 3. The final EASI score was obtained by weight-averaging these 4 scores and will range from 0 to 72 (severe).

APD: All randomized participants, even if the participant does not take the assigned treatment, does not receive the correct treatment, or otherwise does not follow the protocol. One investigational site with eighteen participants was excluded from analysis due to GCP issues. MCMC-MI was used to handle missing data.

End point type	Primary
End point timeframe:	
Baseline to Week 16	

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	146	281		
Units: percentage of participants				
number (confidence interval 95%)	18.2 (11.8 to 24.6)	50.8 (44.9 to 56.8)		

Statistical analyses

Statistical analysis title	EASI-75 ($\geq 75\%$ Reduction in EASI Score)
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	427
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.000001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	32.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	23.2
upper limit	41

Secondary: Percentage of participants with an IGA score of 0 or 1 and a reduction ≥ 2 points from Baseline to Week 2

End point title	Percentage of participants with an IGA score of 0 or 1 and a reduction ≥ 2 points from Baseline to Week 2
End point description:	
<p>The IGA measures the investigator's global assessment of the participant's overall severity of their AD, based on a static, numeric 5-point scale from 0 (clear skin) to 4 (severe disease). The score is based on an overall assessment of the degree of erythema, papulation/induration, oozing/crusting, and lichenification.</p> <p>APD: All randomized participants, even if the participant does not take the assigned treatment, does not receive the correct treatment, or otherwise does not follow the protocol. One investigational site with eighteen participants was excluded from analysis due to GCP issues. MCMC-MI was used to handle missing data.</p>	
End point type	Secondary
End point timeframe:	
Baseline to Week 2	

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	146	281		
Units: percentage of participants				
number (confidence interval 95%)	0 (0.0 to 0.0)	0.7 (-0.3 to 1.8)		

Statistical analyses

Statistical analysis title	IGA score of 0 or 1
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	427
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.305686
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	1.8

Secondary: Percentage of participants with an IGA score of 0 or 1 and a reduction ≥ 2 points from Baseline to Week 4

End point title	Percentage of participants with an IGA score of 0 or 1 and a reduction ≥ 2 points from Baseline to Week 4
End point description:	
<p>The IGA measures the investigator's global assessment of the participant's overall severity of their AD, based on a static, numeric 5-point scale from 0 (clear skin) to 4 (severe disease). The score is based on an overall assessment of the degree of erythema, papulation/induration, oozing/crusting, and lichenification.</p> <p>APD: All randomized participants, even if the participant does not take the assigned treatment, does not receive the correct treatment, or otherwise does not follow the protocol. One investigational site with eighteen participants was excluded from analysis due to GCP issues. MCMC-MI was used to handle missing data.</p>	
End point type	Secondary
End point timeframe:	
Baseline to Week 4	

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	146	281		
Units: percentage of participants				
number (confidence interval 95%)	1.4 (-0.5 to 3.3)	9.0 (5.6 to 12.5)		

Statistical analyses

Statistical analysis title	IGA score of 0 or 1
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	427
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001635
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	8.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.1
upper limit	12.2

Secondary: Percentage of participants with an IGA score of 0 or 1 and a reduction ≥ 2 points from Baseline to Week 16 in Adults

End point title	Percentage of participants with an IGA score of 0 or 1 and a reduction ≥ 2 points from Baseline to Week 16 in Adults
End point description:	
<p>The IGA measures the investigator's global assessment of the participant's overall severity of their AD, based on a static, numeric 5-point scale from 0 (clear skin) to 4 (severe disease). The score is based on an overall assessment of the degree of erythema, papulation/induration, oozing/crusting, and lichenification.</p> <p>APD: All randomized adult participants, even if the participant does not take the assigned treatment, does not receive the correct treatment, or otherwise does not follow the protocol. One investigational site with eighteen participants was excluded from analysis due to GCP issues. MCMC-MI was used to handle missing data.</p>	
End point type	Secondary
End point timeframe:	
Baseline to Week 16	

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	251		
Units: percentage of participants				
number (confidence interval 95%)	11.6 (5.9 to 17.2)	31.8 (25.9 to 37.8)		

Statistical analyses

Statistical analysis title	IGA score of 0 or 1
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	380
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.000032
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	20.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	12.2
upper limit	28.5

Secondary: Percentage of participants achieving EASI-90 (≥90% reduction in EASI score) from Baseline to Week 16

End point title	Percentage of participants achieving EASI-90 (≥90% reduction in EASI score) from Baseline to Week 16
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End point description:

The EASI assesses objective physician estimates of 2 dimensions of atopic dermatitis - disease extent and clinical signs affected: 0 = 0%; 1 = 1-9%; 2 = 10-29%; 3 = 30-49%; 4 = 50-69%; 5 = 70-89%; 6 = 90-100% and the severity of 4 clinical signs: (1) erythema, (2) edema/papulation, (3) excoriation, and (4) lichenification each on a scale of 0 to 3 (0 = none, absent; 1 = mild; 2 = moderate; 3 = severe) at 4 body sites (head/neck, trunk, upper limbs, and lower limbs). Half scores are allowed between severities 1, 2, and 3. The final EASI score was obtained by weight-averaging these 4 scores and will range from 0 to 72 (severe).

APD: All randomized participants, even if the participant does not take the assigned treatment, does not receive the correct treatment, or otherwise does not follow the protocol. One investigational site with eighteen participants was excluded from analysis due to GCP issues. MCMC-MI was used to handle missing data.

End point type	Secondary
End point timeframe:	
Baseline to Week 16	

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	146	281		
Units: percentage of participants				
number (confidence interval 95%)	9.4 (4.5 to 14.2)	30.2 (24.7 to 35.7)		

Statistical analyses

Statistical analysis title	EASI-90 ($\geq 90\%$ reduction in EASI score)
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	427
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.000009
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	20.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	12.9
upper limit	27.8

Secondary: Percentage change in Pruritus Numerical Rating Scale (NRS) score from Baseline to Week 16

End point title	Percentage change in Pruritus Numerical Rating Scale (NRS) score from Baseline to Week 16
End point description:	
Pruritus NRS is an 11-point scale used by participants to rate their worst itch severity over the past 24 hours with 0 indicating "No itch" and 10 indicating "Worst itch imaginable." Least Squares (LS) Mean was calculated using analysis of covariance (ANCOVA) model with treatment and randomization strata (region, disease severity, age) as fixed factors and baseline value as covariate.	
APD: All randomized participants, with a Baseline Pruritus NRS score >0 , even if the participant does not take the assigned treatment, does not receive the correct treatment, or otherwise does not follow the protocol. One investigational site with eighteen participants was excluded from analysis due to GCP issues. MCMC-MI was used to handle missing data.	
End point type	Secondary
End point timeframe:	
Baseline, Week 16	

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	146	281		
Units: percentage change				
least squares mean (standard error)	-8.91 (\pm 3.908)	-35.67 (\pm 3.357)		

Statistical analyses

Statistical analysis title	Pruritus NRS score
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	427
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.000001
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-26.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	-34.3
upper limit	-19.3

Secondary: Percentage of participants with a Pruritus NRS score of ≥ 4 -points at Baseline who achieve a ≥ 4 -point reduction in Pruritus NRS score from Baseline to Week 16

End point title	Percentage of participants with a Pruritus NRS score of ≥ 4 -points at Baseline who achieve a ≥ 4 -point reduction in Pruritus NRS score from Baseline to Week 16
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End point description:

Pruritus NRS is an 11-point scale used by participants to rate their worst itch severity over the past 24 hours with 0 indicating "No itch" and 10 indicating "Worst itch imaginable."

APD: All randomized participants, with a Baseline Pruritus NRS score ≥ 4 , even if the participant does not take the assigned treatment, does not receive the correct treatment, or otherwise does not follow the protocol. One investigational site with eighteen participants was excluded from analysis due to GCP issues. MCMC-MI was used to handle missing data.

End point type	Secondary
End point timeframe:	
Baseline to Week 16	

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	134	253		
Units: percentage of participants				
number (confidence interval 95%)	11.3 (5.9 to 16.8)	38.3 (32.2 to 44.4)		

Statistical analyses

Statistical analysis title	Pruritus NRS score of ≥ 4 -points
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	387
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.000001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	26.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	18.7
upper limit	35

Secondary: Percentage of participants with a Pruritus NRS score of ≥ 5 -points at Baseline who achieve a ≥ 4 -point reduction in Pruritus NRS score from Baseline to Week 16

End point title	Percentage of participants with a Pruritus NRS score of ≥ 5 -points at Baseline who achieve a ≥ 4 -point reduction in Pruritus NRS score from Baseline to Week 16
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End point description:

Pruritus NRS is an 11-point scale used by participants to rate their worst itch severity over the past 24 hours with 0 indicating "No itch" and 10 indicating "Worst itch imaginable."

APD: All randomized participants, with Baseline Pruritus NRS score ≥ 5 , even if the participant does not take the assigned treatment, does not receive the correct treatment, or otherwise does not follow the protocol. One investigational site with eighteen participants was excluded from analysis due to GCP issues. MCMC-MI was used to handle missing data.

End point type	Secondary
End point timeframe:	
Baseline to Week 16	

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	122	234		
Units: percentage of participants				
number (confidence interval 95%)	11.6 (5.9 to 17.4)	40.0 (33.6 to 46.4)		

Statistical analyses

Statistical analysis title	Pruritus NRS score
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	356
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.000001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	28.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	19.6
upper limit	36.7

Secondary: Percentage change in EASI score from Baseline to Week 16

End point title	Percentage change in EASI score from Baseline to Week 16
End point description:	
<p>The EASI assesses objective physician estimates of 2 dimensions of atopic dermatitis - disease extent and clinical signs affected: 0 = 0%; 1 = 1-9%; 2 = 10-29%; 3 = 30-49%; 4 = 50-69%; 5 = 70-89%; 6 = 90-100% and the severity of 4 clinical signs: (1) erythema, (2) edema/papulation, (3) excoriation, and (4) lichenification each on a scale of 0 to 3 (0 = none, absent; 1 = mild; 2 = moderate; 3 = severe) at 4 body sites (head/neck, trunk, upper limbs, and lower limbs). Half scores are allowed between severities 1, 2, and 3. The final EASI score was obtained by weight-averaging these 4 scores and will range from 0 to 72 (severe).</p> <p>APD: All randomized participants, even if the participant does not take the assigned treatment, does not receive the correct treatment, or otherwise does not follow the protocol. One investigational site with eighteen participants was excluded from analysis due to GCP issues. MCMC-MI was used to handle missing data.</p>	
End point type	Secondary
End point timeframe:	
Baseline, Week 16	

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	146	281		
Units: percent change				
least squares mean (standard error)	-28.22 (\pm 3.873)	-60.61 (\pm 3.268)		

Statistical analyses

Statistical analysis title	EASI score
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	427
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.000001
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-32.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-39.9
upper limit	-24.9

Secondary: Change From Baseline in Percent Body Surface Area (BSA) at Week 16

End point title	Change From Baseline in Percent Body Surface Area (BSA) at Week 16
End point description:	
<p>The BSA affected by AD will be assessed for 4 separate body regions: head and neck, trunk (including genital region), upper extremities, and lower extremities (including the buttocks). Each body region will be assessed for disease extent ranging from 0% to 100% involvement. BSA was calculated using the participant's palm using the 1% rule, 1 palm was equivalent to 1% with estimates of the number of palms it takes to cover the affected AD area. Percent of BSA for a body region was calculated as = total number of palms in a body region * % surface area equivalent to 1 palm. Overall percent BSA of all 4 body regions ranges from 0% to 100 % with higher values representing greater severity of AD. APD: All randomized participants, with observed BSA data, even if the participant does not take the assigned treatment, does not receive the correct treatment, or otherwise does not follow the protocol. One investigational site with eighteen participants was excluded from analysis due to GCP issue</p>	
End point type	Secondary
End point timeframe:	
Baseline, Week 16	

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	209		
Units: percentage of BSA				
least squares mean (standard error)	-13.76 (\pm 1.926)	-29.65 (\pm 1.330)		

Statistical analyses

Statistical analysis title	Percent BSA
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	286
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.000001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-15.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.04
upper limit	-11.73

Secondary: Percentage of participants achieving EASI-90 from Baseline to Week 4

End point title	Percentage of participants achieving EASI-90 from Baseline to Week 4
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End point description:

The EASI assesses objective physician estimates of 2 dimensions of atopic dermatitis - disease extent and clinical signs affected: 0 = 0%; 1 = 1-9%; 2 = 10-29%; 3 = 30-49%; 4 = 50-69%; 5 = 70-89%; 6 = 90-100% and the severity of 4 clinical signs: (1) erythema, (2) edema/papulation, (3) excoriation, and (4) lichenification each on a scale of 0 to 3 (0 = none, absent; 1 = mild; 2 = moderate; 3 = severe) at 4 body sites (head/neck, trunk, upper limbs, and lower limbs). Half scores are allowed between severities 1, 2, and 3. The final EASI score was obtained by weight-averaging these 4 scores and will range from 0 to 72 (severe).

APD: All randomized participants, even if the participant does not take the assigned treatment, does not receive the correct treatment, or otherwise does not follow the protocol. One investigational site with eighteen participants was excluded from analysis due to GCP issues. MCMC-MI was used to handle missing data.

End point type	Secondary
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End point timeframe:

Baseline to Week 4

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	146	281		
Units: percentage of participants				
number (confidence interval 95%)	1.4 (-0.5 to 3.4)	6.4 (3.4 to 9.3)		

Statistical analyses

Statistical analysis title	EASI-90
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	427
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.020407
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	5
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.5
upper limit	8.5

Secondary: Change from Baseline in Dermatology Life Quality Index (DLQI) at Week 16

End point title	Change from Baseline in Dermatology Life Quality Index (DLQI) at Week 16
End point description:	
<p>The DLQI is a 10-item, validated questionnaire used to assess the impact of skin disease on the quality of life of an affected person. 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, over the previous week. Response categories include "Not at all," "A little," "A lot," and "Very much," with corresponding scores of 0, 1, 2, and 3 respectively. A high score is indicative of a poor quality of life.</p> <p>APD: All randomized participants, with non-missing baseline DLQI score, even if the participant does not take the assigned treatment, does not receive the correct treatment, or otherwise does not follow the protocol. One investigational site with eighteen participants was excluded from analysis due to GCP issues. MCMC-MI was used to handle missing data.</p>	
End point type	Secondary
End point timeframe:	
Baseline, Week 16	

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	218		
Units: score on a scale				
least squares mean (standard error)	-2.47 (± 1.164)	-6.99 (± 1.152)		

Statistical analyses

Statistical analysis title	Dermatology Life Quality Index (DLQI)
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	336
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.000001
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-4.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.9
upper limit	-3.1

Secondary: Percentage of participants achieving ≥4-point improvement in DLQI from Baseline to Week 16

End point title	Percentage of participants achieving ≥4-point improvement in DLQI from Baseline to Week 16
End point description:	
<p>The DLQI is a 10-item, validated questionnaire used to assess the impact of skin disease on the quality of life of an affected person. 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, over the previous week. Response categories include "Not at all," "A little," "A lot," and "Very much," with corresponding scores of 0, 1, 2, and 3 respectively. A high score is indicative of a poor quality of life.</p> <p>APD: All randomized participants, with non-missing baseline DLQI score, even if the participant does not take the assigned treatment, does not receive the correct treatment, or otherwise does not follow the protocol. One investigational site with eighteen participants was excluded from analysis due to GCP issues. MCMC-MI was used to handle missing data.</p>	
End point type	Secondary
End point timeframe:	
Baseline to Week 16	

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	218		
Units: percentage of participants				
number (confidence interval 95%)	33.7 (24.9 to 42.6)	63.5 (57.0 to 70.0)		

Statistical analyses

Statistical analysis title	DLQI
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	336
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.000001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	29.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	19.1
upper limit	40.8

Secondary: Percentage of participants with a DLQI total score of ≥ 4 -point achieving ≥ 4 -point improvement in DLQI from baseline to Week 16

End point title	Percentage of participants with a DLQI total score of ≥ 4 -point achieving ≥ 4 -point improvement in DLQI from baseline to Week 16
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End point description:

The DLQI is a 10-item, validated questionnaire used to assess the impact of skin disease on the quality of life of an affected person. 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, over the previous week. Response categories include "Not at all," "A little," "A lot," and "Very much," with corresponding scores of 0, 1, 2, and 3 respectively. A high score is indicative of a poor quality of life.

APD: All randomized participants, with a DLQI Total Score of ≥ 4 -point at baseline, even if the participant does not take the assigned treatment, does not receive the correct treatment, or otherwise does not follow the protocol. One investigational site with eighteen participants was excluded from analysis due to GCP issues. MCMC-MI was used to handle missing data.

End point type	Secondary
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End point timeframe:

Baseline to Week 16

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	115	215		
Units: percentage of participants				
number (confidence interval 95%)	34.6 (25.6 to 43.6)	64.4 (57.8 to 70.9)		

Statistical analyses

Statistical analysis title	DLQI
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	330
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.000001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	29.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	18.9
upper limit	40.9

Secondary: Percentage change in Sleep-loss score from Baseline to Week 16

End point title	Percentage change in Sleep-loss score from Baseline to Week 16
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End point description:

Sleep Loss due to interference of itch will be assessed by the participant. Participants rate their interference of itch on sleep based on a 5-point Likert scale [0 (not at all) to 4 (unable to sleep at all)]. Higher scores indicated a greater impact and worse outcome. Assessments will be recorded daily by the participant using an electronic diary. LS Mean was calculated using ANCOVA model with treatment, baseline value, and stratification factors of geographic region, age group, baseline IGA (3 versus 4) score as fixed factors.

APD: All randomized participants, with baseline sleep-loss score >0, even if the participant does not take the assigned treatment, does not receive the correct treatment, or otherwise does not follow the protocol. One investigational site with eighteen participants was excluded from analysis due to GCP issues. MCMC-MI was used to handle missing data.

End point type	Secondary
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End point timeframe:

Baseline, Week 16

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	146	281		
Units: percent change				
least squares mean (standard error)	-11.40 (\pm 5.420)	-47.24 (\pm 4.610)		

Statistical analyses

Statistical analysis title	Sleep-loss score
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	427
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.000001
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-35.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	-46.2
upper limit	-25.5

Secondary: Change from Baseline in Sleep-loss score at Week 16

End point title	Change from Baseline in Sleep-loss score at Week 16
End point description:	
Sleep Loss due to interference of itch will be assessed by the participant. Participants rate their interference of itch on sleep based on a 5-point Likert scale [0 (not at all) to 4 (unable to sleep at all)]. Higher scores indicated a greater impact and worse outcome. Assessments will be recorded daily by the participant using an electronic diary. LS Mean was calculated using ANCOVA model with treatment, baseline value, and stratification factors of geographic region, age group, baseline IGA (3 versus 4) score as fixed factors.	
APD: All randomized participants, with non-missing baseline Sleep-loss score, even if the participant does not take the assigned treatment, does not receive the correct treatment, or otherwise does not follow the protocol. One investigational site with eighteen participants was excluded from analysis due to GCP issues. MCMC-MI was used to handle missing data.	
End point type	Secondary
End point timeframe:	
Baseline, Week 16	

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	146	281		
Units: score on a scale				
least squares mean (standard error)	-0.35 (\pm 0.097)	-1.02 (\pm 0.080)		

Statistical analyses

Statistical analysis title	Sleep-loss score
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	427
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.000001
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-0.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	-0.5

Secondary: Percentage of participants with a Sleep-loss score ≥ 2 points at Baseline who achieve a ≥ 2 points reduction from Baseline to Week 16

End point title	Percentage of participants with a Sleep-loss score ≥ 2 points at Baseline who achieve a ≥ 2 points reduction from Baseline to Week 16
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End point description:

Sleep Loss due to interference of itch will be assessed by the participant. Participants rate their interference of itch on sleep based on a 5-point Likert scale [0 (not at all) to 4 (unable to sleep at all)]. Higher scores indicated a greater impact and worse outcome. Assessments will be recorded daily by the participant using an electronic diary.

APD: All randomized participants, with baseline sleep-loss score ≥ 2 Points, even if the participant does not take the assigned treatment, does not receive the correct treatment, or otherwise does not follow the protocol. One investigational site with eighteen participants was excluded from analysis due to GCP issues. MCMC-MI was used to handle missing data.

End point type	Secondary
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End point timeframe:

Baseline to Week 16

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	97	161		
Units: percentage of participants				
number (confidence interval 95%)	7.8 (2.2 to 13.4)	26.5 (19.6 to 33.4)		

Statistical analyses

Statistical analysis title	Sleep-loss score
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	258
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.000842
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	17.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.8
upper limit	27

Secondary: Percentage of participants with a Pruritus NRS score of ≥ 4 points at Baseline who achieve a ≥ 4 -point reduction from Baseline to Week 1

End point title	Percentage of participants with a Pruritus NRS score of ≥ 4 points at Baseline who achieve a ≥ 4 -point reduction from Baseline to Week 1
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End point description:

Pruritus NRS is an 11-point scale used by participants to rate their worst itch severity over the past 24 hours with 0 indicating "No itch" and 10 indicating "Worst itch imaginable."

APD: All randomized participants, with a Pruritus NRS Score of ≥ 4 Points at baseline, even if the participant does not take the assigned treatment, does not receive the correct treatment, or otherwise does not follow the protocol. One investigational site with eighteen participants was excluded from analysis due to GCP issues. MCMC-MI was used to handle missing data.

End point type	Secondary
End point timeframe:	
Baseline to Week 1	

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	134	253		
Units: percentage of participants				
number (confidence interval 95%)	0.0 (0.0 to 0.0)	0.4 (0.0 to 1.2)		

Statistical analyses

Statistical analysis title	Pruritus NRS score
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	387
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.469221
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	1.2

Secondary: Percentage of participants with a Pruritus NRS score of ≥ 4 points at Baseline who achieve a ≥ 4 -point reduction from Baseline to Week 2

End point title	Percentage of participants with a Pruritus NRS score of ≥ 4 points at Baseline who achieve a ≥ 4 -point reduction from Baseline to Week 2
End point description:	
Pruritus NRS is an 11-point scale used by participants to rate their worst itch severity over the past 24 hours with 0 indicating "No itch" and 10 indicating "Worst itch imaginable."	
APD: All randomized participants, with a Pruritus NRS Score of ≥ 4 Points at Baseline, even if the participant does not take the assigned treatment, does not receive the correct treatment, or otherwise does not follow the protocol. One investigational site with eighteen participants was excluded from analysis due to GCP issues. MCMC-MI was used to handle missing data.	
End point type	Secondary
End point timeframe:	
Baseline to Week 2	

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	134	253		
Units: percentage of participants				
number (confidence interval 95%)	0.7 (0.0 to 2.2)	3.6 (1.3 to 5.8)		

Statistical analyses

Statistical analysis title	Pruritus NRS score
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	387
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.118893
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	2.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	5.3

Secondary: Percentage of participants with a Pruritus NRS score of ≥ 4 points at Baseline who achieve a ≥ 4 -point reduction from Baseline to Week 4

End point title	Percentage of participants with a Pruritus NRS score of ≥ 4 points at Baseline who achieve a ≥ 4 -point reduction from Baseline to Week 4
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End point description:

Pruritus NRS is an 11-point scale used by participants to rate their worst itch severity over the past 24 hours with 0 indicating "No itch" and 10 indicating "Worst itch imaginable."

APD: All randomized participants, with a Pruritus NRS Score of ≥ 4 Points at Baseline, even if the participant does not take the assigned treatment, does not receive the correct treatment, or otherwise does not follow the protocol. One investigational site with eighteen participants was excluded from analysis due to GCP issues. MCMC-MI was used to handle missing data.

End point type	Secondary
End point timeframe:	
Baseline to Week 4	

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	134	253		
Units: percentage of participants				
number (confidence interval 95%)	3.0 (0.1 to 5.9)	16.8 (12.2 to 21.4)		

Statistical analyses

Statistical analysis title	Pruritus NRS score
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	387
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.000216
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	13.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.7
upper limit	18.7

Secondary: Percentage of participants with a Pruritus NRS score of ≥5 points at Baseline who achieve a ≥4-point reduction from Baseline to Week 1

End point title	Percentage of participants with a Pruritus NRS score of ≥5 points at Baseline who achieve a ≥4-point reduction from Baseline to Week 1
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End point description:

Pruritus NRS is an 11-point scale used by participants to rate their worst itch severity over the past 24 hours with 0 indicating "No itch" and 10 indicating "Worst itch imaginable."

APD: All randomized participants, with a Pruritus NRS Score of ≥5 Points at Baseline, even if the participant does not take the assigned treatment, does not receive the correct treatment, or otherwise does not follow the protocol. One investigational site with eighteen participants was excluded from analysis due to GCP issues. MCMC-MI was used to handle missing data.

End point type	Secondary
End point timeframe:	
Baseline to Week 1	

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	122	234		
Units: percentage of participants				
number (confidence interval 95%)	0.0 (0.0 to 0.0)	0.4 (0.0 to 1.3)		

Statistical analyses

Statistical analysis title	Pruritus NRS score
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	356
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.46816
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	1.3

Secondary: Percentage of participants with a Pruritus NRS score of ≥ 5 points at Baseline who achieve a ≥ 4 -point reduction from Baseline to Week 2

End point title	Percentage of participants with a Pruritus NRS score of ≥ 5 points at Baseline who achieve a ≥ 4 -point reduction from Baseline to Week 2
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End point description:

Pruritus NRS is an 11-point scale used by participants to rate their worst itch severity over the past 24 hours with 0 indicating "No itch" and 10 indicating "Worst itch imaginable."

APD: All randomized participants, with a Pruritus NRS Score of ≥ 5 Points at Baseline, even if the participant does not take the assigned treatment, does not receive the correct treatment, or otherwise does not follow the protocol. One investigational site with eighteen participants was excluded from analysis due to GCP issues. MCMC-MI was used to handle missing data.

End point type	Secondary
End point timeframe:	
Baseline to Week 2	

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	122	234		
Units: percentage of participants				
number (confidence interval 95%)	0.8 (0.0 to 2.4)	3.8 (1.4 to 6.3)		

Statistical analyses

Statistical analysis title	Pruritus NRS score
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	356
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.121327
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	5.8

Secondary: Percentage of participants with a Pruritus NRS score of ≥ 5 points at Baseline who achieve a ≥ 4 -point reduction from Baseline to Week 4

End point title	Percentage of participants with a Pruritus NRS score of ≥ 5 points at Baseline who achieve a ≥ 4 -point reduction from Baseline to Week 4
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End point description:

Pruritus NRS is an 11-point scale used by participants to rate their worst itch severity over the past 24 hours with 0 indicating "No itch" and 10 indicating "Worst itch imaginable."

APD: All randomized participants, with a Pruritus NRS Score of ≥ 5 Points at Baseline, even if the participant does not take the assigned treatment, does not receive the correct treatment, or otherwise does not follow the protocol. One investigational site with eighteen participants was excluded from analysis due to GCP issues. MCMC-MI was used to handle missing data.

End point type	Secondary
End point timeframe:	
Baseline to Week 4	

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	122	234		
Units: percentage of participants				
number (confidence interval 95%)	3.3 (0.1 to 6.5)	18.1 (13.2 to 23.1)		

Statistical analyses

Statistical analysis title	Pruritus NRS score
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	356
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.000238
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	14.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.3
upper limit	20.2

Secondary: Percentage Change in SCORing Atopic Dermatitis (SCORAD) from Baseline to Week 16

End point title	Percentage Change in SCORing Atopic Dermatitis (SCORAD) from Baseline to Week 16
End point description:	
<p>The SCORAD index uses the rule of nines to assess disease extent and evaluates 6 clinical characteristics to determine disease severity: (1) erythema, (2) edema/papulation, (3) oozing/crusts, (4) excoriation, (5) lichenification, and (6) dryness on a scale of 0 to 3 (0=absence, 1=mild, 2=moderate, 3=severe). The SCORAD assesses subjective symptoms of pruritus and sleep loss with VAS where 0 is no itching or no trouble sleeping and 10 is unbearable itching or a lot of trouble sleeping. These 3 aspects: extent of disease (A: 0-1-2), disease severity (B: 0-18), & subjective symptoms (C: 0-20) combine to give a maximum possible score of 103, where 0 = no disease and 103 = severe disease.</p> <p>APD: All randomized participants, with baseline SCORAD >0, even if the participant does not take the assigned treatment, does not receive the correct treatment, or otherwise does not follow the protocol. One investigational site with eighteen participants was excluded from analysis due to GCP issue.</p>	
End point type	Secondary
End point timeframe:	
Baseline, Week 16	

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	146	281		
Units: percent change				
least squares mean (standard error)	-13.87 (\pm 3.201)	-43.85 (\pm 2.680)		

Statistical analyses

Statistical analysis title	SCORing Atopic Dermatitis (SCORAD)
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	427
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.000001
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-29.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	-36.16
upper limit	-23.8

Secondary: Change From Baseline in European Quality of Life-5 Dimensions-5 Levels (EQ-5D-5L) at Week 16 - Health State Index

End point title	Change From Baseline in European Quality of Life-5 Dimensions-5 Levels (EQ-5D-5L) at Week 16 - Health State Index
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End point description:

The EQ-5D-5L is a 2-part measurement. The first part is comprised of the following 5 participant-reported dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has 5 levels: no problems, slight problems, moderate problems, severe problems, and extreme problems. The responses are used to derive the health state index scores using the United Kingdom (UK) algorithm, with scores ranging from -0.594 to 1, and the United States (US) algorithm, with scores ranging from -0.109 to 1, with higher score indicating better health state.

APD: All randomized participants, with non-missing EQ-5D-5L data at baseline, even if the participant does not take the assigned treatment, does not receive the correct treatment, or otherwise does not follow the protocol. One investigational site with eighteen participants was excluded from analysis due to GCP issues. Missing Values were imputed using last observation carried forward (LOCF) method.

End point type	Secondary
End point timeframe:	
Baseline, Week 16	

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	146	281		
Units: score on a scale				
least squares mean (standard error)				
Health State Index UK	0.04 (± 0.018)	0.12 (± 0.015)		
Health State Index US	0.03 (± 0.013)	0.08 (± 0.011)		

Statistical analyses

Statistical analysis title	EQ-5D-5L
Statistical analysis description: UK	
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	427
Analysis specification	Pre-specified
Analysis type	superiority ^[1]
P-value	= 0.000011
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.04
upper limit	0.11
Notes:	
[1] - UK	

Statistical analysis title	EQ-5D-5L
Statistical analysis description: US	
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	427
Analysis specification	Pre-specified
Analysis type	superiority ^[2]
P-value	= 0.000012
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.03
upper limit	0.08
Notes:	
[2] - US	

Secondary: Change From Baseline in EQ-5D-5L at Week 16 - Visual Analog Scale (VAS)

End point title	Change From Baseline in EQ-5D-5L at Week 16 - Visual Analog Scale (VAS)
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End point description:

The EQ-5D-5L is a 2-part measurement. The second part is assessed using a VAS that ranged from 0 to 100 millimeter (mm), where 0 is the worst health you can imagine and 100 is the best health you can imagine. LS Mean was calculated using the ANCOVA model with treatment and stratification factors of geographic region, age group, baseline IGA (3 versus 4) score as fixed factors and baseline value as covariate.

End point type	Secondary
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End point timeframe:

Baseline, Week 16

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	145	277		
Units: millimetre(s)				
least squares mean (standard error)	5.23 (\pm 1.578)	8.97 (\pm 1.325)		

Statistical analyses

Statistical analysis title	VAS
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	422
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.016649
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	3.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	6.79

Secondary: Change from Baseline in Patient Oriented Eczema Measure (POEM) at Week 16

End point title	Change from Baseline in Patient Oriented Eczema Measure (POEM) at Week 16
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End point description:

POEM is a 7-item, validated, questionnaire used by the participant to assess disease symptoms over the last week. The participant is asked to respond to 7 questions on skin dryness, itching, flaking, cracking, sleep loss, bleeding and weeping. All 7 answers carry equal weight with a total possible score from 0 to 28 (answers scored as: No days=0; 1-2 days = 1; 3-4 days = 2; 5-6 days = 3; everyday = 4). A high

score is indicative of a poor quality of life. POEM responses will be captured using an electronic diary and transferred into the clinical database.

APD: All randomized participants, with observed POEM data, even if the participant does not take the assigned treatment, does not receive the correct treatment, or otherwise does not follow the protocol. One investigational site with eighteen participants was excluded from analysis due to GCP issues. MMRM was used to handle all missing data.

End point type	Secondary
End point timeframe:	
Baseline, Week 16	

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	184		
Units: score on a scale				
least squares mean (standard error)	-3.45 (\pm 0.773)	-9.55 (\pm 0.525)		

Statistical analyses

Statistical analysis title	POEM
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	249
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.000001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-6.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.81
upper limit	-4.39

Secondary: Change from Baseline in Patient-Reported Outcomes Measurement Information System (PROMIS) Anxiety at Week 16-Adolescents

End point title	Change from Baseline in Patient-Reported Outcomes Measurement Information System (PROMIS) Anxiety at Week 16-Adolescents
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End point description:

PROMIS® is a set of person-centered measures that evaluates and monitors physical, mental, and social health in adults and children. Participants ≤ 17 years will complete pediatric versions for the duration of the study. PROMIS anxiety has 8 questions on Emotion Distress-Anxiety (or Pediatric Anxiety Symptom). Each question has 5 response options with values from 1 to 5. Total raw scores were converted to T-scores with higher scores indicating greater severity of symptoms. LS Mean was calculated using the ANCOVA model with treatment and stratification factors of geographic region, age group, baseline IGA (3 versus 4) score as fixed factors and baseline value as covariate.

APD: All randomized, adolescent participants, even if the participant does not take the assigned

treatment, does not receive the correct treatment, or otherwise does not follow the protocol. One investigational site with eighteen participants was excluded from analysis due to GCP issues.

End point type	Secondary
End point timeframe:	
Baseline, Week 16	

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	30		
Units: score on a scale				
least squares mean (standard error)	0.12 (\pm 2.129)	-2.79 (\pm 1.550)		

Statistical analyses

Statistical analysis title	PROMIS
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.241275
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-2.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.85
upper limit	2.03

Secondary: Change From Baseline in PROMIS Anxiety at Week 16 - Adults

End point title	Change From Baseline in PROMIS Anxiety at Week 16 - Adults
End point description:	<p>PROMIS is a set of person-centered measures that evaluates and monitors physical, mental, and social health in adults and children. The PROMIS measures will be completed by the participant in the study clinic. PROMIS anxiety has 8 questions on Emotion Distress-Anxiety. Each question has 5 response options with values from 1 to 5. Total raw scores were converted to T-scores with higher scores indicating greater severity of symptoms. LS Mean was calculated using the ANCOVA model with treatment and stratification factors of geographic region, age group, baseline IGA (3 versus 4) score as fixed factors and baseline value as covariate.</p> <p>APD: All randomized, adults participants, with Week 16 PROMIS anxiety data, even if the participant does not take the assigned treatment, does not receive the correct treatment, or otherwise does not follow the protocol. One investigational site with eighteen participants was excluded from analysis due to GCP issues.</p>
End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	251		
Units: score on a scale				
least squares mean (standard error)	-0.43 (\pm 0.572)	-3.00 (\pm 0.416)		

Statistical analyses

Statistical analysis title	PROMIS
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	380
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.241275
Method	ANCOVA
Parameter estimate	[LS Mean Difference (Final Values)]
Point estimate	-2.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.85
upper limit	2.03

Secondary: Change from Baseline in PROMIS Depression at Week 16- Adolescents

End point title	Change from Baseline in PROMIS Depression at Week 16- Adolescents
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End point description:

PROMIS is a set of person-centered measures that evaluates and monitors physical, mental, and social health in adults and children. The PROMIS measures will be completed by the participant in the study clinic. PROMIS depression has 8 questions on Emotion Distress-Depression. Each question has 5 response options with values from 1 to 5. Total raw scores were converted to T-scores with higher scores indicating greater severity of symptoms. LS Mean was calculated using the ANCOVA model with treatment and stratification factors of geographic region, age group, baseline IGA (3 versus 4) score as fixed factors and baseline value as covariate.

APD: All randomized, adolescent participants, even if the participant does not take the assigned treatment, does not receive the correct treatment, or otherwise does not follow the protocol. One investigational site with eighteen participants was excluded from analysis due to GCP issues. Missing values were imputed using LOCF method.

End point type	Secondary
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End point timeframe:

Baseline, Week 16

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	30		
Units: score on a scale				
least squares mean (standard error)	-0.57 (\pm 2.047)	-1.67 (\pm 1.493)		

Statistical analyses

Statistical analysis title	PROMIS
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.645132
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.86
upper limit	3.67

Secondary: Change From Baseline in PROMIS Depression at Week 16- Adults

End point title	Change From Baseline in PROMIS Depression at Week 16- Adults
End point description:	
<p>PROMIS is a set of person-centered measures that evaluates and monitors physical, mental, and social health in adults and children. The PROMIS measures will be completed by the participant in the study clinic. PROMIS depression has 8 questions on Emotion Distress-Depression. Each question has 5 response options with values from 1 to 5. Total raw scores were converted to T-scores with higher scores indicating greater severity of symptoms. LS Mean was calculated using the ANCOVA model with treatment and stratification factors of geographic region, age group, baseline IGA (3 versus 4) score as fixed factors and baseline value as covariate.</p> <p>APD: All randomized, adult participants, with Week 16 PROMIS Depression data, even if the participant does not take the assigned treatment, does not receive the correct treatment, or otherwise does not follow the protocol. One investigational site with eighteen participants was excluded from analysis due to GCP issues.</p>	
End point type	Secondary
End point timeframe:	
Baseline, Week 16	

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	251		
Units: score on a scale				
least squares mean (standard error)	0.19 (\pm 0.533)	-2.38 (\pm 0.387)		

Statistical analyses

Statistical analysis title	PROMIS
Comparison groups	Lebrikizumab Q2W v Placebo
Number of subjects included in analysis	380
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.000081
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-2.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.84
upper limit	-1.3

Secondary: Change from Baseline in Asthma Control Questionnaire (ACQ-5) score at Week 16 in participants who have self-reported comorbid asthma

End point title	Change from Baseline in Asthma Control Questionnaire (ACQ-5) score at Week 16 in participants who have self-reported comorbid asthma
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End point description:

The ACQ-5 has been shown to reliably measure asthma control and distinguish participants with well-controlled asthma (score ≤ 0.75 points) from those with uncontrolled asthma (score ≥ 1.5 points). It consists of 5 questions that are scored on a 7- point Likert scale with a recall period of 1 week. The total ACQ-5 score is the mean score of all questions; a lower score represents better asthma control.

LS Mean was calculated using ANCOVA with treatment, geographic region, age group, baseline IGA (3 versus 4) score as fixed factors and baseline value as covariate.

APD: All randomized participants, with non-missing baseline ACQ-5 score, even if the participant does not take the assigned treatment, does not receive the correct treatment, or otherwise does not follow the protocol. One investigational site with eighteen participants was excluded from analysis due to GCP issues. Missing values were imputed using LOCF method.

End point type	Secondary
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End point timeframe:

Baseline, Week 16

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	75		
Units: score on a scale				
least squares mean (standard error)	0.19 (± 0.138)	0.20 (± 0.106)		

Statistical analyses

Statistical analysis title	ACQ-5
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.919129
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.25
upper limit	0.28

Secondary: Change from Baseline in Children's Dermatology Life Quality Index (CDLQI) at Week 16

End point title	Change from Baseline in Children's Dermatology Life Quality Index (CDLQI) at Week 16
End point description:	
<p>The CDLQI questionnaire is designed for use in children (4 to 16 years of age). It consists of 10 items that are grouped into 6 domains: symptoms & feelings, leisure, school or holidays, personal relationships, sleep, & treatment. The scoring of each question is: Very much = 3; Quite a lot = 2; Only a little = 1; Not at all = 0. CDLQI total score is calculated by summing all 10 items responses, and has a range of 0 to 30 (higher scores are indicative of greater impairment).</p> <p>APD: All randomized, adolescent participants, with non-missing baseline CDLQI score, even if the participant does not take the assigned treatment, does not receive the correct treatment, or otherwise does not follow the protocol. One investigational site with eighteen participants was excluded from analysis due to GCP issues. MMRM was used to handle all missing data.</p>	
End point type	Secondary
End point timeframe:	
Baseline, Week 16	

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	17		
Units: score on a scale				
least squares mean (standard error)	-4.13 (± 2.276)	-7.49 (± 1.120)		

Statistical analyses

Statistical analysis title	CDLQI
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.196507
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-3.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.59
upper limit	1.86

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to Week 16

Adverse event reporting additional description:

All randomized participants who received at least one dose of study drug. Gender specific events only occurring in male or female participants have had the number of participants at risk adjusted accordingly.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	24.0
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Reporting groups

Reporting group title	Lebrikizumab 250mg Q2W
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Reporting group description: -

Reporting group title	Placebo
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Reporting group description: -

Serious adverse events	Lebrikizumab 250mg Q2W	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 295 (0.68%)	4 / 149 (2.68%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
uterine leiomyoma			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed ^[1]	0 / 147 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
fibula fracture			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
multiple injuries			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
tibia fracture			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
cardiac failure			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
myocardial infarction			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
cerebellar syndrome			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
dermatitis atopic			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 295 (0.34%)	1 / 149 (0.67%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
large intestine infection			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: Gender specific events only occurring in male or female participants have had the number of participants at risk adjusted accordingly.

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

Non-serious adverse events	Lebrikizumab 250mg Q2W	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	155 / 295 (52.54%)	97 / 149 (65.10%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
bowen's disease			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)	
occurrences (all)	0	1	
fibroadenoma of breast			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)	
occurrences (all)	0	1	
skin papilloma			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	3 / 295 (1.02%)	0 / 149 (0.00%)	
occurrences (all)	3	0	
squamous cell carcinoma			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 295 (0.34%)	1 / 149 (0.67%)	
occurrences (all)	1	1	
Vascular disorders			
haematoma			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)	
occurrences (all)	0	1	
hot flush			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)	
occurrences (all)	1	0	
hypertension			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	2 / 295 (0.68%)	2 / 149 (1.34%)	
occurrences (all)	2	2	
General disorders and administration site conditions			
chills			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)	
occurrences (all)	1	0	
cyst rupture			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)	
occurrences (all)	1	0	
fatigue			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	3 / 295 (1.02%)	1 / 149 (0.67%)	
occurrences (all)	3	1	
injection site discomfort			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)	
occurrences (all)	1	0	
injection site erythema			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	2 / 295 (0.68%)	0 / 149 (0.00%)	
occurrences (all)	3	0	
injection site pain			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	3 / 295 (1.02%)	1 / 149 (0.67%)	
occurrences (all)	4	1	
injection site reaction			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	2 / 295 (0.68%)	0 / 149 (0.00%)	
occurrences (all)	2	0	
injection site swelling			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)	
occurrences (all)	0	1	
malaise			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)	
occurrences (all)	0	1	
oedema			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)	
occurrences (all)	0	1	
oedema peripheral			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)	
occurrences (all)	0	2	
peripheral swelling			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)	
occurrences (all)	0	2	
swelling			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)	
occurrences (all)	0	1	
Immune system disorders			
allergy to animal			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)	
occurrences (all)	1	0	
drug hypersensitivity			
alternative dictionary used: MedDRA 24.0			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>seasonal allergy</p> <p>alternative dictionary used: MedDRA 24.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 295 (0.34%)</p> <p>1</p> <p>3 / 295 (1.02%)</p> <p>4</p>	<p>0 / 149 (0.00%)</p> <p>0</p> <p>1 / 149 (0.67%)</p> <p>1</p>	
<p>Reproductive system and breast disorders</p> <p>breast ulceration</p> <p>alternative dictionary used: MedDRA 24.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>heavy menstrual bleeding</p> <p>alternative dictionary used: MedDRA 24.0</p> <p>subjects affected / exposed^[2]</p> <p>occurrences (all)</p> <p>vulvovaginal dryness</p> <p>alternative dictionary used: MedDRA 24.0</p> <p>subjects affected / exposed^[3]</p> <p>occurrences (all)</p>	<p>0 / 295 (0.00%)</p> <p>0</p> <p>0 / 147 (0.00%)</p> <p>0</p> <p>1 / 147 (0.68%)</p> <p>1</p>	<p>1 / 149 (0.67%)</p> <p>1</p> <p>1 / 78 (1.28%)</p> <p>1</p> <p>0 / 78 (0.00%)</p> <p>0</p>	
<p>Respiratory, thoracic and mediastinal disorders</p> <p>asthma</p> <p>alternative dictionary used: MedDRA 24.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>cough</p> <p>alternative dictionary used: MedDRA 24.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>dyspnoea</p> <p>alternative dictionary used: MedDRA 24.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>nasal congestion</p> <p>alternative dictionary used: MedDRA 24.0</p>	<p>1 / 295 (0.34%)</p> <p>1</p> <p>2 / 295 (0.68%)</p> <p>2</p> <p>0 / 295 (0.00%)</p> <p>0</p>	<p>0 / 149 (0.00%)</p> <p>0</p> <p>0 / 149 (0.00%)</p> <p>0</p> <p>1 / 149 (0.67%)</p> <p>1</p>	

subjects affected / exposed	1 / 295 (0.34%)	1 / 149 (0.67%)	
occurrences (all)	1	1	
oropharyngeal pain			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	2 / 295 (0.68%)	1 / 149 (0.67%)	
occurrences (all)	2	1	
rhinitis allergic			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	3 / 295 (1.02%)	1 / 149 (0.67%)	
occurrences (all)	3	1	
sinus congestion			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
anxiety			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 295 (0.00%)	2 / 149 (1.34%)	
occurrences (all)	0	2	
depression			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)	
occurrences (all)	0	1	
insomnia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 295 (0.34%)	1 / 149 (0.67%)	
occurrences (all)	1	2	
middle insomnia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)	
occurrences (all)	1	0	
panic attack			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)	
occurrences (all)	1	0	
sleep disorder			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)	
occurrences (all)	0	1	
Investigations			
blood alkaline phosphatase increased			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)	
occurrences (all)	1	0	
blood pressure increased			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 295 (0.34%)	1 / 149 (0.67%)	
occurrences (all)	1	1	
eosinophil count increased			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	2 / 295 (0.68%)	0 / 149 (0.00%)	
occurrences (all)	2	0	
gamma-glutamyltransferase increased			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)	
occurrences (all)	1	0	
neutrophil count decreased			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)	
occurrences (all)	0	1	
neutrophil count increased			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)	
occurrences (all)	0	1	
nitrite urine present			
alternative dictionary used: MedDRA 24.0			

<p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 295 (0.34%)</p> <p>1</p>	<p>0 / 149 (0.00%)</p> <p>0</p>	
<p>platelet count increased</p> <p>alternative dictionary used: MedDRA 24.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 295 (0.34%)</p> <p>1</p>	<p>2 / 149 (1.34%)</p> <p>2</p>	
<p>white blood cell count increased</p> <p>alternative dictionary used: MedDRA 24.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 295 (0.34%)</p> <p>1</p>	<p>0 / 149 (0.00%)</p> <p>0</p>	
<p>Injury, poisoning and procedural complications</p> <p>accident at work</p> <p>alternative dictionary used: MedDRA 24.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 295 (0.34%)</p> <p>1</p>	<p>0 / 149 (0.00%)</p> <p>0</p>	
<p>animal bite</p> <p>alternative dictionary used: MedDRA 24.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 295 (0.34%)</p> <p>1</p>	<p>0 / 149 (0.00%)</p> <p>0</p>	
<p>clavicle fracture</p> <p>alternative dictionary used: MedDRA 24.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 295 (0.34%)</p> <p>1</p>	<p>0 / 149 (0.00%)</p> <p>0</p>	
<p>concussion</p> <p>alternative dictionary used: MedDRA 24.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 295 (0.34%)</p> <p>1</p>	<p>1 / 149 (0.67%)</p> <p>1</p>	
<p>contusion</p> <p>alternative dictionary used: MedDRA 24.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 295 (0.00%)</p> <p>0</p>	<p>1 / 149 (0.67%)</p> <p>1</p>	
<p>epicondylitis</p> <p>alternative dictionary used: MedDRA 24.0</p>			

subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)
occurrences (all)	0	1
fall		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)
occurrences (all)	1	0
fibula fracture		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)
occurrences (all)	0	1
hand fracture		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	2 / 295 (0.68%)	0 / 149 (0.00%)
occurrences (all)	2	0
injection related reaction		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)
occurrences (all)	0	2
injury corneal		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)
occurrences (all)	1	0
joint dislocation		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)
occurrences (all)	0	1
ligament sprain		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)
occurrences (all)	0	1
limb injury		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)
occurrences (all)	0	1

muscle strain			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 295 (0.34%)	1 / 149 (0.67%)	
occurrences (all)	1	1	
overdose			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	3 / 295 (1.02%)	1 / 149 (0.67%)	
occurrences (all)	4	1	
post procedural complication			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)	
occurrences (all)	0	1	
procedural headache			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)	
occurrences (all)	0	1	
procedural pain			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 295 (0.00%)	2 / 149 (1.34%)	
occurrences (all)	0	2	
skin abrasion			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)	
occurrences (all)	1	0	
skin laceration			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 295 (0.34%)	1 / 149 (0.67%)	
occurrences (all)	1	1	
thermal burn			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)	
occurrences (all)	1	0	
tibia fracture			
alternative dictionary used: MedDRA 24.0			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>vaccination complication</p> <p>alternative dictionary used: MedDRA 24.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>wound dehiscence</p> <p>alternative dictionary used: MedDRA 24.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>wrist fracture</p> <p>alternative dictionary used: MedDRA 24.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 295 (0.00%)</p> <p>0</p> <p>2 / 295 (0.68%)</p> <p>3</p> <p>1 / 295 (0.34%)</p> <p>1</p> <p>1 / 295 (0.34%)</p> <p>1</p>	<p>1 / 149 (0.67%)</p> <p>1</p> <p>0 / 149 (0.00%)</p> <p>0</p> <p>0 / 149 (0.00%)</p> <p>0</p> <p>0 / 149 (0.00%)</p> <p>0</p>	
<p>Cardiac disorders</p> <p>tachycardia</p> <p>alternative dictionary used: MedDRA 24.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 295 (0.34%)</p> <p>1</p>	<p>0 / 149 (0.00%)</p> <p>0</p>	
<p>Nervous system disorders</p> <p>burning sensation</p> <p>alternative dictionary used: MedDRA 24.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>cerebellar syndrome</p> <p>alternative dictionary used: MedDRA 24.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>dizziness</p> <p>alternative dictionary used: MedDRA 24.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>headache</p> <p>alternative dictionary used: MedDRA 24.0</p>	<p>0 / 295 (0.00%)</p> <p>0</p> <p>1 / 295 (0.34%)</p> <p>2</p> <p>4 / 295 (1.36%)</p> <p>4</p>	<p>1 / 149 (0.67%)</p> <p>1</p> <p>0 / 149 (0.00%)</p> <p>0</p> <p>0 / 149 (0.00%)</p> <p>0</p>	

subjects affected / exposed	15 / 295 (5.08%)	8 / 149 (5.37%)	
occurrences (all)	17	8	
hypoaesthesia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 295 (0.34%)	2 / 149 (1.34%)	
occurrences (all)	1	2	
neuralgia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)	
occurrences (all)	1	0	
paraesthesia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 295 (0.34%)	1 / 149 (0.67%)	
occurrences (all)	1	1	
Blood and lymphatic system disorders			
eosinophilia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)	
occurrences (all)	1	0	
iron deficiency anaemia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)	
occurrences (all)	1	0	
lymphadenitis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)	
occurrences (all)	1	0	
lymphadenopathy			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)	
occurrences (all)	1	0	
lymphocytosis			
alternative dictionary used: MedDRA 24.0			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>lymphopenia</p> <p>alternative dictionary used: MedDRA 24.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 295 (0.00%)</p> <p>0</p> <p>0 / 295 (0.00%)</p> <p>0</p>	<p>1 / 149 (0.67%)</p> <p>1</p> <p>1 / 149 (0.67%)</p> <p>1</p>	
<p>Ear and labyrinth disorders</p> <p>ear discomfort</p> <p>alternative dictionary used: MedDRA 24.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>paraesthesia ear</p> <p>alternative dictionary used: MedDRA 24.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>tinnitus</p> <p>alternative dictionary used: MedDRA 24.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>vertigo</p> <p>alternative dictionary used: MedDRA 24.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 295 (0.34%)</p> <p>1</p> <p>1 / 295 (0.34%)</p> <p>1</p> <p>1 / 295 (0.34%)</p> <p>1</p> <p>1 / 295 (0.34%)</p> <p>1</p>	<p>0 / 149 (0.00%)</p> <p>0</p> <p>0 / 149 (0.00%)</p> <p>0</p> <p>0 / 149 (0.00%)</p> <p>0</p> <p>0 / 149 (0.00%)</p> <p>0</p>	
<p>Eye disorders</p> <p>atopic keratoconjunctivitis</p> <p>alternative dictionary used: MedDRA 24.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>blepharitis</p> <p>alternative dictionary used: MedDRA 24.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>cataract</p> <p>alternative dictionary used: MedDRA 24.0</p>	<p>2 / 295 (0.68%)</p> <p>3</p> <p>2 / 295 (0.68%)</p> <p>3</p>	<p>0 / 149 (0.00%)</p> <p>0</p> <p>1 / 149 (0.67%)</p> <p>1</p>	

subjects affected / exposed	1 / 295 (0.34%)	2 / 149 (1.34%)
occurrences (all)	1	2
conjunctivitis allergic		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	6 / 295 (2.03%)	2 / 149 (1.34%)
occurrences (all)	6	2
dark circles under eyes		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)
occurrences (all)	0	1
dermatochalasis		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)
occurrences (all)	0	1
dry eye		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	7 / 295 (2.37%)	0 / 149 (0.00%)
occurrences (all)	8	0
episcleritis		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)
occurrences (all)	1	0
eye discharge		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	2 / 295 (0.68%)	0 / 149 (0.00%)
occurrences (all)	2	0
eye pruritus		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)
occurrences (all)	1	0
eyelid erosion		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	0 / 295 (0.00%)	2 / 149 (1.34%)
occurrences (all)	0	2

keratitis alternative dictionary used: MedDRA 24.0 subjects affected / exposed occurrences (all)	1 / 295 (0.34%) 2	0 / 149 (0.00%) 0	
lacrimation increased alternative dictionary used: MedDRA 24.0 subjects affected / exposed occurrences (all)	0 / 295 (0.00%) 0	1 / 149 (0.67%) 1	
ocular hyperaemia alternative dictionary used: MedDRA 24.0 subjects affected / exposed occurrences (all)	1 / 295 (0.34%) 1	0 / 149 (0.00%) 0	
vision blurred alternative dictionary used: MedDRA 24.0 subjects affected / exposed occurrences (all)	1 / 295 (0.34%) 1	0 / 149 (0.00%) 0	
vitreous floaters alternative dictionary used: MedDRA 24.0 subjects affected / exposed occurrences (all)	0 / 295 (0.00%) 0	1 / 149 (0.67%) 1	
Gastrointestinal disorders abdominal pain alternative dictionary used: MedDRA 24.0 subjects affected / exposed occurrences (all)	1 / 295 (0.34%) 1	0 / 149 (0.00%) 0	
breath odour alternative dictionary used: MedDRA 24.0 subjects affected / exposed occurrences (all)	1 / 295 (0.34%) 1	0 / 149 (0.00%) 0	
constipation alternative dictionary used: MedDRA 24.0 subjects affected / exposed occurrences (all)	0 / 295 (0.00%) 0	1 / 149 (0.67%) 1	
diarrhoea alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	2 / 295 (0.68%)	1 / 149 (0.67%)
occurrences (all)	2	1
dyspepsia		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	1 / 295 (0.34%)	1 / 149 (0.67%)
occurrences (all)	1	1
flatulence		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)
occurrences (all)	1	0
gastrointestinal inflammation		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)
occurrences (all)	0	1
haematemesis		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)
occurrences (all)	1	0
haemorrhoids		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	1 / 295 (0.34%)	1 / 149 (0.67%)
occurrences (all)	1	1
hiatus hernia		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)
occurrences (all)	1	0
inguinal hernia		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	1 / 295 (0.34%)	1 / 149 (0.67%)
occurrences (all)	1	1
nausea		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	4 / 295 (1.36%)	1 / 149 (0.67%)
occurrences (all)	4	1

toothache alternative dictionary used: MedDRA 24.0 subjects affected / exposed occurrences (all)	0 / 295 (0.00%) 0	1 / 149 (0.67%) 1	
vomiting alternative dictionary used: MedDRA 24.0 subjects affected / exposed occurrences (all)	1 / 295 (0.34%) 2	0 / 149 (0.00%) 0	
Skin and subcutaneous tissue disorders			
acne alternative dictionary used: MedDRA 24.0 subjects affected / exposed occurrences (all)	1 / 295 (0.34%) 1	3 / 149 (2.01%) 3	
alopecia alternative dictionary used: MedDRA 24.0 subjects affected / exposed occurrences (all)	2 / 295 (0.68%) 2	0 / 149 (0.00%) 0	
alopecia areata alternative dictionary used: MedDRA 24.0 subjects affected / exposed occurrences (all)	1 / 295 (0.34%) 1	0 / 149 (0.00%) 0	
angioedema alternative dictionary used: MedDRA 24.0 subjects affected / exposed occurrences (all)	0 / 295 (0.00%) 0	1 / 149 (0.67%) 1	
dermatitis alternative dictionary used: MedDRA 24.0 subjects affected / exposed occurrences (all)	2 / 295 (0.68%) 2	1 / 149 (0.67%) 1	
dermatitis atopic alternative dictionary used: MedDRA 24.0 subjects affected / exposed occurrences (all)	27 / 295 (9.15%) 30	37 / 149 (24.83%) 40	
dermatitis contact alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	1 / 295 (0.34%)	2 / 149 (1.34%)
occurrences (all)	1	2
dermatitis exfoliative generalised		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	1 / 295 (0.34%)	1 / 149 (0.67%)
occurrences (all)	1	1
dermatitis psoriasiform		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	2 / 295 (0.68%)	0 / 149 (0.00%)
occurrences (all)	2	0
diffuse alopecia		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)
occurrences (all)	1	0
dyshidrotic eczema		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)
occurrences (all)	0	1
eczema		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	1 / 295 (0.34%)	1 / 149 (0.67%)
occurrences (all)	1	1
erythema		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)
occurrences (all)	1	0
hair disorder		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)
occurrences (all)	1	0
night sweats		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	2 / 295 (0.68%)	0 / 149 (0.00%)
occurrences (all)	2	0

pityriasis rosea		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)
occurrences (all)	1	0
prurigo		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)
occurrences (all)	0	1
pruritus		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	5 / 295 (1.69%)	1 / 149 (0.67%)
occurrences (all)	5	1
rash		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)
occurrences (all)	1	0
rash erythematous		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)
occurrences (all)	0	2
rosacea		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)
occurrences (all)	0	1
seborrhoea		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)
occurrences (all)	1	0
skin fissures		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	1 / 295 (0.34%)	1 / 149 (0.67%)
occurrences (all)	1	1
skin lesion inflammation		
alternative dictionary used: MedDRA 24.0		

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>urticaria</p> <p>alternative dictionary used: MedDRA 24.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 295 (0.34%)</p> <p>1</p> <p>2 / 295 (0.68%)</p> <p>3</p>	<p>1 / 149 (0.67%)</p> <p>1</p> <p>1 / 149 (0.67%)</p> <p>1</p>	
<p>Renal and urinary disorders</p> <p>bladder disorder</p> <p>alternative dictionary used: MedDRA 24.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>nephrolithiasis</p> <p>alternative dictionary used: MedDRA 24.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>renal pain</p> <p>alternative dictionary used: MedDRA 24.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 295 (0.34%)</p> <p>1</p> <p>0 / 295 (0.00%)</p> <p>0</p> <p>0 / 295 (0.00%)</p> <p>0</p>	<p>0 / 149 (0.00%)</p> <p>0</p> <p>1 / 149 (0.67%)</p> <p>1</p> <p>1 / 149 (0.67%)</p> <p>1</p>	
<p>Musculoskeletal and connective tissue disorders</p> <p>arthralgia</p> <p>alternative dictionary used: MedDRA 24.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>arthritis</p> <p>alternative dictionary used: MedDRA 24.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>bursitis</p> <p>alternative dictionary used: MedDRA 24.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>coccydynia</p> <p>alternative dictionary used: MedDRA 24.0</p>	<p>3 / 295 (1.02%)</p> <p>3</p> <p>0 / 295 (0.00%)</p> <p>0</p> <p>0 / 295 (0.00%)</p> <p>0</p>	<p>1 / 149 (0.67%)</p> <p>1</p> <p>1 / 149 (0.67%)</p> <p>1</p> <p>1 / 149 (0.67%)</p> <p>1</p>	

subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)	
occurrences (all)	1	0	
joint swelling			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)	
occurrences (all)	0	1	
limb discomfort			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)	
occurrences (all)	2	0	
muscle spasms			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)	
occurrences (all)	1	0	
pain in extremity			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 295 (0.34%)	1 / 149 (0.67%)	
occurrences (all)	1	2	
synovial cyst			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)	
occurrences (all)	0	1	
Infections and infestations			
abscess			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)	
occurrences (all)	0	1	
asymptomatic bacteriuria			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)	
occurrences (all)	0	1	
body tinea			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)
occurrences (all)	1	0
covid-19		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	2 / 295 (0.68%)	2 / 149 (1.34%)
occurrences (all)	2	2
conjunctivitis		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	22 / 295 (7.46%)	3 / 149 (2.01%)
occurrences (all)	23	3
conjunctivitis bacterial		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	3 / 295 (1.02%)	0 / 149 (0.00%)
occurrences (all)	3	0
cystitis		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	2 / 295 (0.68%)	1 / 149 (0.67%)
occurrences (all)	2	1
dermatitis infected		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)
occurrences (all)	0	1
eczema herpeticum		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)
occurrences (all)	0	1
eczema impetiginous		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)
occurrences (all)	0	1
eczema infected		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)
occurrences (all)	2	0

erysipelas		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)
occurrences (all)	1	0
folliculitis		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	1 / 295 (0.34%)	3 / 149 (2.01%)
occurrences (all)	1	3
gastroenteritis		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	3 / 295 (1.02%)	1 / 149 (0.67%)
occurrences (all)	4	1
genital herpes simplex		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)
occurrences (all)	0	1
herpes dermatitis		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	1 / 295 (0.34%)	1 / 149 (0.67%)
occurrences (all)	1	1
herpes simplex		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	2 / 295 (0.68%)	0 / 149 (0.00%)
occurrences (all)	3	0
herpes zoster		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)
occurrences (all)	1	0
hordeolum		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	1 / 295 (0.34%)	1 / 149 (0.67%)
occurrences (all)	1	1
impetigo		
alternative dictionary used: MedDRA 24.0		

subjects affected / exposed	0 / 295 (0.00%)	3 / 149 (2.01%)
occurrences (all)	0	3
large intestine infection		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)
occurrences (all)	1	0
nasopharyngitis		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	15 / 295 (5.08%)	3 / 149 (2.01%)
occurrences (all)	17	3
oral herpes		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	4 / 295 (1.36%)	3 / 149 (2.01%)
occurrences (all)	4	3
oral infection		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)
occurrences (all)	1	0
otitis externa		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	1 / 295 (0.34%)	1 / 149 (0.67%)
occurrences (all)	1	1
paronychia		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	2 / 295 (0.68%)	0 / 149 (0.00%)
occurrences (all)	2	0
pharyngitis		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)
occurrences (all)	0	1
pharyngitis streptococcal		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)
occurrences (all)	0	1

pharyngotonsillitis		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)
occurrences (all)	1	0
post procedural infection		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)
occurrences (all)	0	1
pustule		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)
occurrences (all)	0	1
rhinitis		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)
occurrences (all)	1	0
skin infection		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)
occurrences (all)	2	0
superinfection		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)
occurrences (all)	0	1
tinea infection		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)
occurrences (all)	0	1
tinea pedis		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)
occurrences (all)	1	0
tooth abscess		
alternative dictionary used: MedDRA 24.0		

subjects affected / exposed	1 / 295 (0.34%)	1 / 149 (0.67%)	
occurrences (all)	1	1	
tooth infection			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 295 (0.34%)	1 / 149 (0.67%)	
occurrences (all)	1	1	
upper respiratory tract infection			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 295 (0.00%)	2 / 149 (1.34%)	
occurrences (all)	0	2	
urinary tract infection			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	4 / 295 (1.36%)	1 / 149 (0.67%)	
occurrences (all)	4	1	
viral infection			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)	
occurrences (all)	1	0	
vulvovaginal candidiasis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed ^[4]	0 / 147 (0.00%)	1 / 78 (1.28%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
decreased appetite			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)	
occurrences (all)	1	0	
hypercholesterolaemia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)	
occurrences (all)	0	1	
hypoglycaemia			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	0 / 295 (0.00%)	1 / 149 (0.67%)	
occurrences (all)	0	1	
obesity			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 295 (0.34%)	0 / 149 (0.00%)	
occurrences (all)	1	0	

Notes:

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Gender specific events only occurring in male or female participants have had the number of participants at risk adjusted accordingly.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Gender specific events only occurring in male or female participants have had the number of participants at risk adjusted accordingly.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Gender specific events only occurring in male or female participants have had the number of participants at risk adjusted accordingly.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 May 2020	Revised to align with FDA and EU received recommendations and regulations, to add more clarifications and ensuring consistencies between different sections, and to be consistent across the Phase 3 studies of Lebrikizumab in atopic dermatitis.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

One investigational site with eighteen participants was excluded from analysis due to GCP issues.

Notes: