



Clinical trial results:

A Phase III, Randomized, Double-Blind, Placebo-Controlled Study to Assess the Efficacy and Safety of Lebrikizumab in Patients with Uncontrolled Asthma Who Are on Inhaled Corticosteroids and a Second Controller Medication

Summary

EudraCT number	2013-000175-33
Trial protocol	SK DE BE GB HU IT CZ PL ES
Global end of trial date	28 December 2016

Results information

Result version number	v1 (current)
This version publication date	03 January 2018
First version publication date	03 January 2018

Trial information

Trial identification

Sponsor protocol code	GB28688
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01867125
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	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	28 December 2016
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:

Primary purpose of this study is to determine the efficacy and safety of lebrikizumab in subjects with asthma whose disease remains uncontrolled despite daily treatment with inhaled corticosteroid (ICS) therapy and at least one second controller medication. Subjects were randomised in 1:1:1 ratio to receive double-blind treatment with either lebrikizumab ("high" or "low") or placebo, administered subcutaneously (SC) every 4 weeks for 52 weeks, in addition to their standard-of-care therapy. This was followed by a 52-week double-blind active treatment extension. During double-blind active treatment extension period, all subjects received SC injection of lebrikizumab from Week 52 to Week 104. Time on study treatment up to 104 weeks. After study treatment, subjects completed a 20-week safety follow-up.

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy:

a) Inhaled corticosteroids (ICS) therapy at a total daily dose of 500 – 2000 microgram (mcg) of fluticasone propionate dry powder inhaler (DPI) or equivalent for ≥ 6 months prior to Visit 1, with no changes within 4 weeks prior to Visit 1 and no anticipated changes throughout the study. b) Second controller medication (Long-acting β adrenoceptor agonists (LABA), Leukotriene Receptor Antagonists (LTRA), Long-acting muscarinic antagonists (LAMA), or theophylline) for 6 months prior to Visit 1, with no changes within 4 weeks prior to Visit 1 and no anticipated changes throughout the study (except for theophylline dose, which may be adjusted on the basis of theophylline levels).

Evidence for comparator: -

Actual start date of recruitment	25 July 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	Japan: 75
Country: Number of subjects enrolled	Korea, Republic of: 19
Country: Number of subjects enrolled	Czech Republic: 61
Country: Number of subjects enrolled	Hungary: 18
Country: Number of subjects enrolled	Poland: 108
Country: Number of subjects enrolled	Romania: 18
Country: Number of subjects enrolled	Russian Federation: 101
Country: Number of subjects enrolled	Serbia: 2
Country: Number of subjects enrolled	Slovakia: 30
Country: Number of subjects enrolled	Turkey: 14
Country: Number of subjects enrolled	Ukraine: 81

Country: Number of subjects enrolled	Argentina: 54
Country: Number of subjects enrolled	Chile: 14
Country: Number of subjects enrolled	Colombia: 3
Country: Number of subjects enrolled	Mexico: 9
Country: Number of subjects enrolled	Canada: 16
Country: Number of subjects enrolled	United States: 312
Country: Number of subjects enrolled	Australia: 8
Country: Number of subjects enrolled	Belgium: 10
Country: Number of subjects enrolled	Spain: 12
Country: Number of subjects enrolled	France: 16
Country: Number of subjects enrolled	United Kingdom: 5
Country: Number of subjects enrolled	Israel: 48
Country: Number of subjects enrolled	Italy: 7
Country: Number of subjects enrolled	New Zealand: 6
Country: Number of subjects enrolled	South Africa: 34
Worldwide total number of subjects	1081
EEA total number of subjects	285

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	918
From 65 to 84 years	163
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects with asthma, whose disease remained uncontrolled despite daily treatment with inhaled corticosteroid (ICS) therapy and at least one second controller medication, were recruited in 26 countries.

Pre-assignment

Screening details:

Subject randomisation was stratified by baseline serum periostin level, history of asthma exacerbations within the last 12 months, baseline asthma medications and country.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Subjects received SC injection of lebrikizumab matching placebo every 4 weeks for 52 weeks during the placebo-controlled period. Subjects then completed a 20-week safety follow-up.

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

Dosage and administration details:

Subjects received lebrikizumab matching placebo by SC injection every 4 weeks.

Arm title	Placebo/Lebrikizumab (37.5 mg)
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Arm description:

Subjects received SC injection of lebrikizumab matching placebo every 4 weeks for 52 weeks during the placebo-controlled period followed by SC injection of lebrikizumab at 37.5 mg for another 52 weeks during the active treatment extension period. After study treatment, subjects completed a 20-week safety follow-up.

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:

Subjects received 37.5 mg lebrikizumab by SC injection every 4 weeks

Arm title	Placebo/Lebrikizumab (125 mg)
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Arm description:

Subjects received SC injection of lebrikizumab matching placebo every 4 weeks for 52 weeks during the placebo-controlled period followed by SC injection of lebrikizumab at 125 mg for another 52 weeks during active treatment extension period. After study treatment, subjects completed a 20-week safety follow-up.

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:

Subjects received 125 mg lebrikizumab by SC injection every 4 weeks

Arm title	Lebrikizumab (37.5 mg)
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Arm description:

Subjects received SC injection of lebrikizumab (37.5 mg) every 4 weeks for 104 weeks. After study treatment, subjects completed a 20-week safety follow-up.

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:

Subjects received 37.5 mg lebrikizumab by SC injection every 4 weeks

Arm title	Lebrikizumab (125 mg)
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Arm description:

Subjects received SC injection of lebrikizumab (125 milligrams [mg]) every 4 weeks for 104 weeks. After study treatment, subjects completed a 20-week safety follow-up.

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:

Subjects received 125 mg lebrikizumab by SC injection every 4 weeks.

Number of subjects in period 1	Placebo	Placebo/Lebrikizumab (37.5 mg)	Placebo/Lebrikizumab (125 mg)
Started	46	159	157
Completed	10	139	139
Not completed	36	20	18
Physician decision	2	1	-
Non-Compliance	-	2	-
Withdrawal By Subject	22	13	15
Adverse Event	5	-	2
Other	1	2	-
Death	1	-	-
Lost to follow-up	4	2	1
Lack of efficacy	1	-	-

Number of subjects in period 1	Lebrikizumab (37.5 mg)	Lebrikizumab (125 mg)
Started	360	359
Completed	302	285
Not completed	58	74
Physician decision	4	1
Non-Compliance	1	3
Withdrawal By Subject	34	56
Adverse Event	5	6
Other	6	2
Death	-	-
Lost to follow-up	6	4
Lack of efficacy	2	2

Baseline characteristics

Reporting groups

Reporting group title	OVERALL PERIOD
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Reporting group description: -

Reporting group values	OVERALL PERIOD	Total	
Number of subjects	1081	1081	
Age Categorical Units: Subjects			
Age Continuous Units: years arithmetic mean standard deviation	51.2 ± 12.6	-	
Gender Categorical Units: Subjects			
Female	713	713	
Male	368	368	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Subjects received SC injection of lebrikizumab matching placebo every 4 weeks for 52 weeks during the placebo-controlled period. Subjects then completed a 20-week safety follow-up.	
Reporting group title	Placebo/Lebrikizumab (37.5 mg)
Reporting group description: Subjects received SC injection of lebrikizumab matching placebo every 4 weeks for 52 weeks during the placebo-controlled period followed by SC injection of lebrikizumab at 37.5 mg for another 52 weeks during the active treatment extension period. After study treatment, subjects completed a 20-week safety follow-up.	
Reporting group title	Placebo/Lebrikizumab (125 mg)
Reporting group description: Subjects received SC injection of lebrikizumab matching placebo every 4 weeks for 52 weeks during the placebo-controlled period followed by SC injection of lebrikizumab at 125 mg for another 52 weeks during active treatment extension period. After study treatment, subjects completed a 20-week safety follow-up.	
Reporting group title	Lebrikizumab (37.5 mg)
Reporting group description: Subjects received SC injection of lebrikizumab (37.5 mg) every 4 weeks for 104 weeks. After study treatment, subjects completed a 20-week safety follow-up.	
Reporting group title	Lebrikizumab (125 mg)
Reporting group description: Subjects received SC injection of lebrikizumab (125 milligrams [mg]) every 4 weeks for 104 weeks. After study treatment, subjects completed a 20-week safety follow-up.	
Subject analysis set title	Biomarker-High, Placebo
Subject analysis set type	Intention-to-treat
Subject analysis set description: Subjects in the biomarker high arms had Periostin levels \geq 50 nanograms per millilitre (ng/mL) or Eosinophil counts \geq 300 cells per microlitre (cells/mcL). Subjects in this arm received SC injection of lebrikizumab matching placebo every 4 weeks for 52 weeks during the placebo-controlled period (Period 1).	
Subject analysis set title	Biomarker-High, Lebrikizumab 37.5 mg
Subject analysis set type	Intention-to-treat
Subject analysis set description: Subjects in the biomarker high arms had Periostin levels \geq 50 ng/mL or Eosinophil counts \geq 300 cells/mcL. Subjects in this arm received SC injection of lebrikizumab (37.5 mg) every 4 weeks for 52 weeks during the placebo-controlled period (Period 1).	
Subject analysis set title	Biomarker-High, Lebrikizumab 125 mg
Subject analysis set type	Intention-to-treat
Subject analysis set description: Subjects in the biomarker high arms had Periostin levels \geq 50 ng/mL or Eosinophil counts \geq 300 cells/mcL. Subjects in this arm received SC injection of lebrikizumab (125 mg) every 4 weeks for 52 weeks during the placebo-controlled period (Period 1).	
Subject analysis set title	Biomarker-Low, Placebo
Subject analysis set type	Intention-to-treat
Subject analysis set description: Subjects in the biomarker low arms had Periostin levels $<$ 50 ng/mL and Eosinophils $<$ 300 cells/mcL. Subjects in this arm received SC injection of lebrikizumab matching placebo every 4 weeks for 52 weeks during the placebo-controlled period (Period 1).	
Subject analysis set title	Biomarker-Low, Lebrikizumab 37.5 mg
Subject analysis set type	Intention-to-treat
Subject analysis set description: Subjects in the biomarker low arms had Periostin levels $<$ 50 ng/mL and Eosinophils $<$ 300 cells/mcL.	

Subjects in this arm received SC injection of lebrikizumab (37.5 mg) every 4 weeks for 52 weeks during the placebo-controlled period (Period 1).

Subject analysis set title	Biomarker-Low, Lebrikizumab 125 mg
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Subjects in the biomarker low arms had Periostin levels < 50 ng/mL and Eosinophils < 300 cells/mcL. Subjects in this arm received SC injection of lebrikizumab (125 mg) every 4 weeks for 52 weeks during the placebo-controlled period (Period 1).	

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

End point title	Rate of Asthma Exacerbations During the 52-Week Placebo-Controlled Period
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 hospitalisation. 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 one dose of IV or IM corticosteroids. Reported is the rate of asthma exacerbations during the 52-week placebo-controlled period. ITT population included all subjects randomised in the study.	
End point type	Primary
End point timeframe:	
Baseline up to 52 weeks	

End point values	Biomarker-High, Placebo	Biomarker-High, Lebrikizumab 37.5 mg	Biomarker-High, Lebrikizumab 125 mg	Biomarker-Low, Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	256	251	255	106
Units: Exacerbation rate				
number (not applicable)	0.95	0.46	0.66	0.60

End point values	Biomarker-Low, Lebrikizumab 37.5 mg	Biomarker-Low, Lebrikizumab 125 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	109	104		
Units: Exacerbation rate				
number (not applicable)	0.33	0.44		

Statistical analyses

Statistical analysis title	High: Lebrikizumab 125 mg vs Placebo
Statistical analysis description:	
Adjusted exacerbation rate ratios are estimates 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, geographic region and a 3-level categorical variable (periostin high and eosinophil high, periostin high and eosinophil low, periostin low and eosinophil high).

Comparison groups	Biomarker-High, Placebo v Biomarker-High, Lebrikizumab 125 mg
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0198
Method	Poisson regression
Parameter estimate	Rate Ratio
Point estimate	0.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.51
upper limit	0.94

Statistical analysis title	High: Lebrikizumab 37.5 mg vs Placebo
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Statistical analysis description:

Adjusted exacerbation rate ratios are estimates 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, geographic region and a 3-level categorical variable (periostin high and eosinophil high, periostin high and eosinophil low, periostin low and eosinophil high).

Comparison groups	Biomarker-High, Placebo v Biomarker-High, Lebrikizumab 37.5 mg
Number of subjects included in analysis	507
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Poisson regression
Parameter estimate	Rate Ratio
Point estimate	0.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.35
upper limit	0.69

Statistical analysis title	Low: Lebrikizumab 125 mg vs Placebo
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Statistical analysis description:

Adjusted exacerbation rate ratios are estimates 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 geographic region.

Comparison groups	Biomarker-Low, Placebo v Biomarker-Low, Lebrikizumab 125 mg
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Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2051
Method	Poisson regression
Parameter estimate	Rate Ratio
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.44
upper limit	1.19

Statistical analysis title	Low: Lebrikizumab 37.5 mg vs Placebo
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Statistical analysis description:

Adjusted exacerbation rate ratios are estimates 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 geographic region.

Comparison groups	Biomarker-Low, Placebo v Biomarker-Low, Lebrikizumab 37.5 mg
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.032
Method	Poisson regression
Parameter estimate	Rate Ratio
Point estimate	0.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.32
upper limit	0.95

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

End point title	Absolute Change From Baseline in Pre-Bronchodilator Forced Expiratory Volume in 1 Second (FEV1) at Week 52
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End point description:

FEV1 is the maximal amount of air, which can be forcefully exhaled in one second. Measurements were performed before use of bronchodilator. Reported is the absolute change from baseline in FEV1 to the end of the placebo-controlled period at Week 52. ITT population included all subjects randomised in the study. The value of "n" signifies the number of subjects evaluated at specific time points.

End point type	Secondary
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End point timeframe:

Baseline, Week 52

End point values	Biomarker-High, Placebo	Biomarker-High, Lebrikizumab 37.5 mg	Biomarker-High, Lebrikizumab 125 mg	Biomarker-Low, Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	228	236	232	94
Units: millilitre (mL)				
arithmetic mean (standard deviation)				
Baseline (n= 256, 251, 255,106, 109, 104)	1795 (± 572)	1785 (± 541)	1779 (± 588)	1982 (± 624)
Change at Week 52 (n= 228, 236, 232, 94, 96, 98)	110 (± 369)	198 (± 412)	224 (± 395)	23 (± 323)

End point values	Biomarker-Low, Lebrikizumab 37.5 mg	Biomarker-Low, Lebrikizumab 125 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	96	98		
Units: millilitre (mL)				
arithmetic mean (standard deviation)				
Baseline (n= 256, 251, 255,106, 109, 104)	1865 (± 509)	1918 (± 517)		
Change at Week 52 (n= 228, 236, 232, 94, 96, 98)	36 (± 282)	153 (± 386)		

Statistical analyses

Statistical analysis title	High: Lebrikizumab 125 mg vs Placebo
Statistical analysis description:	
Estimates are based on a MMRM analysis with an unstructured covariance matrix. Model used absolute change from baseline in pre-bronchodilator FEV1 as response variable and included terms for treatment, visit, treatment visit, baseline FEV1, baseline FEV1 visit, number of asthma exacerbations within last 12 months, baseline asthma medications, geographic region and a 3-level categorical variable (periostin high, eosinophil high, periostin high, eosinophil low, periostin low, eosinophil high).	
Comparison groups	Biomarker-High, Placebo v Biomarker-High, Lebrikizumab 125 mg
Number of subjects included in analysis	460
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0013
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Difference in Adjusted Means
Point estimate	113
Confidence interval	
level	95 %
sides	2-sided
lower limit	44
upper limit	182
Variability estimate	Standard error of the mean
Dispersion value	35

Statistical analysis title	High: Lebrikizumab 37.5 mg vs Placebo
Statistical analysis description:	
Estimates are based on a MMRM analysis with an unstructured covariance matrix. Model used absolute change from baseline in pre-bronchodilator FEV1 as response variable and included terms for treatment, visit, treatment visit, baseline FEV1, baseline FEV1 visit, number of asthma exacerbations within last 12 months, baseline asthma medications, geographic region and a 3-level categorical variable (periostin high, eosinophil high, periostin high, eosinophil low, periostin low, eosinophil high).	
Comparison groups	Biomarker-High, Placebo v Biomarker-High, Lebrikizumab 37.5 mg
Number of subjects included in analysis	464
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0034
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Difference in Adjusted Means
Point estimate	103
Confidence interval	
level	95 %
sides	2-sided
lower limit	34
upper limit	172
Variability estimate	Standard error of the mean
Dispersion value	35

Statistical analysis title	Low: Lebrikizumab 125 mg VS Placebo
Statistical analysis description:	
Estimates are based on a MMRM analysis with an unstructured covariance matrix. Model used absolute change from baseline in pre-bronchodilator FEV1 as response variable and included terms for treatment, visit, treatment visit, baseline FEV1, baseline FEV1 visit, number of asthma exacerbations within last 12 months, baseline asthma medications and geographic region.	
Comparison groups	Biomarker-Low, Placebo v Biomarker-Low, Lebrikizumab 125 mg
Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.007
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Difference in Adjusted Means
Point estimate	126
Confidence interval	
level	95 %
sides	2-sided
lower limit	35
upper limit	217
Variability estimate	Standard error of the mean
Dispersion value	46

Statistical analysis title	Low: Lebrikizumab 37.5 mg vs Placebo
Statistical analysis description:	
Estimates are based on a MMRM analysis with an unstructured covariance matrix. Model used absolute change from baseline in pre-bronchodilator FEV1 as response variable and included terms for treatment, visit, treatment visit, baseline FEV1, baseline FEV1 visit, number of asthma exacerbations within last 12 months, baseline asthma medications and geographic region.	
Comparison groups	Biomarker-Low, Placebo v Biomarker-Low, Lebrikizumab 37.5 mg
Number of subjects included in analysis	190
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7782
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Difference in Adjusted Means
Point estimate	13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-78
upper limit	104
Variability estimate	Standard error of the mean
Dispersion value	46

Secondary: Time to First Asthma Exacerbation During the Placebo-Controlled Period

End point title	Time to First Asthma Exacerbation During the Placebo-Controlled Period
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 hospitalisation. 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 one dose of IV or IM corticosteroids. Reported is the time to first asthma exacerbation during the 52-week placebo-controlled period. ITT population included all subjects randomised in the study. 9999 = not estimable	
End point type	Secondary
End point timeframe:	
Baseline up to 52 weeks	

End point values	Biomarker-High, Placebo	Biomarker-High, Lebrikizumab 37.5 mg	Biomarker-High, Lebrikizumab 125 mg	Biomarker-Low, Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	256	251	255	106
Units: Weeks				
median (confidence interval 95%)	9999 (9999 to 9999)	9999 (9999 to 9999)	9999 (9999 to 9999)	9999 (9999 to 9999)

End point values	Biomarker-Low, Lebrikizumab 37.5 mg	Biomarker-Low, Lebrikizumab 125 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	109	104		
Units: Weeks				
median (confidence interval 95%)	9999 (9999 to 9999)	9999 (9999 to 9999)		

Statistical analyses

Statistical analysis title	High: Lebrikizumab 125 mg vs Placebo
Statistical analysis description:	
Hazard ratios were estimated by Cox regression with the following baseline covariates included as stratification factors: number of asthma exacerbations within the last 12 months, baseline asthma medications, geographic region and a 3-level categorical variable (periostin high and eosinophil high, periostin high and eosinophil low, periostin low and eosinophil high).	
Comparison groups	Biomarker-High, Placebo v Biomarker-High, Lebrikizumab 125 mg
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0068
Method	Cox regression
Parameter estimate	Hazard ratio (HR)
Point estimate	0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.47
upper limit	0.89

Statistical analysis title	High: Lebrikizumab 37.5 mg vs Placebo
Statistical analysis description:	
Hazard ratios were estimated by Cox regression with the following baseline covariates included as stratification factors: number of asthma exacerbations within the last 12 months, baseline asthma medications, geographic region and a 3-level categorical variable (periostin high and eosinophil high, periostin high and eosinophil low, periostin low and eosinophil high).	
Comparison groups	Biomarker-High, Placebo v Biomarker-High, Lebrikizumab 37.5 mg

Number of subjects included in analysis	507
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0007
Method	Cox regression
Parameter estimate	Hazard ratio (HR)
Point estimate	0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.42
upper limit	0.79

Statistical analysis title	Low: Lebrikizumab 125 mg vs Placebo
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Statistical analysis description:

Hazard ratios were estimated by Cox regression with the following baseline covariates included as stratification factors: number of asthma exacerbations within the last 12 months, baseline asthma medications and geographic region.

Comparison groups	Biomarker-Low, Placebo v Biomarker-Low, Lebrikizumab 125 mg
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0435
Method	Cox regression
Parameter estimate	Hazard ratio (HR)
Point estimate	0.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.35
upper limit	0.98

Statistical analysis title	Low: Lebrikizumab 37.5 mg vs Placebo
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Statistical analysis description:

Hazard ratios were estimated by Cox regression with the following baseline covariates included as stratification factors: number of asthma exacerbations within the last 12 months, baseline asthma medications and geographic region.

Comparison groups	Biomarker-Low, Placebo v Biomarker-Low, Lebrikizumab 37.5 mg
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0435
Method	Cox regression
Parameter estimate	Hazard ratio (HR)
Point estimate	0.52

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	0.89

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

End point title	Rate of Urgent Asthma-Related Health Care Utilization (HCU)
End point description: Urgent health care utilization was defined as hospitalisations, emergency department visits, and acute care visits. Reported is the rate of urgent asthma-related health care utilization during the 52-week placebo-controlled period. ITT population included all subjects randomised in the study.	
End point type	Secondary
End point timeframe: Baseline up to Week 52	

End point values	Biomarker-High, Placebo	Biomarker-High, Lebrikizumab 37.5 mg	Biomarker-High, Lebrikizumab 125 mg	Biomarker-Low, Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	256	251	255	106
Units: HCU event rate				
number (not applicable)	0.58	0.24	0.62	0.29

End point values	Biomarker-Low, Lebrikizumab 37.5 mg	Biomarker-Low, Lebrikizumab 125 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	109	104		
Units: HCU event rate				
number (not applicable)	0.41	0.20		

Statistical analyses

Statistical analysis title	High: Lebrikizumab 125 mg vs Placebo
Statistical analysis description: Adjusted health care utilization rates and rate ratios are 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, geographic region and a 3-level categorical variable (periostin high and eosinophil high, periostin high and eosinophil low, periostin low and eosinophil high).	
Comparison groups	Biomarker-High, Placebo v Biomarker-High, Lebrikizumab 125 mg

Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7757
Method	Poisson regression
Parameter estimate	Rate Ratio
Point estimate	1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	1.63

Statistical analysis title	High: Lebrikizumab 37.5 mg vs Placebo
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Statistical analysis description:

Adjusted health care utilization rates and rate ratios are 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, geographic region and a 3-level categorical variable (periostin high and eosinophil high, periostin high and eosinophil low, periostin low and eosinophil high).

Comparison groups	Biomarker-High, Placebo v Biomarker-High, Lebrikizumab 37.5 mg
Number of subjects included in analysis	507
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0023
Method	Poisson regression
Parameter estimate	Rate Ratio
Point estimate	0.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.24
upper limit	0.73

Statistical analysis title	Low: Lebrikizumab 125 mg vs Placebo
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Statistical analysis description:

Adjusted health care utilization rates and rate ratios are 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 geographic region.

Comparison groups	Biomarker-Low, Placebo v Biomarker-Low, Lebrikizumab 125 mg
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Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.31
Method	Poisson regression
Parameter estimate	Rate Ratio
Point estimate	0.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.33
upper limit	1.42

Statistical analysis title	Low: Lebrikizumab 37.5 mg vs Placebo
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Statistical analysis description:

Adjusted health care utilization rates and rate ratios are 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 geographic region.

Comparison groups	Biomarker-Low, Placebo v Biomarker-Low, Lebrikizumab 37.5 mg
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2725
Method	Poisson regression
Parameter estimate	Rate Ratio
Point estimate	1.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	2.6

Secondary: Change From Baseline in Standardized Asthma Quality of Life Questionnaire (AQLQ) Score at Week 52

End point title	Change From Baseline in Standardized Asthma Quality of Life Questionnaire (AQLQ) Score at Week 52
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End point description:

Asthma-specific health-related quality of life was assessed by the overall score of the Standardized AQLQ. The AQLQ is a self-administered test with 32 questions; each with seven possible answers ranging from 1 to 7 with a higher score being more favourable. Total score is calculated as follows: sum of items 1 to 32 divided by 32 for a score range of 1 to 7 with a higher score indicating a better outcome. Reported is the change in AQLQ score from baseline to the end of the placebo-controlled period at Week 52. ITT population included all subjects randomised in the study. The value of "n" signifies the number of subjects evaluated at specific time points.

End point type	Secondary
End point timeframe:	
Baseline, Week 52	

End point values	Biomarker-High, Placebo	Biomarker-High, Lebrikizumab 37.5 mg	Biomarker-High, Lebrikizumab 125 mg	Biomarker-Low, Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	230	236	230	94
Units: Score on scale				
arithmetic mean (standard deviation)				
Baseline (n= 256, 251, 254,106, 109, 104)	4.23 (± 1.04)	4.15 (± 1.04)	4.16 (± 1.04)	4.06 (± 1.12)
Change at Week 52 (n= 230, 236, 230, 94, 97, 99)	0.76 (± 1.01)	0.93 (± 1.12)	0.91 (± 1.19)	0.86 (± 1.09)

End point values	Biomarker-Low, Lebrikizumab 37.5 mg	Biomarker-Low, Lebrikizumab 125 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	97	99		
Units: Score on scale				
arithmetic mean (standard deviation)				
Baseline (n= 256, 251, 254,106, 109, 104)	4.22 (± 1.17)	4.23 (± 0.96)		
Change at Week 52 (n= 230, 236, 230, 94, 97, 99)	0.74 (± 1.12)	0.85 (± 1.11)		

Statistical analyses

Statistical analysis title	High: Lebrikizumab 125 mg vs Placebo
Statistical analysis description:	
Estimates are based on a MMRM analysis with an unstructured covariance matrix. Model used absolute change from baseline in AQLQ(S) score as response variable and included terms for treatment, visit, treatment visit, baseline AQLQ(S), baseline AQLQ(S) visit, number of asthma exacerbations within last 12 months, baseline asthma medications, geographic region and a 3-level categorical variable (periostin high, eosinophil high, periostin high, eosinophil low, periostin low, eosinophil high).	
Comparison groups	Biomarker-High, Placebo v Biomarker-High, Lebrikizumab 125 mg
Number of subjects included in analysis	460
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1533
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Difference in Adjusted Mean
Point estimate	0.13

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.05
upper limit	0.31
Variability estimate	Standard error of the mean
Dispersion value	0.09

Statistical analysis title	High: Lebrikizumab 37.5 mg vs Placebo
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Statistical analysis description:

Estimates are based on a MMRM analysis with an unstructured covariance matrix. Model used absolute change from baseline in AQLQ(S) score as response variable and included terms for treatment, visit, treatment visit, baseline AQLQ(S), baseline AQLQ(S) visit, number of asthma exacerbations within last 12 months, baseline asthma medications, geographic region and a 3-level categorical variable (periostin high, eosinophil high, periostin high, eosinophil low, periostin low, eosinophil high).

Comparison groups	Biomarker-High, Placebo v Biomarker-High, Lebrikizumab 37.5 mg
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1032
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Difference in Adjusted Mean
Point estimate	0.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.03
upper limit	0.32
Variability estimate	Standard error of the mean
Dispersion value	0.09

Statistical analysis title	Low: Lebrikizumab 125 mg vs Placebo
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Statistical analysis description:

Estimates are based on a MMRM analysis with an unstructured covariance matrix. Model used absolute change from baseline in AQLQ(S) score as response variable and included terms for treatment, visit, treatment visit, baseline AQLQ(S), baseline AQLQ(S) visit, number of asthma exacerbations within last 12 months, baseline asthma medications and geographic region.

Comparison groups	Biomarker-Low, Placebo v Biomarker-Low, Lebrikizumab 125 mg
Number of subjects included in analysis	193
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9293
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Difference in Adjusted Mean
Point estimate	0.01

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.26
upper limit	0.28
Variability estimate	Standard error of the mean
Dispersion value	0.138

Statistical analysis title	Low: Lebrikizumab 37.5 mg vs Placebo
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Statistical analysis description:

Estimates are based on a MMRM analysis with an unstructured covariance matrix. Model used absolute change from baseline in AQLQ(S) score as response variable and included terms for treatment, visit, treatment visit, baseline AQLQ(S), baseline AQLQ(S) visit, number of asthma exacerbations within last 12 months, baseline asthma medications and geographic region.

Comparison groups	Biomarker-Low, Placebo v Biomarker-Low, Lebrikizumab 37.5 mg
Number of subjects included in analysis	191
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4015
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Difference in Adjusted Mean
Point estimate	-0.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.38
upper limit	0.15
Variability estimate	Standard error of the mean
Dispersion value	0.137

Secondary: Change from Baseline In Asthma Rescue Medication at Week 52

End point title	Change from Baseline In Asthma Rescue Medication at Week 52
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End point description:

Reported here is the change in the number of puffs or nebulized treatments of asthma rescue medication from baseline to the end of the placebo-controlled period at Week 52. ITT population included all subjects randomised in the study. The value of "n" signifies the number of subjects evaluated at specific time points.

End point type	Secondary
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End point timeframe:

Baseline, Week 52

End point values	Biomarker-High, Placebo	Biomarker-High, Lebrikizumab 37.5 mg	Biomarker-High, Lebrikizumab 125 mg	Biomarker-Low, Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	227	234	232	91
Units: Puffs per day				
arithmetic mean (standard deviation)				
Baseline (n= 256, 251, 254, 106, 109, 103)	3.0 (± 3.8)	2.7 (± 2.9)	3.0 (± 3.9)	3.1 (± 4.1)
Change at Week 52 (n= 227, 234, 232, 91, 96, 94)	-0.5 (± 2.9)	-1.0 (± 2.3)	-1.3 (± 3.3)	-0.9 (± 2.2)

End point values	Biomarker-Low, Lebrikizumab 37.5 mg	Biomarker-Low, Lebrikizumab 125 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	96	94		
Units: Puffs per day				
arithmetic mean (standard deviation)				
Baseline (n= 256, 251, 254, 106, 109, 103)	2.9 (± 2.9)	3.4 (± 5.2)		
Change at Week 52 (n= 227, 234, 232, 91, 96, 94)	-0.7 (± 2.3)	-1.4 (± 4.8)		

Statistical analyses

Statistical analysis title	High: Lebrikizumab 125 mg vs Placebo
Statistical analysis description:	
Estimates are based on MMRM analysis with an unstructured covariance matrix. Model used absolute change from baseline in asthma rescue medication use as response variable and included terms for treatment, visit, treatment visit, baseline rescue medication use/visit, number of asthma exacerbations within last 12 months, baseline asthma medications, geographic region and 3-level categorical variable (periostin high, eosinophil high, periostin high, eosinophil low, periostin low, eosinophil high).	
Comparison groups	Biomarker-High, Placebo v Biomarker-High, Lebrikizumab 125 mg
Number of subjects included in analysis	459
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0121
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Difference in Adjusted Means
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	-0.1
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	High: Lebrikizumab 37.5 mg vs Placebo
Statistical analysis description:	
Estimates are based on MMRM analysis with an unstructured covariance matrix. Model used absolute change from baseline in asthma rescue medication use as response variable and included terms for treatment, visit, treatment visit, baseline rescue medication use/visit, number of asthma exacerbations within last 12 months, baseline asthma medications, geographic region and 3-level categorical variable (periostin high, eosinophil high, periostin high, eosinophil low, periostin low, eosinophil high).	
Comparison groups	Biomarker-High, Placebo v Biomarker-High, Lebrikizumab 37.5 mg
Number of subjects included in analysis	461
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0256
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Difference in Adjusted Means
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	-0.1
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Low: Lebrikizumab 125 mg vs Placebo
Statistical analysis description:	
Estimates are based on MMRM analysis with an unstructured covariance matrix. Model used absolute change from baseline in asthma rescue medication use as response variable and included terms for treatment, visit, treatment visit, baseline rescue medication use/visit, number of asthma exacerbations within last 12 months, baseline asthma medications and geographic region.	
Comparison groups	Biomarker-Low, Placebo v Biomarker-Low, Lebrikizumab 125 mg
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2698
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Difference in Adjusted Means
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.3
Variability estimate	Standard error of the mean
Dispersion value	0.3

Statistical analysis title	Low: Lebrikizumab 37.5 mg vs Placebo
Statistical analysis description:	
Estimates are based on MMRM analysis with an unstructured covariance matrix. Model used absolute change from baseline in asthma rescue medication use as response variable and included terms for treatment, visit, treatment visit, baseline rescue medication use/visit, number of asthma exacerbations within last 12 months, baseline asthma medications and geographic region.	
Comparison groups	Biomarker-Low, Placebo v Biomarker-Low, Lebrikizumab 37.5 mg
Number of subjects included in analysis	187
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.934
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Difference in Adjusted Means
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0.7
Variability estimate	Standard error of the mean
Dispersion value	0.3

Secondary: Change From Baseline in Asthma Control Questionnaire-5 (ACQ-5) Score at Week 52

End point title	Change From Baseline in Asthma Control Questionnaire-5 (ACQ-5) Score at Week 52
End point description:	
The ACQ-5 is test with 5 questions; each with seven possible answers ranging from 0 to 6 with a lower score being more favourable. Total score range is 0 to 30 with a lower score indicating a better outcome. Reported is the change in ACQ-5 score from baseline to the end of the placebo-controlled period at Week 52. ITT population included all subjects randomised in the study. The value of "n" signifies the number of subjects evaluated at specific time points.	
End point type	Secondary
End point timeframe:	
Baseline, Week 52	

End point values	Biomarker-High, Placebo	Biomarker-High, Lebrikizumab 37.5 mg	Biomarker-High, Lebrikizumab 125 mg	Biomarker-Low, Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	229	235	230	93
Units: Score on scale				
arithmetic mean (standard deviation)				

Baseline (n= 256, 251, 255, 106, 109, 104)	2.7 (± 0.7)	2.6 (± 0.7)	2.6 (± 0.7)	2.7 (± 0.9)
Change at Week 52 (n= 229, 235, 230, 93, 97, 99)	-0.8 (± 1.0)	-0.9 (± 1.1)	-0.9 (± 1.1)	-0.8 (± 1.0)

End point values	Biomarker-Low, Lebrikizumab 37.5 mg	Biomarker-Low, Lebrikizumab 125 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	97	99		
Units: Score on scale				
arithmetic mean (standard deviation)				
Baseline (n= 256, 251, 255, 106, 109, 104)	2.6 (± 0.7)	2.6 (± 0.7)		
Change at Week 52 (n= 229, 235, 230, 93, 97, 99)	-0.8 (± 1.0)	-0.8 (± 1.0)		

Statistical analyses

Statistical analysis title	High: Lebrikizumab 125 mg vs Placebo
Statistical analysis description:	
Estimates are based on MMRM analysis with an unstructured covariance matrix. Model used absolute change from baseline in ACQ-5 as response variable and included terms for treatment, visit, treatment visit, baseline ACQ-5, baseline ACQ-5 visit, number of asthma exacerbations within the last 12 months, baseline asthma medications, geographic region and 3-level categorical variable (periostin high, eosinophil high, periostin high, eosinophil low, periostin low, eosinophil high).	
Comparison groups	Biomarker-High, Placebo v Biomarker-High, Lebrikizumab 125 mg
Number of subjects included in analysis	459
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4018
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Difference in Adjusted Mean
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.09

Statistical analysis title	High: Lebrikizumab 37.5 mg vs Placebo
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Statistical analysis description:

Estimates are based on MMRM analysis with an unstructured covariance matrix. Model used absolute change from baseline in ACQ-5 as response variable and included terms for treatment, visit, treatment

visit, baseline ACQ-5, baseline ACQ-5 visit, number of asthma exacerbations within the last 12 months, baseline asthma medications, geographic region and 3-level categorical variable (periostin high, eosinophil high, periostin high, eosinophil low, periostin low, eosinophil high).

Comparison groups	Biomarker-High, Placebo v Biomarker-High, Lebrikizumab 37.5 mg
Number of subjects included in analysis	464
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2341
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Difference in Adjusted Mean
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.09

Statistical analysis title	Low: Lebrikizumab 125 mg vs Placebo
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Statistical analysis description:

Estimates are based on MMRM analysis with an unstructured covariance matrix. Model used absolute change from baseline in ACQ-5 as response variable and included terms for treatment, visit, treatment visit, baseline ACQ-5, baseline ACQ-5 visit, number of asthma exacerbations within the last 12 months, baseline asthma medications and geographic region.

Comparison groups	Biomarker-Low, Placebo v Biomarker-Low, Lebrikizumab 125 mg
Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9293
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Difference in Adjusted Mean
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.3
Variability estimate	Standard error of the mean
Dispersion value	0.13

Statistical analysis title	Low: Lebrikizumab 37.5 mg vs Placebo
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Statistical analysis description:

Estimates are based on MMRM analysis with an unstructured covariance matrix. Model used absolute change from baseline in ACQ-5 as response variable and included terms for treatment, visit, treatment visit, baseline ACQ-5, baseline ACQ-5 visit, number of asthma exacerbations within the last 12 months, baseline asthma medications and geographic region.

Comparison groups	Biomarker-Low, Placebo v Biomarker-Low, Lebrikizumab 37.5 mg
Number of subjects included in analysis	190
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9787
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Difference in Adjusted Mean
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.3
Variability estimate	Standard error of the mean
Dispersion value	0.13

Other pre-specified: Percentage of Subjects With Anti-Therapeutic Antibodies to Lebrikizumab

End point title	Percentage of Subjects With Anti-Therapeutic Antibodies to Lebrikizumab
End point description:	
The safety population included all subjects who received at least one dose of study medication.	
End point type	Other pre-specified
End point timeframe:	
Baseline up to Week 124 (assessed at Baseline, Weeks 4, 12, 24, 36, 52 and safety follow-up [20 weeks] or end of study)	

End point values	Placebo	Placebo/Lebrikizumab (37.5 mg)	Placebo/Lebrikizumab (125 mg)	Lebrikizumab (37.5 mg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43	159	157	359
Units: Percentage of Subjects				
number (not applicable)	0	11.3	10.8	18.7

End point values	Lebrikizumab (125 mg)			
Subject group type	Reporting group			
Number of subjects analysed	358			
Units: Percentage of Subjects				
number (not applicable)	15.1			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects With Adverse Events

End point title	Percentage of Subjects With Adverse Events
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End point description:

An adverse event is any untoward medical occurrence in a subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with the treatment. An adverse event can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a pharmaceutical product, whether or not considered related to the pharmaceutical product. Preexisting conditions which worsen during a study are also considered as adverse events. The safety population included all subjects who received at least one dose of study medication.

End point type	Other pre-specified
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End point timeframe:

Baseline, Week 124

End point values	Placebo	Placebo/Lebriki zumab (37.5 mg)	Placebo/Lebriki zumab (125 mg)	Lebrikizumab (37.5 mg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46	159	157	360
Units: Percentage of Subjects				
number (not applicable)	80.4	91.2	91.7	93.1

End point values	Lebrikizumab (125 mg)			
Subject group type	Reporting group			
Number of subjects analysed	359			
Units: Percentage of Subjects				
number (not applicable)	90.0			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Minimum Serum Concentration (Cmin) of Lebrikizumab

End point title	Minimum Serum Concentration (Cmin) of Lebrikizumab ^[1]
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End point description:

ITT population included all subjects randomised in the study.

End point type	Other pre-specified
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End point timeframe:

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

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: Minimum serum concentration of lebrikizumab was only measured in the arm that received lebrikizumab treatment. Therefore, data are only reported for the lebrikizumab arm.

End point values	Lebrikizumab (37.5 mg)	Lebrikizumab (125 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	360	359		
Units: microgram per millilitre (mcg/mL)				
arithmetic mean (standard deviation)				
Week 4: (n= 360, 359)	2.40 (± 1.67)	8.47 (± 3.61)		
Week 12: (n= 360, 359)	3.78 (± 2.21)	14.1 (± 6.17)		
Week 24: (n=360, 359)	4.38 (± 2.28)	16.4 (± 7.78)		
Week 36: (n=360, 359)	4.87 (± 3.12)	16.7 (± 7.62)		
Week 52: (n= 360, 359)	4.66 (± 2.94)	16.9 (± 8.28)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 124 weeks

Adverse event reporting additional description:

Safety population included all subjects who received at least one dose of study medication.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.1
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Reporting groups

Reporting group title	Placebo
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Reporting group description:

Subjects received SC injection of lebrikizumab matching placebo every 4 weeks for 52 weeks during the placebo-controlled period. Subjects then completed a 20-week safety follow-up.

Reporting group title	Placebo/Lebrikizumab (37.5 mg)
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Reporting group description:

Subjects received SC injection of lebrikizumab matching placebo every 4 weeks for 52 weeks during the placebo-controlled period and then SC injection of lebrikizumab at 37.5 mg for 52 weeks during the active treatment extension period. After study treatment, subjects completed a 20-week safety follow-up.

Reporting group title	Placebo/Lebrikizumab (125 mg)
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Reporting group description:

Subjects received SC injection of lebrikizumab matching placebo every 4 weeks for 52 weeks during the placebo-controlled period and then SC injection of lebrikizumab at 125 mg for 52 weeks during active treatment extension period. After study treatment, subjects completed a 20-week safety follow-up.

Reporting group title	Lebrikizumab (37.5 mg)
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Reporting group description:

Subjects received SC injection of lebrikizumab (37.5 mg) every 4 weeks for 104 weeks. After study treatment, subjects completed a 20-week safety follow-up.

Reporting group title	Lebrikizumab (125 mg)
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Reporting group description:

Subjects received SC injection of lebrikizumab (125 milligrams [mg]) every 4 weeks for 104 weeks. After study treatment, subjects completed a 20-week safety follow-up.

Serious adverse events	Placebo	Placebo/Lebrikizumab (37.5 mg)	Placebo/Lebrikizumab (125 mg)
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 46 (19.57%)	21 / 159 (13.21%)	27 / 157 (17.20%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 46 (0.00%)	1 / 159 (0.63%)	0 / 157 (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

Prostate cancer			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Adenocarcinoma of the cervix			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Basal cell carcinoma			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Colon adenoma			
subjects affected / exposed	0 / 46 (0.00%)	1 / 159 (0.63%)	0 / 157 (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
Lung adenocarcinoma			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Meningioma			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Ovarian cancer			
subjects affected / exposed	0 / 46 (0.00%)	1 / 159 (0.63%)	0 / 157 (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
Uterine leiomyoma			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	1 / 157 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			

Deep vein thrombosis			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Hypertension			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	1 / 157 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive emergency			
subjects affected / exposed	1 / 46 (2.17%)	0 / 159 (0.00%)	0 / 157 (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
Surgical and medical procedures			
Hysterosalpingectomy			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Parathyroidectomy			
subjects affected / exposed	0 / 46 (0.00%)	1 / 159 (0.63%)	0 / 157 (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
Tooth extraction			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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	1 / 46 (2.17%)	0 / 159 (0.00%)	0 / 157 (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
Cervical incompetence			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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

General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	1 / 157 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Papillitis			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	1 / 157 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Metrorrhagia			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Uterine prolapse			
subjects affected / exposed	0 / 46 (0.00%)	1 / 159 (0.63%)	0 / 157 (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
Cystocele			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Endometriosis			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	1 / 157 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cyst ruptured			

subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Cervical polyp			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	1 / 157 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	4 / 46 (8.70%)	3 / 159 (1.89%)	6 / 157 (3.82%)
occurrences causally related to treatment / all	0 / 4	0 / 5	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	1 / 157 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute pulmonary oedema			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Eosinophilic pneumonia			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Hypoxia			
subjects affected / exposed	1 / 46 (2.17%)	0 / 159 (0.00%)	0 / 157 (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
Acute respiratory failure			
subjects affected / exposed	0 / 46 (0.00%)	1 / 159 (0.63%)	0 / 157 (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
Hydrothorax			

subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Organising pneumonia			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Pulmonary oedema			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Psychiatric disorders			
Mental disorder			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Investigations			
Eosinophil count increased			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Weight decreased			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Injury, poisoning and procedural complications			
Tendon rupture			
subjects affected / exposed	0 / 46 (0.00%)	1 / 159 (0.63%)	1 / 157 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle fracture			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	1 / 157 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Fibula fracture			
subjects affected / exposed	0 / 46 (0.00%)	1 / 159 (0.63%)	0 / 157 (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
Hand fracture			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Tibia fracture			
subjects affected / exposed	0 / 46 (0.00%)	2 / 159 (1.26%)	0 / 157 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clavicle fracture			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Contusion			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Fall			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Fascial rupture			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	1 / 157 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot fracture			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Humerus fracture			

subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Incarcerated incisional hernia			
subjects affected / exposed	0 / 46 (0.00%)	1 / 159 (0.63%)	0 / 157 (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 limb fracture			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Meniscus injury			
subjects affected / exposed	0 / 46 (0.00%)	1 / 159 (0.63%)	0 / 157 (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
Muscle rupture			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Radius fracture			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Road traffic accident			
subjects affected / exposed	0 / 46 (0.00%)	1 / 159 (0.63%)	0 / 157 (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
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Thermal burn			

subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Ulna fracture			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Wound dehiscence			
subjects affected / exposed	0 / 46 (0.00%)	1 / 159 (0.63%)	0 / 157 (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
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 46 (2.17%)	0 / 159 (0.00%)	0 / 157 (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
Atrial fibrillation			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	1 / 157 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	1 / 46 (2.17%)	0 / 159 (0.00%)	0 / 157 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	1 / 157 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Atrial flutter			

subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Cardiac failure acute			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Coronary artery stenosis			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Mitral valve incompetence			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Myocardial infarction			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Tachycardia			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 46 (0.00%)	1 / 159 (0.63%)	2 / 157 (1.27%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carotid artery stenosis			
subjects affected / exposed	0 / 46 (0.00%)	1 / 159 (0.63%)	0 / 157 (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
Sciatica			

subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	1 / 157 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carotid sinus syndrome			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Nervous system disorder			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Neuralgia			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Radicular pain			
subjects affected / exposed	0 / 46 (0.00%)	1 / 159 (0.63%)	0 / 157 (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
Visual field defect			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	1 / 157 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Eosinophilia			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 46 (0.00%)	1 / 159 (0.63%)	0 / 157 (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
Gastrointestinal haemorrhage			

subjects affected / exposed	0 / 46 (0.00%)	1 / 159 (0.63%)	0 / 157 (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
Diarrhoea			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Epiplonic appendagitis			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	1 / 157 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric volvulus			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Hiatus hernia			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	1 / 157 (0.64%)
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 inflammation			
subjects affected / exposed	0 / 46 (0.00%)	1 / 159 (0.63%)	0 / 157 (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
Gastroesophageal reflux disease			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Inguinal hernia			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Pancreatitis			

subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Pancreatitis acute			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Umbilical hernia			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Cholecystitis			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Cholecystitis acute			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Jaundice cholestatic			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	1 / 157 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			

subjects affected / exposed	1 / 46 (2.17%)	0 / 159 (0.00%)	0 / 157 (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
Renal and urinary disorders			
Renal aneurysm			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 46 (0.00%)	1 / 159 (0.63%)	2 / 157 (1.27%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Arthropathy			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Osteochondrosis			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Osteonecrosis			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	1 / 157 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	0 / 46 (0.00%)	1 / 159 (0.63%)	0 / 157 (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

Rhabdomyolysis			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	1 / 157 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Scoliosis			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Trigger finger			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 46 (0.00%)	4 / 159 (2.52%)	0 / 157 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pilonidal cyst			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	2 / 157 (1.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 46 (0.00%)	2 / 159 (1.26%)	0 / 157 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Bronchitis			

subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	1 / 157 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	1 / 157 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis			
subjects affected / exposed	0 / 46 (0.00%)	1 / 159 (0.63%)	0 / 157 (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
Escherichia infection			
subjects affected / exposed	0 / 46 (0.00%)	1 / 159 (0.63%)	0 / 157 (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 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Klebsiella sepsis			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Meningitis			
subjects affected / exposed	0 / 46 (0.00%)	1 / 159 (0.63%)	0 / 157 (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
Peritonsillar abscess			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Cellulitis			

subjects affected / exposed	0 / 46 (0.00%)	2 / 159 (1.26%)	1 / 157 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 46 (0.00%)	1 / 159 (0.63%)	0 / 157 (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
Staphylococcal infection			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Tuberculosis of peripheral lymph nodes			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Upper respiratory tract infection			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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
Varicella			
subjects affected / exposed	0 / 46 (0.00%)	0 / 159 (0.00%)	0 / 157 (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 / 46 (0.00%)	0 / 159 (0.00%)	1 / 157 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Lebrikizumab (37.5 mg)	Lebrikizumab (125 mg)	
Total subjects affected by serious adverse events			
subjects affected / exposed	48 / 360 (13.33%)	49 / 359 (13.65%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	1 / 360 (0.28%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma of the cervix			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon adenoma			
subjects affected / exposed	0 / 360 (0.00%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningioma			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cancer			
subjects affected / exposed	0 / 360 (0.00%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Uterine leiomyoma			
subjects affected / exposed	0 / 360 (0.00%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	0 / 360 (0.00%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive emergency			
subjects affected / exposed	0 / 360 (0.00%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Hysterosalpingectomy			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parathyroidectomy			
subjects affected / exposed	0 / 360 (0.00%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth extraction			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			

subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical incompetence			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	2 / 360 (0.56%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Papillitis			
subjects affected / exposed	0 / 360 (0.00%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Metrorrhagia			
subjects affected / exposed	1 / 360 (0.28%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 360 (0.28%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine prolapse			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystocele			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Endometriosis			
subjects affected / exposed	0 / 360 (0.00%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst ruptured			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical polyp			
subjects affected / exposed	0 / 360 (0.00%)	0 / 359 (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	12 / 360 (3.33%)	11 / 359 (3.06%)	
occurrences causally related to treatment / all	0 / 13	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute pulmonary oedema			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eosinophilic pneumonia			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	0 / 360 (0.00%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Acute respiratory failure			
subjects affected / exposed	0 / 360 (0.00%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrothorax			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Organising pneumonia			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Mental disorder			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Eosinophil count increased			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight decreased			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Tendon rupture			

subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand fracture			
subjects affected / exposed	1 / 360 (0.28%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	0 / 360 (0.00%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clavicle fracture			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fascial rupture			

subjects affected / exposed	0 / 360 (0.00%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated incisional hernia			
subjects affected / exposed	0 / 360 (0.00%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus injury			
subjects affected / exposed	0 / 360 (0.00%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle rupture			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			

subjects affected / exposed	0 / 360 (0.00%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thermal burn			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulna fracture			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound dehiscence			
subjects affected / exposed	0 / 360 (0.00%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	2 / 360 (0.56%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 360 (0.00%)	2 / 359 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			

subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis coronary artery			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure acute			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery stenosis			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve incompetence			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Syncope			

subjects affected / exposed	0 / 360 (0.00%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery stenosis			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid sinus syndrome			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorder			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuralgia			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radicular pain			
subjects affected / exposed	0 / 360 (0.00%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Visual field defect			
subjects affected / exposed	0 / 360 (0.00%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Eosinophilia			

subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 360 (0.00%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epiploic appendagitis			
subjects affected / exposed	0 / 360 (0.00%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric volvulus			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiatus hernia			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal inflammation			
subjects affected / exposed	0 / 360 (0.00%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			

subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	3 / 360 (0.83%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice cholestatic			

subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	0 / 360 (0.00%)	0 / 359 (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 / 360 (0.00%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal aneurysm			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (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			
Osteoarthritis			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	1 / 360 (0.28%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthropathy			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteochondrosis			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Osteonecrosis			
subjects affected / exposed	0 / 360 (0.00%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	0 / 360 (0.00%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhabdomyolysis			
subjects affected / exposed	0 / 360 (0.00%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scoliosis			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trigger finger			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	4 / 360 (1.11%)	2 / 359 (0.56%)	
occurrences causally related to treatment / all	0 / 4	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pilonidal cyst			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			

subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	0 / 360 (0.00%)	2 / 359 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 360 (0.00%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis			
subjects affected / exposed	0 / 360 (0.00%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia infection			
subjects affected / exposed	0 / 360 (0.00%)	0 / 359 (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 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella sepsis			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis			

subjects affected / exposed	0 / 360 (0.00%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonsillar abscess			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 360 (0.00%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 360 (0.00%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal infection			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculosis of peripheral lymph nodes			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicella			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			

subjects affected / exposed	0 / 360 (0.00%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 0	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	Placebo/Lebrikizumab (37.5 mg)	Placebo/Lebrikizumab (125 mg)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 46 (56.52%)	134 / 159 (84.28%)	131 / 157 (83.44%)
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	2 / 46 (4.35%)	8 / 159 (5.03%)	4 / 157 (2.55%)
occurrences (all)	2	8	5
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 46 (2.17%)	13 / 159 (8.18%)	8 / 157 (5.10%)
occurrences (all)	1	15	8
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 46 (13.04%)	18 / 159 (11.32%)	12 / 157 (7.64%)
occurrences (all)	9	27	62
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	1 / 46 (2.17%)	1 / 159 (0.63%)	2 / 157 (1.27%)
occurrences (all)	1	1	7
Fatigue			
subjects affected / exposed	3 / 46 (6.52%)	4 / 159 (2.52%)	2 / 157 (1.27%)
occurrences (all)	3	5	2
Injection site pain			
subjects affected / exposed	0 / 46 (0.00%)	4 / 159 (2.52%)	11 / 157 (7.01%)
occurrences (all)	0	9	19
Gastrointestinal disorders			
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 46 (0.00%)	8 / 159 (5.03%)	3 / 157 (1.91%)
occurrences (all)	0	8	3
Respiratory, thoracic and mediastinal			

disorders			
Asthma			
subjects affected / exposed	16 / 46 (34.78%)	83 / 159 (52.20%)	93 / 157 (59.24%)
occurrences (all)	31	251	241
Rhinitis allergic			
subjects affected / exposed	2 / 46 (4.35%)	9 / 159 (5.66%)	11 / 157 (7.01%)
occurrences (all)	2	11	15
Cough			
subjects affected / exposed	1 / 46 (2.17%)	5 / 159 (3.14%)	7 / 157 (4.46%)
occurrences (all)	1	5	9
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 46 (2.17%)	11 / 159 (6.92%)	11 / 157 (7.01%)
occurrences (all)	1	11	12
Arthralgia			
subjects affected / exposed	2 / 46 (4.35%)	12 / 159 (7.55%)	7 / 157 (4.46%)
occurrences (all)	2	13	8
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 46 (4.35%)	39 / 159 (24.53%)	38 / 157 (24.20%)
occurrences (all)	4	64	62
Upper respiratory tract infection			
subjects affected / exposed	3 / 46 (6.52%)	17 / 159 (10.69%)	26 / 157 (16.56%)
occurrences (all)	3	33	45
Bronchitis			
subjects affected / exposed	1 / 46 (2.17%)	23 / 159 (14.47%)	20 / 157 (12.74%)
occurrences (all)	2	30	37
Sinusitis			
subjects affected / exposed	1 / 46 (2.17%)	13 / 159 (8.18%)	13 / 157 (8.28%)
occurrences (all)	1	21	19
Pharyngitis			
subjects affected / exposed	0 / 46 (0.00%)	12 / 159 (7.55%)	13 / 157 (8.28%)
occurrences (all)	0	12	17
Rhinitis			
subjects affected / exposed	0 / 46 (0.00%)	3 / 159 (1.89%)	16 / 157 (10.19%)
occurrences (all)	0	3	28

Influenza			
subjects affected / exposed	1 / 46 (2.17%)	8 / 159 (5.03%)	4 / 157 (2.55%)
occurrences (all)	2	9	4
Urinary tract infection			
subjects affected / exposed	0 / 46 (0.00%)	9 / 159 (5.66%)	9 / 157 (5.73%)
occurrences (all)	0	10	10
Respiratory tract infection viral			
subjects affected / exposed	2 / 46 (4.35%)	8 / 159 (5.03%)	4 / 157 (2.55%)
occurrences (all)	2	10	7
Pneumonia			
subjects affected / exposed	0 / 46 (0.00%)	9 / 159 (5.66%)	2 / 157 (1.27%)
occurrences (all)	0	10	3
Respiratory tract Infection			
subjects affected / exposed	0 / 46 (0.00%)	7 / 159 (4.40%)	8 / 157 (5.10%)
occurrences (all)	0	8	12

Non-serious adverse events	Lebrikizumab (37.5 mg)	Lebrikizumab (125 mg)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	298 / 360 (82.78%)	292 / 359 (81.34%)	
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	11 / 360 (3.06%)	8 / 359 (2.23%)	
occurrences (all)	11	10	
Vascular disorders			
Hypertension			
subjects affected / exposed	15 / 360 (4.17%)	14 / 359 (3.90%)	
occurrences (all)	20	14	
Nervous system disorders			
Headache			
subjects affected / exposed	34 / 360 (9.44%)	29 / 359 (8.08%)	
occurrences (all)	74	116	
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	11 / 360 (3.06%)	18 / 359 (5.01%)	
occurrences (all)	35	75	
Fatigue			

<p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>3 / 360 (0.83%)</p> <p>3</p>	<p>4 / 359 (1.11%)</p> <p>4</p>	
<p>Injection site pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>4 / 360 (1.11%)</p> <p>7</p>	<p>6 / 359 (1.67%)</p> <p>6</p>	
<p>Gastrointestinal disorders</p> <p>Gastrooesophageal reflux disease</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>9 / 360 (2.50%)</p> <p>11</p>	<p>9 / 359 (2.51%)</p> <p>9</p>	
<p>Respiratory, thoracic and mediastinal disorders</p> <p>Asthma</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Rhinitis allergic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Cough</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>156 / 360 (43.33%)</p> <p>395</p> <p>24 / 360 (6.67%)</p> <p>35</p> <p>18 / 360 (5.00%)</p> <p>21</p>	<p>184 / 359 (51.25%)</p> <p>472</p> <p>8 / 359 (2.23%)</p> <p>9</p> <p>18 / 359 (5.01%)</p> <p>20</p>	
<p>Musculoskeletal and connective tissue disorders</p> <p>Back pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Arthralgia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>22 / 360 (6.11%)</p> <p>23</p> <p>15 / 360 (4.17%)</p> <p>19</p>	<p>24 / 359 (6.69%)</p> <p>30</p> <p>20 / 359 (5.57%)</p> <p>25</p>	
<p>Infections and infestations</p> <p>Nasopharyngitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Upper respiratory tract infection</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Bronchitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>72 / 360 (20.00%)</p> <p>117</p> <p>59 / 360 (16.39%)</p> <p>94</p> <p>60 / 360 (16.67%)</p> <p>85</p>	<p>81 / 359 (22.56%)</p> <p>135</p> <p>67 / 359 (18.66%)</p> <p>112</p> <p>48 / 359 (13.37%)</p> <p>84</p>	

Sinusitis		
subjects affected / exposed	26 / 360 (7.22%)	34 / 359 (9.47%)
occurrences (all)	35	51
Pharyngitis		
subjects affected / exposed	20 / 360 (5.56%)	19 / 359 (5.29%)
occurrences (all)	21	20
Rhinitis		
subjects affected / exposed	24 / 360 (6.67%)	20 / 359 (5.57%)
occurrences (all)	42	28
Influenza		
subjects affected / exposed	28 / 360 (7.78%)	21 / 359 (5.85%)
occurrences (all)	34	30
Urinary tract infection		
subjects affected / exposed	15 / 360 (4.17%)	21 / 359 (5.85%)
occurrences (all)	17	26
Respiratory tract infection viral		
subjects affected / exposed	22 / 360 (6.11%)	9 / 359 (2.51%)
occurrences (all)	30	17
Pneumonia		
subjects affected / exposed	8 / 360 (2.22%)	8 / 359 (2.23%)
occurrences (all)	8	8
Respiratory tract Infection		
subjects affected / exposed	11 / 360 (3.06%)	6 / 359 (1.67%)
occurrences (all)	20	9

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 September 2015	The protocol was amended for the following reasons: 1) to update the description of completed clinical trials with lebrikizumab, 2) to add blood eosinophil count in the biomarker objective, 3) to update the biomarker subgroups for analysis to include blood eosinophil count, 4) to update the secondary efficacy endpoints, and 5) to update details of the statistical analyses.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported