Clinical trial results:
A Phase III, Randomized, Double-Blind, Placebo-Controlled Study to Assess the Efficacy, Safety, and Tolerability of Lebrikizumab in Adolescent Patients With Uncontrolled Asthma Who are on Inhaled Corticosteroids and a Second Controller Medication

Summary

EudraCT number	2012-000180-25
Trial protocol	SK DE PT HU IT CZ ES PL GB FR
Global end of trial date	28 December 2016

Results information

Result version number	v1 (current)
This version publication date	28 June 2017
First version publication date	28 June 2017

Trial information

Trial identification

Sponsor protocol code	WB28183

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01875003
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	Roche Trial Information Hotline, F. Hoffmann-La Roche AG, 41 61 6878333, global.trial_information@roche.com
Scientific contact	Roche Trial Information Hotline, F. Hoffmann-La Roche AG, 41 61 6878333, global.trial_information@roche.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001053-PIP01-10
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 March 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 December 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objectives of this study were: 1) To evaluate the efficacy of lebrikizumab compared with placebo as measured by the rate of asthma exacerbations; 2) To evaluate the safety of lebrikizumab compared with placebo as measured by the rate and severity of adverse events and incidence of anti-therapeutic antibodies (ATA); 3) To evaluate the efficacy and safety of different dose levels of lebrikizumab compared with placebo

Protection of trial subjects:

The study was conducted in full conformance with the International Conference on Harmonisation (ICH) E6 guidelines for Good Clinical Practice (GCP) and the principles of the "Declaration of Helsinki", or the laws and regulations of the country in which the research was conducted, whichever afforded the greater protection to the individual. Approval from the Independent Ethics Committee (IEC)/Institutional Review Board (IRB) was obtained before study start and was documented in a letter to the Investigator specifying the date on which the committee met and granted the approval. The Sponsor also obtained approval from the relevant Competent Authority prior to starting the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 August 2013
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	United Kingdom: 4
Country: Number of subjects enrolled	Spain: 10
Country: Number of subjects enrolled	South Africa: 19
Country: Number of subjects enrolled	Portugal: 5
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Israel: 13
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Brazil: 26
Country: Number of subjects enrolled	United States: 51
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	Peru: 11
Country: Number of subjects enrolled	Mexico: 47
Country: Number of subjects enrolled	Colombia: 2
Country: Number of subjects enrolled	Argentina: 17

Country: Number of subjects enrolled	Ukraine: 31
Country: Number of subjects enrolled	Slovakia: 6
Country: Number of subjects enrolled	Poland: 61
Country: Number of subjects enrolled	Hungary: 31
Country: Number of subjects enrolled	Czech Republic: 5
Worldwide total number of subjects	346
EEA total number of subjects	127

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)	346
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 579 participants were screened for the study of which 346 were randomized and received at least one dose of study drug.

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, Monitor, Carer, Assessor

Arms

Are arms mutually exclusive?	No
Arm title	Placebo

Arm description:

Participants received subcutaneous (SC) injection of lebrikizumab matching placebo (1 placebo pre-filled syringe and 1 placebo vial) every 4 weeks (Q4W) for 52 weeks during placebo-controlled period. All participants were followed for safety for 24 weeks after last dose of study drug.

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

Dosage and administration details:

Participants received SC injection of lebrikizumab matching placebo via pre-filled syringe Q4W up to 52 weeks.

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

Dosage and administration details:

Participants received SC injection of lebrikizumab matching placebo via vial Q4W up to 52 weeks.

Arm title	Lebrikizumab 37.5 mg

Arm description:

Participants received SC injection of lebrikizumab at dose level of 37.5 mg (1 placebo pre-filled syringe and 1 active vial) Q4W for 52 weeks during placebo-controlled period. After Week 52, participants who were willing to take part in active-treatment extension, received same treatment up to Week 76 (if participants met protocol-defined criteria of asthma control from Week 52 to Week 76) or up to Week 104 (if participants did not meet protocol-defined criteria of asthma control from Week 52 to Week 76). All participants were followed for safety for 24 weeks after last dose of study drug.

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

Dosage and administration details:

Participants received SC injection of lebrikizumab matching placebo via pre-filled syringe Q4W maximum up to 104 weeks.

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

Dosage and administration details:

Participants received SC injection of lebrikizumab at dose level of 37.5 mg via vial Q4W maximum up to 104 weeks.

Arm title	Lebrikizumab 125 mg

Arm description:

Participants received SC injection of lebrikizumab at dose level of 125 mg (1 active pre-filled syringe and 1 placebo vial) Q4W for 52 weeks during placebo-controlled period. After Week 52, participants who were willing to take part in active-treatment extension, received same treatment up to Week 76 (if participants met protocol-defined criteria of asthma control from Week 52 to Week 76) or up to Week 104 (if participants did not meet protocol-defined criteria of asthma control from Week 52 to Week 76). All participants were followed for safety for 24 weeks after last dose of study drug.

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

Dosage and administration details:

Participants received SC injection of lebrikizumab at dose level of 125 mg via pre-filled syringe Q4W maximum up to 104 weeks.

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

Dosage and administration details:

Participants received SC injection of lebrikizumab matching placebo via vial Q4W maximum up to 104 weeks.

Arm title	Placebo/Lebrikizumab 37.5 mg

Arm description:

Participants in 'Placebo' group who were willing to take part in optional active-treatment extension period and who were randomized to this group received SC injection of lebrikizumab at dose level of 37.5 mg (1 placebo pre-filled syringe and 1 active vial) Q4W from Weeks 52 to Week 76 (if participants met protocol-defined criteria of asthma control from Week 52 to Week 76) or up to Week 104 (if participants did not meet protocol-defined criteria of asthma control from Week 52 to Week 76). All participants were followed for safety for 24 weeks after last dose of study drug.

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

Dosage and administration details:

Participants received SC injection of lebrikizumab at dose level of 37.5 mg via vial Q4W from Week 52 to maximum up to Week 104.

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

Dosage and administration details:

Participants received SC injection of lebrikizumab matching placebo via pre-filled syringe Q4W from Week 52 to maximum up to Week 104.

Arm title	Placebo/Lebrikizumab 125 mg

Arm description:

Participants in 'Placebo' group who were willing to take part in optional active-treatment extension period and who were randomized to this group received SC injection of lebrikizumab at dose level of 125 mg (1 active pre-filled syringe and 1 placebo vial) Q4W from Weeks 52 to Week 76 (if participants met protocol-defined criteria of asthma control from Week 52 to Week 76) or up to Week 104 (if participants did not meet protocol-defined criteria of asthma control from Week 52 to Week 76). All participants were followed for safety for 24 weeks after last dose of study drug.

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

Dosage and administration details:

Participants received SC injection of lebrikizumab at dose level of 125 mg via pre-filled syringe Q4W from Week 52 to maximum up to Week 104.

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

Dosage and administration details:

Participants received SC injection of lebrikizumab matching placebo via vial Q4W from Week 52 to maximum up to Week 104.

Number of subjects in period 1	Placebo	Lebrikizumab 37.5 mg	Lebrikizumab 125 mg
Started	117	113	116
Completed	0	30	31
Not completed	117	83	85
Consent withdrawn by subject	16	13	5
Physician decision	-	2	1
Adverse Event	1	2	2
Pregnancy	-	-	-
Transferred to Other Arm	61	-	-
Unspecified	-	1	1
Study Terminated by Sponsor	35	61	66
Lost to follow-up	4	-	1
Missing	-	4	9

Number of subjects in period 1	Placebo/Lebrikizumab 37.5 mg	Placebo/Lebrikizumab 125 mg
Started	30	31
Completed	16	14
Not completed	14	17
Consent withdrawn by subject	4	1
Physician decision	-	-
Adverse Event	-	-
Pregnancy	-	1
Transferred to Other Arm	-	-
Unspecified	-	-
Study Terminated by Sponsor	9	13
Lost to follow-up	-	-
Missing	1	2

Baseline characteristics

Reporting groups	
Reporting group title	Overall Study
Reporting group description:	
All randomized participants who received at least one dose of study drug.	

Reporting group values	Overall Study	Total	
Number of subjects	346	346	
Age Categorical Units: Subjects			
Age Continuous			
Intent-to-treat (ITT) population included all randomized participants who received at least one dose of study drug.			
Units: years			
arithmetic mean	14.2		
standard deviation	± 1.6	-	
Gender Categorical Units: Subjects			
Female	151	151	
Male	195	195	

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

Participants received subcutaneous (SC) injection of lebrikizumab matching placebo (1 placebo pre-filled syringe and 1 placebo vial) every 4 weeks (Q4W) for 52 weeks during placebo-controlled period. All participants were followed for safety for 24 weeks after last dose of study drug.

Reporting group title	Lebrikizumab 37.5 mg

Reporting group description:

Participants received SC injection of lebrikizumab at dose level of 37.5 mg (1 placebo pre-filled syringe and 1 active vial) Q4W for 52 weeks during placebo-controlled period. After Week 52, participants who were willing to take part in active-treatment extension, received same treatment up to Week 76 (if participants met protocol-defined criteria of asthma control from Week 52 to Week 76) or up to Week 104 (if participants did not meet protocol-defined criteria of asthma control from Week 52 to Week 76). All participants were followed for safety for 24 weeks after last dose of study drug.

Reporting group title	Lebrikizumab 125 mg

Reporting group description:

Participants received SC injection of lebrikizumab at dose level of 125 mg (1 active pre-filled syringe and 1 placebo vial) Q4W for 52 weeks during placebo-controlled period. After Week 52, participants who were willing to take part in active-treatment extension, received same treatment up to Week 76 (if participants met protocol-defined criteria of asthma control from Week 52 to Week 76) or up to Week 104 (if participants did not meet protocol-defined criteria of asthma control from Week 52 to Week 76). All participants were followed for safety for 24 weeks after last dose of study drug.

Reporting group title	Placebo/Lebrikizumab 37.5 mg

Reporting group description:

Participants in 'Placebo' group who were willing to take part in optional active-treatment extension period and who were randomized to this group received SC injection of lebrikizumab at dose level of 37.5 mg (1 placebo pre-filled syringe and 1 active vial) Q4W from Weeks 52 to Week 76 (if participants met protocol-defined criteria of asthma control from Week 52 to Week 76) or up to Week 104 (if participants did not meet protocol-defined criteria of asthma control from Week 52 to Week 76). All participants were followed for safety for 24 weeks after last dose of study drug.

Reporting group title	Placebo/Lebrikizumab 125 mg

Reporting group description:

Participants in 'Placebo' group who were willing to take part in optional active-treatment extension period and who were randomized to this group received SC injection of lebrikizumab at dose level of 125 mg (1 active pre-filled syringe and 1 placebo vial) Q4W from Weeks 52 to Week 76 (if participants met protocol-defined criteria of asthma control from Week 52 to Week 76) or up to Week 104 (if participants did not meet protocol-defined criteria of asthma control from Week 52 to Week 76). All participants were followed for safety for 24 weeks after last dose of study drug.

Primary: Rate of Asthma Exacerbations During 52-Week Placebo Controlled Period

End point title	Rate of Asthma Exacerbations During 52-Week Placebo Controlled Period[1]

End point description:

An asthma exacerbation is defined as new or increased asthma symptoms (including wheeze, cough, dyspnea, chest tightness, and/or night-time awakening due to these symptoms) that lead to treatment with systemic corticosteroids or to hospitalization. Treatment with systemic corticosteroids is defined as treatment with oral, intravenous (IV), or intramuscular (IM) corticosteroids for at least 3 days or an emergency department visit with at least 1 dose of IV or IM corticosteroids. Rate of asthma exacerbation = total number of exacerbation events divided by total follow-up time in patient years. Adjusted exacerbation rate estimated from a Poisson regression model was reported. Analysis was performed on ITT population.

End point type	Primary

End point timeframe:

52 Weeks

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Analysis was planned to be carried out in the indicated arms only.

End point values	Placebo	Lebrikizumab 37.5 mg	Lebrikizumab 125 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	117	113	116	
Units: events per patient year				
number (not applicable)	0.43	0.26	0.21	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Adjusted exacerbation rates and rate ratios were estimated from a Poisson regression model with over-dispersion adjusted for the following covariates in addition to log(patient years) as an offset: number of asthma exacerbations within the last 12 months, baseline asthma medications and age group.

Comparison groups	Placebo v Lebrikizumab 37.5 mg
Number of subjects included in analysis	230
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Adjusted Rate Ratio
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.35
upper limit	1.03

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Adjusted exacerbation rates and rate ratios were estimated from a Poisson regression model with over-dispersion adjusted for the following covariates in addition to log(patient years) as an offset: number of asthma exacerbations within the last 12 months, baseline asthma medications and age group.

Comparison groups	Placebo v Lebrikizumab 125 mg
Number of subjects included in analysis	233
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Adjusted Rate Ratio
Point estimate	0.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.28
upper limit	0.83

Secondary: Percent Change from Baseline in Pre-Bronchodilator Forced Expiratory Volume in 1 Second (FEV1) at Week 52

End point title	Percent Change from Baseline in Pre-Bronchodilator Forced Expiratory Volume in 1 Second (FEV1) at Week 52[2]

End point description:

FEV1 is the maximal volume of air exhaled in the first second of a forced expiration from a position of full inspiration. The baseline FEV1 was obtained from the last spirometric analysis performed before the first study treatment administration. The percentage change in pre-bronchodilator FEV1 was defined as the change in FEV1 (in liters) from baseline divided by the FEV1 (in liters) at baseline multiplied by 100. ITT populaton; Here 'Number of Subjects Analysed' signifies number of participants evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline, Week 52

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Analysis was planned to be carried out in the indicated arms only.

End point values	Placebo	Lebrikizumab 37.5 mg	Lebrikizumab 125 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	70	75	69	
Units: percent change				
arithmetic mean (standard deviation)	20.8 (± 32.8)	27.1 (± 20.9)	24.7 (± 28.4)	

Statistical analyses

Statistical analysis title	Statisical Analysis 1

Statistical analysis description:

Mixed model repeated measures (MMRM) analysis with an unstructured covariance matrix was utilized.

Comparison groups	Placebo v Lebrikizumab 37.5 mg
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	superiority[3]
Parameter estimate	Difference in Adjusted Means
Point estimate	6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	14
Variability estimate	Standard error of the mean
Dispersion value	4

Notes:

[3] - The model used percent change from baseline in pre-bronchodilator FEV1 as the response variable and included terms for treatment, visit, treatment*visit, number of asthma exacerbations within the last 12 months, baseline asthma medications and age group.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

MMRM analysis with an unstructured covariance matrix was utilized.

Comparison groups	Placebo v Lebrikizumab 125 mg
Number of subjects included in analysis	139
Analysis specification	Pre-specified
Analysis type	superiority[4]
Parameter estimate	Difference in Adjusted Means
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7
upper limit	9
Variability estimate	Standard error of the mean
Dispersion value	4

Notes:

[4] - The model used percent change from baseline in pre-bronchodilator FEV1 as the response variable and included terms for treatment, visit, treatment*visit, number of asthma exacerbations within the last 12 months, baseline asthma medications and age group

Secondary: Time to First Asthma Exacerbation

End point title	Time to First Asthma Exacerbation[5]

End point description:

An asthma exacerbation was defined as new or increased asthma symptoms (including wheeze, cough, dyspnea, chest tightness, and/or night-time awakening due to these symptoms) that lead to treatment with systemic corticosteroids or to hospitalization. Treatment with systemic corticosteroids was defined as treatment with oral, IV, or IM corticosteroids for at least 3 days or an emergency department visit with at least 1 dose of IV or IM corticosteroids. Median time to first protocol-defined asthma exacerbation was estimated using Kaplan-Meier analysis. 95% Confidence interval (CI) for median was computed using the method of Brookmeyer and Crowley. ITT population. The data '99999 (99999 to 99999)' in the results signifies that median and corresponding CI could not be calculated due to low number of participants who had an event.

End point type	Secondary

End point timeframe:

Baseline up to Week 52

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Analysis was planned to be carried out in the indicated arms only.

End point values	Placebo	Lebrikizumab 37.5 mg	Lebrikizumab 125 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	117	113	116	
Units: weeks				
median (confidence interval 95%)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:	
Stratified Analysis	
Comparison groups	Placebo v Lebrikizumab 37.5 mg
Number of subjects included in analysis	230
Analysis specification	Pre-specified
Analysis type	superiority[6]
Parameter estimate	Hazard ratio (HR)
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.22
upper limit	0.73

Notes:

[6] - Hazard Ratio (HR) was estimated using Cox regression analysis with the following baseline covariates included as stratification factors: number of asthma exacerbations within the last 12 months, baseline asthma medications and age group.

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Stratified Analysis	
Comparison groups	Placebo v Lebrikizumab 125 mg
Number of subjects included in analysis	233
Analysis specification	Pre-specified
Analysis type	superiority[7]
Parameter estimate	Hazard ratio (HR)
Point estimate	0.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.21
upper limit	0.66

Notes:

[7] - HR was estimated using Cox regression analysis with the following baseline covariates included as stratification factors: number of asthma exacerbations within the last 12 months, baseline asthma medications and age group.

Secondary: Change From Baseline in Fractional Exhaled Nitric Oxide (FeNO) at Week 52

End point title	Change From Baseline in Fractional Exhaled Nitric Oxide (FeNO) at Week 52[8]

End point description:

Measurement of FeNO (in parts per billion [ppb]) was performed using a hand-held portable NIOX MINO® device, in accordance with guidelines published by the American Thoracic Society (ATS) and described in the pulmonary function testing manual. ITT population. Here 'Number of Subjects Analysed' signifies number of participants evaluable for this outcome measure, and 'n' signifies number of participants evaluable at specified time point, per arm, respectively.

End point type	Secondary

End point timeframe:

Baseline, Week 52

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Analysis was planned to be carried out in the indicated arms only.

End point values	Placebo	Lebrikizumab 37.5 mg	Lebrikizumab 125 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	111	111	115	
Units: ppb				
arithmetic mean (standard deviation)				
Baseline (n= 111, 111, 115)	42.42 (± 35.78)	45.5 (± 37.79)	48.7 (± 42.7)	
Change at Week 52 (n= 63, 70, 65)	7.09 (± 29.45)	-21.59 (± 29.69)	-33.63 (± 38.64)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

MMRM analysis with an unstructured covariance matrix was utilized. Actual subjects included in analysis (at Week 52) = 133.

Comparison groups	Placebo v Lebrikizumab 37.5 mg
Number of subjects included in analysis	222
Analysis specification	Pre-specified
Analysis type	superiority[9]
Parameter estimate	Difference in Adjusted Means
Point estimate	-21.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	-29.39
upper limit	-14.55
Variability estimate	Standard error of the mean
Dispersion value	3.77

Notes:

[9] - The model used absolute change from baseline in pre-bronchodilator FeNO as the response variable and included terms for treatment, visit, treatment*visit, baseline FeNO, baseline FeNO*visit, number of asthma exacerbations within the last 12 months, baseline asthma medications and age group.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

MMRM analysis with an unstructured covariance matrix was utilized. Actual subjects included in analysis (at Week 52) = 128.

Comparison groups	Placebo v Lebrikizumab 125 mg
Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	superiority[10]
Parameter estimate	Difference in Adjusted Means
Point estimate	-30.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-37.87
upper limit	-22.78

Variability estimate	Standard error of the mean
Dispersion value	3.84

Notes:

[10] - The model used absolute change from baseline in pre-bronchodilator FeNO as the response variable and included terms for treatment, visit, treatment*visit, baseline FeNO, baseline FeNO*visit, number of asthma exacerbations within the last 12 months, baseline asthma medications and age group.

Secondary: Change From Baseline in Standardized Asthma Quality of Life Questionnaire for 12 Years and Older (AQLQ+12) Overall Score at Week 52

End point title	Change From Baseline in Standardized Asthma Quality of Life Questionnaire for 12 Years and Older (AQLQ+12) Overall Score at Week 52[11]

End point description:

The Standardized AQLQ+12 was used to assess the participants' asthma-specific health-related quality of life. The AQLQ+12 had a recall specification of 2 weeks. The AQLQ+12 was a 32-item questionnaire with 4 domains: activity limitations, symptoms, emotional function, and environmental stimuli. Each of the 32 questions were scored on a scale 1-7. The overall AQLQ+12 score is the mean of the responses to each of the 32 questions, and ranges from 1 to 7. A score 7 indicated no impairments due to asthma, and a score of 1 indicated severe impairment. ITT population. Here 'Number of Subjects Analysed' signifies number of participants evaluable for this outcome measure, and 'n' signifies number of participants evaluable at specified time point, per arm, respectively.

End point type	Secondary

End point timeframe:

Baseline, Week 52

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Analysis was planned to be carried out in the indicated arms only.

End point values	Placebo	Lebrikizumab 37.5 mg	Lebrikizumab 125 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	106	101	111	
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n= 106, 101, 111)	4.42 (± 1.09)	4.65 (± 1.15)	4.22 (± 1.26)	
Change at Week 52 (n= 63, 64, 69)	1.16 (± 1.21)	0.98 (± 0.98)	1.45 (± 1.33)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

MMRM analysis with an unstructured covariance matrix was utilized. Actual subjects included in analysis (at Week 52) = 127.

Comparison groups	Placebo v Lebrikizumab 37.5 mg
Number of subjects included in analysis	207
Analysis specification	Pre-specified
Analysis type	superiority[12]
Parameter estimate	Difference in Adjusted Means
Point estimate	0.12

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.18
upper limit	0.41
Variability estimate	Standard error of the mean
Dispersion value	0.15

Notes:

[12] - The model used absolute change from baseline in AQLQ+12 score as the response variable and included terms for treatment, visit, treatment*visit, baseline AQLQ+12, baseline AQLQ+12*visit, number of asthma exacerbations within the last 12 months, baseline asthma medications, and age group.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

MMRM analysis with an unstructured covariance matrix was utilized. Actual subjects included in analysis (at Week 52) = 132.

Comparison groups	Placebo v Lebrikizumab 125 mg
Number of subjects included in analysis	217
Analysis specification	Pre-specified
Analysis type	superiority[13]
Parameter estimate	Difference in Adjusted Means
Point estimate	0.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.14
upper limit	0.44
Variability estimate	Standard error of the mean
Dispersion value	0.15

Notes:

[13] - The model used absolute change from baseline in AQLQ+12 score as the response variable and included terms for treatment, visit, treatment*visit, baseline AQLQ+12, baseline AQLQ+12*visit, number of asthma exacerbations within the last 12 months, baseline asthma medications, and age group.

Secondary: Change From Baseline in Asthma Rescue Medication Use at Week 52

End point title	Change From Baseline in Asthma Rescue Medication Use at Week 52[14]

End point description:

Participants were allowed to use short-acting bronchodilators as asthma rescue medication. Baseline asthma rescue medication use was defined as the average number of puffs per day over the 7 days prior to and on the day of randomization. Participants must have recorded their asthma rescue medication use for at least 4 days to have a baseline score calculated. The post-baseline asthma medication use for any timepoint was defined as the average number of puffs per day over the last 28 days on or prior to the timepoint. Participants must have recorded their asthma rescue medication use for at least 14 days during a 28-day interval to have a score calculated for the respective timepoint. For nebulizer use, one treatment (inhalation) was considered equivalent to 4 puffs. ITT population. Here 'Number of Subjects Analysed' signifies number of participants evaluable for this outcome measure, and 'n' signifies number of participants evaluable at specified time point, per arm, respectively.

End point type	Secondary

End point timeframe:

Baseline, Week 52

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Analysis was planned to be carried out in the indicated arms only.

End point values	Placebo	Lebrikizumab 37.5 mg	Lebrikizumab 125 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	109	109	113	
Units: puffs per day				
arithmetic mean (standard deviation)				
Baseline (n= 109, 109, 113)	2.17 (± 4.09)	1.47 (± 1.78)	2.23 (± 3.92)	
Change at Week 52 (n=51, 58, 58)	-0.79 (± 1.95)	-0.56 (± 1.35)	-0.81 (± 3.15)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

MMRM analysis with compound symmetry covariance matrix was utilized. Actual subjects included in analysis (at Week 52) = 109.

Comparison groups	Placebo v Lebrikizumab 37.5 mg
Number of subjects included in analysis	218
Analysis specification	Pre-specified
Analysis type	superiority[15]
Parameter estimate	Difference in Adjusted Means
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.67
upper limit	0.58
Variability estimate	Standard error of the mean
Dispersion value	0.32

Notes:

[15] - The model used absolute change from baseline in asthma rescue medication use as the response variable and included terms for treatment, visit, treatment*visit, baseline rescue medication use, baseline rescue medication use*visit, number of asthma exacerbations within the last 12 months, baseline asthma medications, and age group.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

MMRM analysis with compound symmetry covariance matrix was utilized. Actual subjects included in analysis (at Week 52) = 109.

Comparison groups	Placebo v Lebrikizumab 125 mg
Number of subjects included in analysis	222
Analysis specification	Pre-specified
Analysis type	superiority[16]
Parameter estimate	Difference in Adjusted Means
Point estimate	0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.48
upper limit	0.77
Variability estimate	Standard error of the mean
Dispersion value	0.32

Notes:

[16] - The model used absolute change from baseline in asthma rescue medication use as the response variable and included terms for treatment, visit, treatment*visit, baseline rescue medication use, baseline rescue medication use*visit, number of asthma exacerbations within the last 12 months, baseline asthma medications, and age group.

Secondary: Rate of Urgent Asthma-Related Health Care Utilization (HCU) Events

End point title	Rate of Urgent Asthma-Related Health Care Utilization (HCU) Events[17]

End point description:

Urgent asthma-related HCU events included hospitalizations, emergency department visits, and acute care visits. Rate of urgent asthma-related HCU events = total number of urgent asthma-related HCU events divided by total follow-up time in patient years. ITT population.

End point type	Secondary

End point timeframe:

Baseline up to Week 52

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Analysis was planned to be carried out in the indicated arms only.

End point values	Placebo	Lebrikizumab 37.5 mg	Lebrikizumab 125 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	117	113	116	
Units: events per patient year				
number (not applicable)	0.18	0.07	0.06	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Adjusted health care utilization rates and rate ratios were estimates from a Poisson regression model with over-dispersion and adjusted for the following covariates in addition to log(patient years) as an offset: number of asthma exacerbations within the last 12 months, baseline asthma medications and age group.

Comparison groups	Placebo v Lebrikizumab 37.5 mg
Number of subjects included in analysis	230
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Ratio of Adjusted HCU Rate
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.16
upper limit	1

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Adjusted health care utilization rates and rate ratios were estimates from a Poisson regression model with over-dispersion and adjusted for the following covariates in addition to log(patient years) as an offset: number of asthma exacerbations within the last 12 months, baseline asthma medications and age group.

Comparison groups	Placebo v Lebrikizumab 125 mg
Number of subjects included in analysis	233
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Ratio of Adjusted HCU Rate
Point estimate	0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	0.72

Secondary: Injection Acceptability Questionnaire (IAQ) Score

End point title	Injection Acceptability Questionnaire (IAQ) Score[18]

End point description:

The acceptability of the injections of study drug was addressed by measuring the level of pain that participants experienced. Participants assessed pain associated with study drug administration using the IAQ within 10 minutes of study drug administration. The IAQ score ranged from 0 to 10; where 0 = no pain and 10 = worst pain imaginable. ITT population. Here 'Number of Subjects Analysed' signifies number of participants evaluable for this outcome measure, and 'n' signifies number of participants evaluable at specified time point, per arm, respectively.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Analysis was planned to be carried out in the indicated arms only.

End point values	Placebo	Lebrikizumab 37.5 mg	Lebrikizumab 125 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	107	100	105	
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n= 107, 100, 105)	3.5 (± 2.6)	3.5 (± 2.3)	3.9 (± 2.6)	
Week 4 (n= 101, 102, 105)	3.7 (± 2.7)	4.1 (± 2.6)	3.9 (± 2.7)	
Week 8 (n= 91, 95, 102)	3.7 (± 2.5)	3.7 (± 2.4)	3.5 (± 2.4)	
Week 12 (n= 92, 92, 96)	3.4 (± 2.4)	3.4 (± 2.7)	3.5 (± 2.5)	
Week 16 (n= 87, 88, 95)	3.2 (± 2.5)	3.2 (± 2.6)	3.3 (± 2.5)	
Week 20 (n= 84, 84, 87)	3.1 (± 2.4)	3 (± 2.6)	3.1 (± 2.4)	
Week 24 (n= 80, 82, 85)	3.3 (± 2.3)	3.1 (± 2.5)	3.3 (± 2.1)	
Week 28 (n= 82, 81, 84)	2.9 (± 2.2)	2.8 (± 2.4)	2.8 (± 2.2)	
Week 32 (n= 83, 79, 80)	2.9 (± 2.2)	2.9 (± 2.7)	3 (± 2.1)	
Week 36 (n= 77, 73, 80)	3.1 (± 2.3)	3.1 (± 2.7)	3.1 (± 2.1)	
Week 40 (n= 70, 69, 74)	3 (± 2.3)	3 (± 2.4)	2.7 (± 2.1)	

Week 44 (n= 58, 65, 73)	2.9 (± 2.1)	2.9 (± 2.2)	3.2 (± 2.4)	
Week 48 (n= 58, 60, 67)	2.9 (± 2.3)	2.9 (± 2.6)	2.7 (± 2.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum Observed Serum Concentration (Ctrough) for Lebrikizumab

End point title	Minimum Observed Serum Concentration (Ctrough) for Lebrikizumab[19]

End point description:

Participants who received at least one dose of lebrikizumab and had at least one post-baseline evaluable sample were included in the analysis. Results of post-dose samples which were less than reportable were set to 0.045 micrograms per milliliter (mcg/mL) that is half of minimum quantifiable concentration value (0.09 mcg/mL). Here 'Number of Subjects Analysed' signifies number of participants evaluable for this outcome measure, and 'n' signifies number of participants evaluable at specified time point, per arm, respectively. The data '99999' in the results signifies that data was not available because no participant was evaluable at indicated time point, and data '9999' signifies that data was not reported because more that one-third values were less than reportable.

End point type	Secondary

End point timeframe:

Predose (Hour 0) at Weeks 4, 12, 24, 36, and 52

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Analysis was planned to be carried out in the indicated arms only.

End point values	Lebrikizumab 37.5 mg	Lebrikizumab 125 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	50		
Units: mcg/mL				
arithmetic mean (standard deviation)				
Week 4 (n= 47, 50)	3.25 (± 1.58)	12.2 (± 5.28)		
Week 12 (n=42, 40)	5.72 (± 2.81)	21.7 (± 9.37)		
Week 24 (n= 28, 29)	7.15 (± 6.23)	25.7 (± 9.84)		
Week 36 (n= 18, 23)	3.88 (± 2.92)	23.9 (± 9.87)		
Week 52 (4, 0)	9999 (± 9999)	99999 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to 24 weeks after last dose of study treatment (overall 128 weeks)

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	Placebo

Reporting group description:

Participants received SC injection of lebrikizumab matching placebo (1 placebo pre-filled syringe and 1 placebo vial) Q4W for 52 weeks during placebo-controlled period. All participants were followed for safety for 24 weeks after last dose of study drug.

Reporting group title	Lebrikizumab 37.5 mg

Reporting group description:

Participants received SC injection of lebrikizumab at dose level of 37.5 mg (1 placebo pre-filled syringe and 1 active vial) Q4W for 52 weeks during placebo-controlled period. After Week 52, participants who were willing to take part in active-treatment extension, received same treatment up to Week 76 (if participants met protocol-defined criteria of asthma control from Week 52 to Week 76) or up to Week 104 (if participants did not meet protocol-defined criteria of asthma control from Week 52 to Week 76). All participants were followed for safety for 24 weeks after last dose of study drug.

Reporting group title	Lebrikizumab 125 mg

Reporting group description:

Participants received SC injection of lebrikizumab at dose level of 125 mg (1 active pre-filled syringe and 1 placebo vial) Q4W for 52 weeks during placebo-controlled period. After Week 52, participants who were willing to take part in active-treatment extension, received same treatment up to Week 76 (if participants met protocol-defined criteria of asthma control from Week 52 to Week 76) or up to Week 104 (if participants did not meet protocol-defined criteria of asthma control from Week 52 to Week 76). All participants were followed for safety for 24 weeks after last dose of study drug.

Reporting group title	Placebo/ Lebrikizumab 37.5 mg

Reporting group description:

Participants in 'Placebo' group who were willing to take part in optional active-treatment extension period and who were randomized to this group received SC injection of lebrikizumab at dose level of 37.5 mg (1 placebo pre-filled syringe and 1 active vial) Q4W from Weeks 52 to Week 76 (if participants met protocol-defined criteria of asthma control from Week 52 to Week 76) or up to Week 104 (if participants did not meet protocol-defined criteria of asthma control from Week 52 to Week 76). All participants were followed for safety for 24 weeks after last dose of study drug.

Reporting group title	Placebo/ Lebrikizumab 125 mg

Reporting group description:

Participants in 'Placebo' group who were willing to take part in optional active-treatment extension period and who were randomized to this group received SC injection of lebrikizumab at dose level of 125 mg (1 active pre-filled syringe and 1 placebo vial) Q4W from Weeks 52 to Week 76 (if participants met protocol-defined criteria of asthma control from Week 52 to Week 76) or up to Week 104 (if participants did not meet protocol-defined criteria of asthma control from Week 52 to Week 76). All participants were followed for safety for 24 weeks after last dose of study drug.

Serious adverse events	Placebo	Lebrikizumab 37.5 mg	Lebrikizumab 125 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 56 (5.36%)	6 / 113 (5.31%)	8 / 116 (6.90%)
number of deaths (all causes)	0	0	0

number of deaths resulting from adverse events			
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 56 (0.00%)	0 / 113 (0.00%)	1 / 116 (0.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 56 (0.00%)	0 / 113 (0.00%)	0 / 116 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 56 (0.00%)	0 / 113 (0.00%)	0 / 116 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Eosinophilia			
subjects affected / exposed	0 / 56 (0.00%)	1 / 113 (0.88%)	0 / 116 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 56 (0.00%)	0 / 113 (0.00%)	1 / 116 (0.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaphylactic shock			
subjects affected / exposed	0 / 56 (0.00%)	0 / 113 (0.00%)	1 / 116 (0.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 56 (0.00%)	0 / 113 (0.00%)	0 / 116 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			

subjects affected / exposed	1 / 56 (1.79%)	0 / 113 (0.00%)	0 / 116 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 56 (1.79%)	0 / 113 (0.00%)	0 / 116 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 56 (1.79%)	2 / 113 (1.77%)	2 / 116 (1.72%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthmatic crisis			
subjects affected / exposed	0 / 56 (0.00%)	1 / 113 (0.88%)	0 / 116 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 56 (1.79%)	0 / 113 (0.00%)	0 / 116 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 56 (0.00%)	1 / 113 (0.88%)	0 / 116 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			
subjects affected / exposed	0 / 56 (0.00%)	1 / 113 (0.88%)	0 / 116 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 56 (0.00%)	0 / 113 (0.00%)	1 / 116 (0.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 56 (0.00%)	1 / 113 (0.88%)	0 / 116 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 56 (0.00%)	0 / 113 (0.00%)	1 / 116 (0.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 56 (0.00%)	1 / 113 (0.88%)	0 / 116 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 56 (0.00%)	1 / 113 (0.88%)	0 / 116 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary tuberculosis			
subjects affected / exposed	0 / 56 (0.00%)	0 / 113 (0.00%)	1 / 116 (0.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 56 (0.00%)	0 / 113 (0.00%)	0 / 116 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	0 / 56 (0.00%)	1 / 113 (0.88%)	0 / 116 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 56 (1.79%)	0 / 113 (0.00%)	1 / 116 (0.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Metabolic syndrome			
subjects affected / exposed	0 / 56 (0.00%)	0 / 113 (0.00%)	1 / 116 (0.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 56 (0.00%)	0 / 113 (0.00%)	0 / 116 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo/ Lebrikizumab 37.5 mg	Placebo/ Lebrikizumab 125 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 30 (10.00%)	4 / 31 (12.90%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 30 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	1 / 30 (3.33%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 30 (0.00%)	1 / 31 (3.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Eosinophilia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			

Anaphylactic reaction			
subjects affected / exposed	0 / 30 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaphylactic shock			
subjects affected / exposed	0 / 30 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 30 (0.00%)	1 / 31 (3.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 30 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 30 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 30 (3.33%)	2 / 31 (6.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthmatic crisis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 30 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 30 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria			
subjects affected / exposed	0 / 30 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 30 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	0 / 30 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 30 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary tuberculosis			

subjects affected / exposed	0 / 30 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			
subjects affected / exposed	1 / 30 (3.33%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	0 / 30 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 30 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic syndrome			
subjects affected / exposed	0 / 30 (0.00%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 1 diabetes mellitus			
subjects affected / exposed	1 / 30 (3.33%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	Lebrikizumab 37.5 mg	Lebrikizumab 125 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 56 (41.07%)	67 / 113 (59.29%)	72 / 116 (62.07%)
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 56 (1.79%)	2 / 113 (1.77%)	3 / 116 (2.59%)
occurrences (all)	2	2	3

Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 56 (1.79%)	3 / 113 (2.65%)	0 / 116 (0.00%)
occurrences (all)	1	3	0
Headache			
subjects affected / exposed	2 / 56 (3.57%)	8 / 113 (7.08%)	11 / 116 (9.48%)
occurrences (all)	2	20	22
General disorders and administration site conditions			
Injection site extravasation			
subjects affected / exposed	0 / 56 (0.00%)	2 / 113 (1.77%)	2 / 116 (1.72%)
occurrences (all)	0	8	12
Injection site induration			
subjects affected / exposed	0 / 56 (0.00%)	1 / 113 (0.88%)	3 / 116 (2.59%)
occurrences (all)	0	1	3
Injection site pain			
subjects affected / exposed	0 / 56 (0.00%)	2 / 113 (1.77%)	2 / 116 (1.72%)
occurrences (all)	0	4	2
Eye disorders			
Conjunctivitis allergic			
subjects affected / exposed	0 / 56 (0.00%)	1 / 113 (0.88%)	0 / 116 (0.00%)
occurrences (all)	0	3	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 56 (0.00%)	1 / 113 (0.88%)	6 / 116 (5.17%)
occurrences (all)	0	3	6
Diarrhoea			
subjects affected / exposed	1 / 56 (1.79%)	2 / 113 (1.77%)	2 / 116 (1.72%)
occurrences (all)	1	2	2
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	12 / 56 (21.43%)	25 / 113 (22.12%)	31 / 116 (26.72%)
occurrences (all)	21	53	58
Cough			
subjects affected / exposed	1 / 56 (1.79%)	6 / 113 (5.31%)	3 / 116 (2.59%)
occurrences (all)	1	8	3
Oropharyngeal pain			

subjects affected / exposed	0 / 56 (0.00%)	7 / 113 (6.19%)	0 / 116 (0.00%)
occurrences (all)	0	10	0
Rhinitis allergic			
subjects affected / exposed	1 / 56 (1.79%)	3 / 113 (2.65%)	6 / 116 (5.17%)
occurrences (all)	2	4	8
Wheezing			
subjects affected / exposed	0 / 56 (0.00%)	1 / 113 (0.88%)	0 / 116 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 56 (0.00%)	1 / 113 (0.88%)	1 / 116 (0.86%)
occurrences (all)	0	1	1
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	0 / 56 (0.00%)	2 / 113 (1.77%)	3 / 116 (2.59%)
occurrences (all)	0	2	4
Bronchitis			
subjects affected / exposed	2 / 56 (3.57%)	10 / 113 (8.85%)	6 / 116 (5.17%)
occurrences (all)	2	12	7
Gastroenteritis			
subjects affected / exposed	1 / 56 (1.79%)	3 / 113 (2.65%)	3 / 116 (2.59%)
occurrences (all)	1	3	3
Influenza			
subjects affected / exposed	0 / 56 (0.00%)	5 / 113 (4.42%)	6 / 116 (5.17%)
occurrences (all)	0	5	9
Laryngitis			
subjects affected / exposed	0 / 56 (0.00%)	1 / 113 (0.88%)	1 / 116 (0.86%)
occurrences (all)	0	1	1
Nasopharyngitis			
subjects affected / exposed	4 / 56 (7.14%)	14 / 113 (12.39%)	13 / 116 (11.21%)
occurrences (all)	5	31	18
Pharyngitis			
subjects affected / exposed	5 / 56 (8.93%)	10 / 113 (8.85%)	18 / 116 (15.52%)
occurrences (all)	5	14	28
Respiratory tract infection			

subjects affected / exposed	0 / 56 (0.00%)	1 / 113 (0.88%)	5 / 116 (4.31%)
occurrences (all)	0	1	5
Rhinitis			
subjects affected / exposed	1 / 56 (1.79%)	5 / 113 (4.42%)	6 / 116 (5.17%)
occurrences (all)	1	5	6
Sinusitis			
subjects affected / exposed	4 / 56 (7.14%)	2 / 113 (1.77%)	3 / 116 (2.59%)
occurrences (all)	4	3	4
Tonsillitis			
subjects affected / exposed	2 / 56 (3.57%)	9 / 113 (7.96%)	8 / 116 (6.90%)
occurrences (all)	2	9	11
Upper respiratory tract infection			
subjects affected / exposed	3 / 56 (5.36%)	16 / 113 (14.16%)	11 / 116 (9.48%)
occurrences (all)	3	22	14
Viral infection			
subjects affected / exposed	0 / 56 (0.00%)	1 / 113 (0.88%)	3 / 116 (2.59%)
occurrences (all)	0	1	3
Viral pharyngitis			
subjects affected / exposed	0 / 56 (0.00%)	1 / 113 (0.88%)	1 / 116 (0.86%)
occurrences (all)	0	1	1
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 56 (0.00%)	2 / 113 (1.77%)	2 / 116 (1.72%)
occurrences (all)	0	2	4

Non-serious adverse events	Placebo/ Lebrikizumab 37.5 mg	Placebo/ Lebrikizumab 125 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 30 (76.67%)	24 / 31 (77.42%)	
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	2 / 30 (6.67%)	0 / 31 (0.00%)	
occurrences (all)	2	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 30 (0.00%)	2 / 31 (6.45%)	
occurrences (all)	0	2	
Headache			

subjects affected / exposed	3 / 30 (10.00%)	6 / 31 (19.35%)	
occurrences (all)	6	7	
General disorders and administration site conditions			
Injection site extravasation			
subjects affected / exposed	1 / 30 (3.33%)	2 / 31 (6.45%)	
occurrences (all)	4	2	
Injection site induration			
subjects affected / exposed	1 / 30 (3.33%)	2 / 31 (6.45%)	
occurrences (all)	1	3	
Injection site pain			
subjects affected / exposed	2 / 30 (6.67%)	1 / 31 (3.23%)	
occurrences (all)	38	1	
Eye disorders			
Conjunctivitis allergic			
subjects affected / exposed	2 / 30 (6.67%)	0 / 31 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 30 (3.33%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Diarrhoea			
subjects affected / exposed	2 / 30 (6.67%)	1 / 31 (3.23%)	
occurrences (all)	2	1	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	11 / 30 (36.67%)	15 / 31 (48.39%)	
occurrences (all)	20	43	
Cough			
subjects affected / exposed	2 / 30 (6.67%)	1 / 31 (3.23%)	
occurrences (all)	2	1	
Oropharyngeal pain			
subjects affected / exposed	1 / 30 (3.33%)	2 / 31 (6.45%)	
occurrences (all)	1	2	
Rhinitis allergic			
subjects affected / exposed	2 / 30 (6.67%)	2 / 31 (6.45%)	
occurrences (all)	6	5	

Wheezing			
subjects affected / exposed	1 / 30 (3.33%)	2 / 31 (6.45%)	
occurrences (all)	2	2	
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	2 / 30 (6.67%)	1 / 31 (3.23%)	
occurrences (all)	2	1	
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	1 / 30 (3.33%)	3 / 31 (9.68%)	
occurrences (all)	1	6	
Bronchitis			
subjects affected / exposed	4 / 30 (13.33%)	4 / 31 (12.90%)	
occurrences (all)	7	7	
Gastroenteritis			
subjects affected / exposed	3 / 30 (10.00%)	1 / 31 (3.23%)	
occurrences (all)	3	1	
Influenza			
subjects affected / exposed	1 / 30 (3.33%)	1 / 31 (3.23%)	
occurrences (all)	1	1	
Laryngitis			
subjects affected / exposed	0 / 30 (0.00%)	2 / 31 (6.45%)	
occurrences (all)	0	2	
Nasopharyngitis			
subjects affected / exposed	6 / 30 (20.00%)	7 / 31 (22.58%)	
occurrences (all)	11	10	
Pharyngitis			
subjects affected / exposed	8 / 30 (26.67%)	4 / 31 (12.90%)	
occurrences (all)	11	7	
Respiratory tract infection			
subjects affected / exposed	2 / 30 (6.67%)	2 / 31 (6.45%)	
occurrences (all)	4	4	
Rhinitis			
subjects affected / exposed	3 / 30 (10.00%)	3 / 31 (9.68%)	
occurrences (all)	7	3	
Sinusitis			

subjects affected / exposed	1 / 30 (3.33%)	1 / 31 (3.23%)	
occurrences (all)	1	2	
Tonsillitis			
subjects affected / exposed	2 / 30 (6.67%)	3 / 31 (9.68%)	
occurrences (all)	3	3	
Upper respiratory tract infection			
subjects affected / exposed	2 / 30 (6.67%)	2 / 31 (6.45%)	
occurrences (all)	2	6	
Viral infection			
subjects affected / exposed	0 / 30 (0.00%)	2 / 31 (6.45%)	
occurrences (all)	0	4	
Viral pharyngitis			
subjects affected / exposed	0 / 30 (0.00%)	2 / 31 (6.45%)	
occurrences (all)	0	2	
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 30 (3.33%)	3 / 31 (9.68%)	
occurrences (all)	1	4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 March 2015	Active treatment extension was converted to optional; Timing of biomarker-related blood draws was changed to reduce required number of blood draws; The frequency of certain study assessments was reduced, including blood draws, spirometry, FeNO, urinalysis, and patient-reported outcomes; The Week 16 visit during the safety follow-up period was eliminated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

The enrollment was closed, and dosing was terminated in this study following the sponsor’s decision to discontinue development of lebrikizumab. Thus, this study was treated as exploratory (rather than confirmatory).

Notes: