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	2019-002932-10
Trial protocol	LT ES PL EE FR LV
Global end of trial date	03 May 2022

Results information

Result version number	v2
This version publication date	21 August 2022
First version publication date	06 July 2022
Version creation reason	• Correction of full data set Corrections to outcome measures per CT.gov Quality Review.

Trial information

Trial identification

Sponsor protocol code	J2T-DM-KGAB, DRM06-AD04

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04146363
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 17801

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, 1 877-CTLilly,
Scientific contact	Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 877-285-4559,

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	21 June 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 June 2021
Global end of trial reached?	Yes
Global end of trial date	03 May 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the safety and efficacy of lebrikizumab compared with placebo in participants with moderate-to-severe atopic dermatitis.

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	24 September 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	France: 7
Country: Number of subjects enrolled	Estonia: 8
Country: Number of subjects enrolled	Latvia: 11
Country: Number of subjects enrolled	Lithuania: 18
Country: Number of subjects enrolled	Poland: 81
Country: Number of subjects enrolled	Australia: 39
Country: Number of subjects enrolled	Canada: 23
Country: Number of subjects enrolled	Korea, Republic of: 34
Country: Number of subjects enrolled	United States: 190
Country: Number of subjects enrolled	Spain: 13
Worldwide total number of subjects	424
EEA total number of subjects	138

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)	55
Adults (18-64 years)	338
From 65 to 84 years	29
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Reported are results for the Induction Period (Baseline to Week16), data for Maintenance Period (Week 16 to Week 52) will be posted at the time of final results reporting.

Pre-assignment

Screening details:

No Text Entered

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.

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:

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.

Arm title	Lebrikizumab Q2W

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.

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

Dosage and administration details:

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.

Number of subjects in period 1	Placebo	Lebrikizumab Q2W
Started	141	283
Received at Least One Dose of Study Drug	141	282
Completed	120	263
Not completed	21	20
Started systemic dexamethasone	1	-
Positive quantiferon test	-	1
Adverse event, non-fatal	1	2
Due to Epidemic/Pandemic	1	1
Withdrawal by Subject	6	4
Lost to follow-up	1	4
Lack of efficacy	6	2
Protocol deviation	5	6

Baseline characteristics

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.	

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.	

Reporting group values	Placebo	Lebrikizumab Q2W	Total
Number of subjects	141	283	424
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	18	37	55
Adults (18-64 years)	113	225	338
From 65-84 years	10	19	29
85 years and over	0	2	2
Gender categorical Units: Subjects			
Female	73	141	214
Male	68	142	210
Race Units: Subjects			
American Indian or Alaska Native	0	7	7
Asian	31	39	70
Native Hawaiian or Other Pacific Islander	0	2	2
Black or African American	16	33	49
White	93	196	289
More than one race	1	4	5
Unknown or Not Reported	0	2	2
Region of Enrollment Units: Subjects			
Canada	7	16	23
South Korea	13	21	34
Lativa	6	5	11
United States	62	128	190
Poland	25	56	81
Australia	13	26	39

France	0	7	7
Lithuania	7	11	18
Spain	4	9	13
Estonia	4	4	8

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.

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.

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 Atopic Dermatitis (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. 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	141	283		
Units: Percentage of Participants				
number (confidence interval 95%)	12.8 (7.0 to 18.6)	43.0 (37.1 to 49.0)		

Statistical analyses

Statistical analysis title	IGA Baseline to Week 16
Comparison groups	Placebo v Lebrikizumab Q2W

Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.000001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	29.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	21.4
upper limit	37.8

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

End point description:

The EASI assesses objective physician estimates of 2 dimensions of atopic dermatitis - disease extent, i.e., percentage of skin 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 (none) to 72 (severe).
The EASI-75 responder is defined as a participant who achieves a ≥ 75% improvement from baseline in the EASI score.
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. 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	141	283		
Units: Percentage of Participants				
number (confidence interval 95%)	16.4 (9.8 to 23.0)	59.3 (53.4 to 65.2)		

Statistical analyses

Statistical analysis title	EASI-75
Comparison groups	Placebo v Lebrikizumab Q2W

Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.000001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	42.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	33.5
upper limit	51

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:

he 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.

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. 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	141	283		
Units: Percentage of Participants				
number (confidence interval 95%)	0.7 (0.0 to 2.1)	2.5 (0.7 to 4.4)		

Statistical analyses

Statistical analysis title	IGA Baseline to Week 2
Comparison groups	Placebo v Lebrikizumab Q2W

Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.218644
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	4

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:

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.

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. 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	141	283		
Units: Percentage of Participants				
number (confidence interval 95%)	1.0 (-0.8 to 2.8)	10.2 (6.6 to 13.8)		

Statistical analyses

Statistical analysis title	IGA Baseline to Week 4
Comparison groups	Placebo v Lebrikizumab Q2W

Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.000982
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	9
Confidence interval	
level	95 %
sides	2-sided
lower limit	5
upper limit	13.1

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:

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.

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. 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	123	246		
Units: Percentage of Participants				
number (confidence interval 95%)	11.3 (5.4 to 17.3)	42.2 (35.8 to 48.6)		

Statistical analyses

Statistical analysis title	IGA - Adults Baseline to Week 16
Comparison groups	Placebo v Lebrikizumab Q2W

Number of subjects included in analysis	369
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.000001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	30.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	22
upper limit	39.4

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

End point description:

The EASI assesses objective physician estimates of 2 dimensions of atopic dermatitis - disease extent i.e., percentage of skin 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 (none) to 72 (severe).
The EASI-90responder is defined as a participant who achieves a ≥ 90% improvement from baseline in the EASI score.
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. 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	141	283		
Units: Percentage of Participants				
number (confidence interval 95%)	9.1 (3.9 to 14.3)	38.2 (32.4 to 44.0)		

Statistical analyses

Statistical analysis title	EASI-90
Comparison groups	Placebo v Lebrikizumab Q2W

Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.000001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	28.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	20.9
upper limit	36.3

Secondary: Percent Change in Pruritus Numerical Rating Scale (NRS) Score From Baseline to Week 16

End point title	Percent 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. 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	136	276		
Units: Percent Change				
least squares mean (standard error)	-15.24 (± 3.855)	-45.75 (± 3.167)		

Statistical analyses

Statistical analysis title	Pruritus Numerical Rating Scale (NRS)
Comparison groups	Placebo v Lebrikizumab Q2W

Number of subjects included in analysis	412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.000001
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-30.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	-38.2
upper limit	-22.8
Variability estimate	Standard error of the mean
Dispersion value	3.948

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

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. 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	130	263		
Units: Percentage of Participants				
number (confidence interval 95%)	12.7 (6.9 to 18.6)	46.3 (40.2 to 52.5)		

Statistical analyses

Statistical analysis title	Pruritus NRS Score
Comparison groups	Placebo v Lebrikizumab Q2W

Number of subjects included in analysis	393
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.000001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	33.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	25.2
upper limit	41.9

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

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. 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	123	141		
Units: Percentage of Participants				
number (confidence interval 95%)	13.5 (7.3 to 19.6)	49.4 (43.0 to 55.8)		

Statistical analyses

Statistical analysis title	Pruritus NRS Score
Comparison groups	Placebo v Lebrikizumab Q2W

Number of subjects included in analysis	264
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.000001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	35.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	27
upper limit	44.5

Secondary: Percent Change in EASI Score From Baseline to Week 16

End point title	Percent Change in EASI Score From Baseline to Week 16

End point description:

The EASI assesses objective physician estimates of 2 dimensions of atopic dermatitis - disease extent, i.e., percentage of skin 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). LS Mean was calculated using ANCOVA model with treatment, stratification factors of geographic region, age group, baseline IGA score (IGA 3 versus 4) as fixed factors baseline value as covariate.

End point type	Secondary

End point timeframe:

Baseline, Week 16

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. MCMC-MI was used to handle missing data.

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	141	283		
Units: Percent Change				
least squares mean (standard error)	-26.16 (± 4.049)	-64.75 (± 3.166)		

Statistical analyses

Statistical analysis title	Percent Change in EASI Score
Comparison groups	Placebo v Lebrikizumab Q2W

Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.000001
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-38.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-46.8
upper limit	-30.4
Variability estimate	Standard error of the mean
Dispersion value	4.19

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:

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. Maximum number of palms were 10 palms for head and neck (10%), 20 palms for upper extremities (20%), 30 palms for trunk, including axilla and groin (30%), 40 palms for lower extremities, including buttocks (40%). 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.
MMRM was used to handle all missing data.

End point type	Secondary

End point timeframe:

Baseline, Week 16
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.

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	236		
Units: percentage of body surface area				
least squares mean (standard error)	-11.77 (± 1.856)	-30.23 (± 1.310)		

Statistical analyses

Statistical analysis title	BSA
Comparison groups	Placebo v Lebrikizumab Q2W

Number of subjects included in analysis	313
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.000001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-18.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.38
upper limit	-14.53
Variability estimate	Standard error of the mean
Dispersion value	1.995

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

End point description:

The EASI assesses objective physician estimates of 2 dimensions of atopic dermatitis - disease extent, i.e., percentage of skin 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 (none) to 72 (severe).
The EASI-90 responder is defined as a participant who achieves a ≥ 90% improvement from baseline in the EASI score.
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. 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	141	283		
Units: Percentage of Participants				
number (confidence interval 95%)	1.8 (-0.7 to 4.3)	12.0 (8.2 to 15.9)		

Statistical analyses

Statistical analysis title	EASI-90
Comparison groups	Placebo v Lebrikizumab Q2W

Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.000878
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	10.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.5
upper limit	14.8

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:

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. Questions 3-10 also have an additional response category of "Not relevant" which is scored as "0". Questions are scored from 0 to 3, giving a possible total score range from 0 (no impact of skin disease on quality of life) to 30 (maximum impact on quality of life). A high score is indicative of a poor quality of life.
LS Mean was calculated using the ANCOVA model with treatment, baseline value, and stratification factors of geographic region, age group, baseline IGA (3 versus 4) score as fixed factors.

End point type	Secondary

End point timeframe:

Baseline, Week 16

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.

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	121[1]	239[2]		
Units: Score on a Scale				
least squares mean (standard error)	-2.94 (± 1.103)	-8.78 (± 1.056)		

Notes:

[1] - MCMC-MI was used to handle missing data.

[2] - MCMC-MI was used to handle missing data.

Statistical analyses

Statistical analysis title	DLQI
Comparison groups	Placebo v Lebrikizumab Q2W

Number of subjects included in analysis	360
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.000001
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-5.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.2
upper limit	-4.5
Variability estimate	Standard error of the mean
Dispersion value	0.678

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:

he 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. Questions 3-10 also have an additional response category of "Not relevant" which is scored as "0". Questions are scored from 0 to 3, giving a possible total score range from 0 (no impact of skin disease on quality of life) to 30 (maximum impact on quality of life). A high score is indicative of a poor quality of life.
MCMC-MI was used to handle all missing data.

End point type	Secondary

End point timeframe:

Baseline to Week 16
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.

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	121[3]	239[4]		
Units: Percentage of Participants				
number (confidence interval 95%)	32.4 (23.8 to 41.1)	71.4 (65.5 to 77.2)		

Notes:

[3] - MCMC-MI was used to handle missing data.

[4] - MCMC-MI was used to handle missing data.

Statistical analyses

Statistical analysis title	DLQI
Comparison groups	Placebo v Lebrikizumab Q2W

Number of subjects included in analysis	360
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.000001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	38.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	28
upper limit	49.3

Secondary: Percentage of Participants With a DLQI Total Score of ≥4-point at Baseline 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 at Baseline Achieving ≥4-point Improvement in DLQI From Baseline to Week 16

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. Questions 3-10 also have an additional response category of "Not relevant" which is scored as "0". Questions are scored from 0 to 3, giving a possible total score range from 0 (no impact of skin disease on quality of life) to 30 (maximum impact on quality of life). A high score is indicative of a poor quality of life.
MCMC-MI was used to handle missing data.

End point type	Secondary

End point timeframe:

Baseline to Week 16
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.

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	116	226		
Units: Percentage of Participants				
number (confidence interval 95%)	33.8 (24.9 to 42.8)	75.5 (69.8 to 81.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Sleep-loss Score From Baseline to Week 16

End point title	Percent Change in Sleep-loss Score From Baseline to 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 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. 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	132	269		
Units: Percent Change				
least squares mean (standard error)	-16.34 (± 5.156)	-48.61 (± 4.164)		

Statistical analyses

Statistical analysis title	Sleep-loss Score
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	401
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.000001
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-32.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-42.6
upper limit	-22
Variability estimate	Standard error of the mean
Dispersion value	5.242

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, 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. 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	136	276		
Units: Score on a Scale				
least squares mean (standard error)	-0.39 (± 0.095)	-1.14 (± 0.078)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With a Sleep-loss Score ≥2 Points at Baseline Who Achieve a ≥2 Points Reduction From Baseline at 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 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.
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. 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	91	195		
Units: Percentage of Participants				
number (confidence interval 95%)	5.1 (0.3 to 9.9)	38.7 (31.8 to 45.7)		

Statistical analyses

Statistical analysis title	Sleep-loss Score
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	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	33.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	25.4
upper limit	42.4

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

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. 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	130	263		
Units: Percentage of Participants				
number (confidence interval 95%)	0.8 (0.0 to 2.3)	2.3 (0.5 to 4.1)		

Statistical analyses

Statistical analysis title	Pruritus NRS Score
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	393
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.275529
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	3.9

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 participant, 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. 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	130	263		
Units: Percentage of Participants				
number (confidence interval 95%)	0.9 (-0.8 to 2.5)	6.1 (3.2 to 9.1)		

Statistical analyses

Statistical analysis title	Pruritus NRS Score
Comparison groups	Placebo v Lebrikizumab Q2W

Number of subjects included in analysis	393
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.016543
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	5.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.9
upper limit	8.7

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

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, if the participant does not take the assigned treatment, does not receive the correct treatment, or otherwise does not follow the protocol. 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	130	263		
Units: Percentage of Participants				
number (confidence interval 95%)	2.4 (-0.3 to 5.0)	21.6 (16.6 to 26.6)		

Statistical analyses

Statistical analysis title	Pruritus NRS Score
Comparison groups	Placebo v Lebrikizumab Q2W

Number of subjects included in analysis	393
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.000003
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	19.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.6
upper limit	25

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

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. 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	123	244		
Units: Percentage of Participants				
number (confidence interval 95%)	0.8 (0.0 to 2.4)	2.5 (0.5 to 4.4)		

Statistical analyses

Statistical analysis title	Pruritus NRS Score
Comparison groups	Placebo v Lebrikizumab Q2W

Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.244105
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	4.3

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

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. 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	123	244		
Units: Percentage of Participants				
number (confidence interval 95%)	0.9 (-0.9 to 2.7)	6.6 (3.5 to 9.8)		

Statistical analyses

Statistical analysis title	Pruritus NRS Score
Comparison groups	Placebo v Lebrikizumab Q2W

Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.014375
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	5.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.2
upper limit	9.5

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

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. 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	123	244		
Units: Percentage of Participants				
number (confidence interval 95%)	2.5 (-0.3 to 5.3)	23.2 (17.9 to 28.6)		

Statistical analyses

Statistical analysis title	Pruritus NRS Score
Comparison groups	Placebo v Lebrikizumab Q2W

Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.000002
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	21
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.9
upper limit	27

Secondary: Percent Change in SCORing Atopic Dermatitis (SCORAD) From Baseline to Week 16

End point title	Percent Change in SCORing Atopic Dermatitis (SCORAD) From Baseline to Week 16

End point description:

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 index also 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 using A/5 + 7*B/2+ C to give a maximum possible score of 103, where 0 = no disease and 103 = severe disease.
LS Mean was calculated using the ANCOVA model with treatment group and stratification factors of geographic region, age group, baseline IGA (3 versus 4) score as fixed factors and baseline value as covariate. Missing Values were imputed using LOCF method.

End point type	Secondary

End point timeframe:

Baseline, Week 16

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.

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	138	276		
Units: Score on a Scale				
least squares mean (standard error)	-16.79 (± 3.164)	-47.26 (± 2.552)		

Statistical analyses

Statistical analysis title	SCORing Atopic Dermatitis
Comparison groups	Placebo v Lebrikizumab Q2W

Number of subjects included in analysis	414
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.000001
Method	ANCOVA
Parameter estimate	Risk difference (RD)
Point estimate	-30.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	-36.77
upper limit	-24.17

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

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.
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. Missing Values were imputed using last observation carried forward (LOCF) method.

End point type	Secondary

End point timeframe:

Baseline, Week 16
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.

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	141	282		
Units: Score on a Scale				
least squares mean (standard error)				
Health State Index UK	0.05 (± 0.017)	0.19 (± 0.014)		
Health State Index US	0.03 (± 0.012)	0.13 (± 0.010)		

Statistical analyses

Statistical analysis title	Health State Index UK
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	423
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.000001
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.11
upper limit	0.18
Variability estimate	Standard error of the mean
Dispersion value	0.018

Statistical analysis title	Health State Index US
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	423
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.000001
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.08
upper limit	0.13
Variability estimate	Standard error of the mean
Dispersion value	0.013

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)

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.
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. Missing values were imputed using 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	141	282		
Units: Score on a Scale				
least squares mean (standard error)	2.19 (± 1.641)	10.48 (± 1.329)		

Statistical analyses

Statistical analysis title	EQ-5D-5L VAS
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	423
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.000001
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	8.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.02
upper limit	11.56
Variability estimate	Standard error of the mean
Dispersion value	1.664

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

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. LS Mean was calculated using MMRM model using treatment, baseline value, visit, the interaction of the baseline value-by-visit, the interaction of treatment by-visit as covariates, geographic region, age group, baseline IGA (3 versus 4) score as fixed.
MMRM was used to handle all missing data

End point type	Secondary

End point timeframe:

Baseline, Week 16

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.

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	203		
Units: Score on a Scale				
least squares mean (standard error)	-4.02 (± 0.723)	-11.28 (± 0.475)		

Statistical analyses

Statistical analysis title	POEM
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	273
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.000001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-7.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.85
upper limit	-5.66
Variability estimate	Standard error of the mean
Dispersion value	0.811

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

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 (mean = 50 and a standard deviation = 10) with higher scores representing greater anxiety. 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. Missing values were imputed using the 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	18	37		
Units: Score on a Scale				
least squares mean (standard error)	-2.80 (± 2.435)	-3.87 (± 1.830)		

Statistical analyses

Statistical analysis title	PROMIS Anxiety Adolescents
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.716224
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-1.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.93
upper limit	4.8
Variability estimate	Standard error of the mean
Dispersion value	2.917

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

End point title	Change From Baseline in PROMIS Depression at Week 16 - Adolescent

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 depression has 8 questions on Emotion Distress-Depression (or Pediatric Depressive Symptom). Each question has 5 response options with values from 1 to 5. Total raw scores were converted to T-Scores (mean = 50 and a standard deviation = 10) with higher scores representing greater depression. 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. Missing values were imputed using the 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	18	37		
Units: Score on a Scale				
least squares mean (standard error)	-0.11 (± 2.165)	-4.62 (± 1.623)		

Statistical analyses

Statistical analysis title	PROMIS Depression Adolescents
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.089275
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-4.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.73
upper limit	0.72
Variability estimate	Standard error of the mean
Dispersion value	2.599

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:

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 (or Pediatric Anxiety Symptom). Each question has 5 response options with values from 1 to 5. Total raw scores were converted to T-Scores (mean = 50 and a standard deviation = 10) with higher scores representing greater anxiety. 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, adult 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. Missing values are imputed with the 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	122	244		
Units: Score on a Scale				
least squares mean (standard error)	-0.62 (± 0.663)	-3.99 (± 0.477)		

Statistical analyses

Statistical analysis title	PROMIS Anxiety Adults
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.000032
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-3.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.93
upper limit	-1.79
Variability estimate	Standard error of the mean
Dispersion value	0.799

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:

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 (or Pediatric Depressive Symptom). Each question has 5 response options with values from 1 to 5. Total raw scores were converted to T-Scores (mean = 50 and a standard deviation = 10) with higher scores representing greater depression. 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 , 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. Missing values were imputed using the 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	122	244		
Units: Score on a Scale				
least squares mean (standard error)	-0.40 (± 0.581)	-3.16 (± 0.418)		

Statistical analyses

Statistical analysis title	PROMIS Depression Adults
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.000096
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-2.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.13
upper limit	-1.38
Variability estimate	Standard error of the mean
Dispersion value	0.699

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

End point description:

The ACQ-5 is a five-item, self-completed questionnaire, which is used as a measure of asthma control of a participant. The five questions (concerning nocturnal awakening, waking in the morning, activity limitation, shortness of breath and wheeze) enquire about the frequency and/or severity of symptoms over the previous week. The response options for all these questions range from zero (no impairment/limitation) to six (total impairment/ limitation) scale. The ACQ-5 score is the average of the individual item scores and ranges from 0 (totally controlled) to 6 (severely uncontrolled). Higher scores indicate lower 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 f

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	51	95		
Units: Score on a Scale				
least squares mean (standard error)	-0.05 (± 0.118)	-0.13 (± 0.096)		

Statistical analyses

Statistical analysis title	Asthma Control Questionnaire
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	146
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.513146
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.32
upper limit	0.16
Variability estimate	Standard error of the mean
Dispersion value	0.122

Secondary: Change From Baseline in Children’s Dermatology Life Quality Index (CDLQI) at Week 16 - Adolescents

End point title	Change From Baseline in Children’s Dermatology Life Quality Index (CDLQI) at Week 16 - Adolescents

End point description:

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).
LS Mean was calculated using MMRM model which includes treatment, baseline value, visit, the interaction of the baseline value-by-visit as covariates, the interaction of treatment by-visit, geographic region, age group, and baseline IGA (3 versus 4) score as fixed factors.
MMRM was used to handle all missing data.

End point type	Secondary

End point timeframe:

Baseline, Week 16
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.

End point values	Placebo	Lebrikizumab Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	26		
Units: Score on a Scale				
least squares mean (standard error)	-0.99 (± 1.293)	-7.96 (± 0.802)		

Statistical analyses

Statistical analysis title	Children’s Dermatology Life Quality Index
Comparison groups	Placebo v Lebrikizumab Q2W
Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.000069
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-6.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.07
upper limit	-3.87
Variability estimate	Standard error of the mean
Dispersion value	1.52

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

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Lebrikizumab 250mg Q2W

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.

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.

Serious adverse events	Lebrikizumab 250mg Q2W	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 282 (2.13%)	1 / 141 (0.71%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
accidental overdose			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
myocardial infarction			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
carpal tunnel syndrome			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
oedema peripheral			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
synovitis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
cellulitis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
sepsis			

alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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	126 / 282 (44.68%)	72 / 141 (51.06%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
acrochordon			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	2	
haemangioma			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
hypertension			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	3 / 282 (1.06%)	1 / 141 (0.71%)	
occurrences (all)	3	1	
peripheral venous disease			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
administration site reaction			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
asthenia			

alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	2	0	
chest discomfort			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
chills			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	2	
fatigue			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	2 / 282 (0.71%)	1 / 141 (0.71%)	
occurrences (all)	2	1	
hyperthermia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
injection site bruising			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
injection site erythema			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
injection site pain			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	2 / 141 (1.42%)	
occurrences (all)	2	4	
injection site reaction			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	3	0	
oedema peripheral			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	3 / 282 (1.06%)	0 / 141 (0.00%)	
occurrences (all)	4	0	
pyrexia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			
food allergy			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
hypersensitivity			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
dysmenorrhoea			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed[1]	3 / 141 (2.13%)	0 / 73 (0.00%)	
occurrences (all)	5	0	
heavy menstrual bleeding			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed[2]	1 / 141 (0.71%)	0 / 73 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
asthma			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	3 / 282 (1.06%)	0 / 141 (0.00%)	
occurrences (all)	3	0	
chronic obstructive pulmonary disease			

alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
cough			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	1 / 141 (0.71%)	
occurrences (all)	1	1	
dyspnoea			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
nasal congestion			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
oropharyngeal pain			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
pneumonia aspiration			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
rhinitis allergic			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	2 / 282 (0.71%)	0 / 141 (0.00%)	
occurrences (all)	2	0	
rhinorrhoea			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
sleep apnoea syndrome			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
Psychiatric disorders			
anxiety			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	4 / 282 (1.42%)	0 / 141 (0.00%)	
occurrences (all)	6	0	
attention deficit hyperactivity disorder			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
depression			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	2 / 282 (0.71%)	1 / 141 (0.71%)	
occurrences (all)	2	1	
insomnia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	1 / 141 (0.71%)	
occurrences (all)	1	1	
persistent depressive disorder			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
stress			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
Investigations			
blood lactate dehydrogenase increased			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
blood pressure increased			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
eosinophil count increased			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
hepatic enzyme increased			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
neutrophil count decreased			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
neutrophil count increased			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
platelet count increased			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
back injury			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
contusion			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
head injury			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
ligament sprain			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
meniscus injury			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
muscle strain			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
overdose			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
post procedural inflammation			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
sunburn			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
tooth injury			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
angina pectoris			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
palpitations			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
Nervous system disorders			
dizziness			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	2 / 282 (0.71%)	1 / 141 (0.71%)	
occurrences (all)	5	1	
dysgeusia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
epilepsy			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
headache			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	9 / 282 (3.19%)	2 / 141 (1.42%)	
occurrences (all)	10	2	
hypersomnia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
post herpetic neuralgia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
radiculopathy			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
seizure			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
syncope			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
eosinophilia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	2 / 141 (1.42%)	
occurrences (all)	1	2	
erythropenia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
iron deficiency anaemia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
lymphopenia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
thrombocytopenia			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	2 / 282 (0.71%)	0 / 141 (0.00%)	
occurrences (all)	2	0	
Eye disorders			
blepharitis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	3 / 282 (1.06%)	0 / 141 (0.00%)	
occurrences (all)	3	0	
chalazion			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	2 / 282 (0.71%)	0 / 141 (0.00%)	
occurrences (all)	2	0	
conjunctival hyperaemia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
conjunctivitis allergic			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	6 / 282 (2.13%)	1 / 141 (0.71%)	
occurrences (all)	6	1	
dry eye			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	2 / 141 (1.42%)	
occurrences (all)	1	2	
eye irritation			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	2 / 282 (0.71%)	0 / 141 (0.00%)	
occurrences (all)	2	0	
eyelids pruritus			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
eye pruritus			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
keratoconus			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
keratitis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
pupils unequal			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
vernal keratoconjunctivitis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
vision blurred			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
visual impairment			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
abdominal pain			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
anal haemorrhage			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
gastric polyps			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
gastrointestinal inflammation			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
nausea			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	2 / 141 (1.42%)	
occurrences (all)	0	2	
odynophagia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
toothache			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	1 / 141 (0.71%)	
occurrences (all)	1	1	
vomiting			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	1 / 141 (0.71%)	
occurrences (all)	1	1	
Hepatobiliary disorders			
non-alcoholic steatohepatitis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
dermal cyst			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
dermatitis atopic			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	15 / 282 (5.32%)	28 / 141 (19.86%)	
occurrences (all)	16	31	
dermatitis contact			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
drug eruption			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
dyshidrotic eczema			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
eczema			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
milia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
pruritus			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	3 / 282 (1.06%)	6 / 141 (4.26%)	
occurrences (all)	3	7	
rash			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	

seborrhoea			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
seborrhoeic dermatitis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	2 / 282 (0.71%)	1 / 141 (0.71%)	
occurrences (all)	2	1	
skin burning sensation			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
solar dermatitis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
Renal and urinary disorders			
cystitis noninfective			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
nephrolithiasis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
Endocrine disorders			
hyperparathyroidism secondary			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	

back pain			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	2 / 282 (0.71%)	1 / 141 (0.71%)	
occurrences (all)	2	1	
bursitis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	1 / 141 (0.71%)	
occurrences (all)	1	1	
muscle twitching			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
musculoskeletal chest pain			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
musculoskeletal stiffness			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
myalgia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	2	
pain in extremity			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
abscess neck			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
bacterial vaginosis			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed[3]	1 / 141 (0.71%)	0 / 73 (0.00%)	
occurrences (all)	1	0	
bronchitis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	2 / 282 (0.71%)	0 / 141 (0.00%)	
occurrences (all)	2	0	
covid-19			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	5 / 282 (1.77%)	3 / 141 (2.13%)	
occurrences (all)	5	3	
cellulitis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
conjunctivitis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	21 / 282 (7.45%)	4 / 141 (2.84%)	
occurrences (all)	22	4	
ear infection			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
ecthyma			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
eczema herpeticum			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
folliculitis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	3 / 282 (1.06%)	1 / 141 (0.71%)	
occurrences (all)	3	1	

furuncle			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	2 / 141 (1.42%)	
occurrences (all)	0	3	
gastroenteritis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	2 / 282 (0.71%)	0 / 141 (0.00%)	
occurrences (all)	3	0	
gastroenteritis viral			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	2 / 282 (0.71%)	0 / 141 (0.00%)	
occurrences (all)	2	0	
helicobacter infection			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
herpes zoster			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
impetigo			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	4 / 282 (1.42%)	2 / 141 (1.42%)	
occurrences (all)	4	2	
infection			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
influenza			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
lower respiratory tract infection			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
nasopharyngitis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	11 / 282 (3.90%)	3 / 141 (2.13%)	
occurrences (all)	11	3	
oral herpes			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	9 / 282 (3.19%)	5 / 141 (3.55%)	
occurrences (all)	9	10	
paronychia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
pharyngitis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
skin infection			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	1 / 141 (0.71%)	
occurrences (all)	1	1	
tinea capitis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
tonsillitis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	2 / 141 (1.42%)	
occurrences (all)	1	2	
tooth abscess			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	

upper respiratory tract infection			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	3 / 141 (2.13%)	
occurrences (all)	1	4	
urinary tract infection			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	1 / 141 (0.71%)	
occurrences (all)	1	1	
vaginal infection			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed[4]	0 / 141 (0.00%)	1 / 73 (1.37%)	
occurrences (all)	0	1	
viral upper respiratory tract infection			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
vulvovaginal candidiasis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed[5]	2 / 141 (1.42%)	0 / 73 (0.00%)	
occurrences (all)	2	0	
Metabolism and nutrition disorders			
decreased appetite			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 282 (0.00%)	1 / 141 (0.71%)	
occurrences (all)	0	1	
dehydration			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
hyperlipidaemia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 282 (0.35%)	0 / 141 (0.00%)	
occurrences (all)	1	0	
vitamin d deficiency			
alternative dictionary used: MedDRA 24.0			

subjects affected / exposed occurrences (all)	0 / 282 (0.00%) 0	1 / 141 (0.71%) 1	

Notes:

[1] - 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.

[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.

[5] - 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
16 October 2019	• Clarification of primary, co-primary and secondary endpoints to be analyzed for the FDA and EMEA • Updated inclusion criterion 10 for contraceptive use after last dose of study drug (increased from 17 to 18 weeks) • Added inclusion criterion 11 to require male patients to use an effective method of contraception if sexually active with a female of child-bearing potential. • Other minor clarifications and editorial changes.
20 May 2020	• Added hormone testing to adolescent patients • Removed requirement for TB screening serology at screening visit. • Added PK sample at Week 4 • Clarifications on analysis timing, study procedures and protocol wording.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
24 March 2020	Global enrollment hold on new patient screening and enrollment.	28 May 2020

Notes:

Limitations and caveats

None reported