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	2013-000176-15
Trial protocol	DE BE GB HU IT CZ ES PL BG SK
Global end of trial date	03 January 2017

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	GB28689

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01868061
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	03 January 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 January 2017
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 as subcutaneous (SC) injection 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. Subjects who were assigned to placebo during the placebo-controlled period of the trial were re-randomised at Week 52 to receive blinded SC lebrikizumab 37.5 milligrams (mg) or 125 mg every 4 weeks 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	29 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: 56
Country: Number of subjects enrolled	Korea, Republic of: 30
Country: Number of subjects enrolled	Bulgaria: 82
Country: Number of subjects enrolled	Czech Republic: 14
Country: Number of subjects enrolled	Hungary: 11
Country: Number of subjects enrolled	Poland: 140
Country: Number of subjects enrolled	Romania: 19
Country: Number of subjects enrolled	Russian Federation: 64
Country: Number of subjects enrolled	Serbia: 10
Country: Number of subjects enrolled	Slovakia: 14

Country: Number of subjects enrolled	Ukraine: 95
Country: Number of subjects enrolled	Argentina: 21
Country: Number of subjects enrolled	Mexico: 20
Country: Number of subjects enrolled	Peru: 42
Country: Number of subjects enrolled	Canada: 20
Country: Number of subjects enrolled	United States: 297
Country: Number of subjects enrolled	Australia: 7
Country: Number of subjects enrolled	Belgium: 13
Country: Number of subjects enrolled	Spain: 21
Country: Number of subjects enrolled	France: 8
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	Israel: 32
Country: Number of subjects enrolled	Italy: 7
Country: Number of subjects enrolled	New Zealand: 8
Country: Number of subjects enrolled	South Africa: 33
Worldwide total number of subjects	1067
EEA total number of subjects	332

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)	909
From 65 to 84 years	158
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	Subject, Investigator

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)

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	RO5490255
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)

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	RO5490255
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)

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	RO5490255
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)

Arm description:

Subjects received SC injection of lebrikizumab (125 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	RO5490255
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	44	156	154
Completed	14	139	140
Not completed	30	17	14
Physician decision	1	-	-
Non-Compliance	2	-	-
Withdrawal By Subject	18	10	8
Adverse Event	3	1	4
Death	-	-	-
Pregnancy	-	-	-
Lost to follow-up	2	5	2
Reason not specified	3	-	-

Lack of efficacy	1	1	-

Number of subjects in period 1	Lebrikizumab (37.5 mg)	Lebrikizumab (125 mg)
Started	356	357
Completed	291	292
Not completed	65	65
Physician decision	2	1
Non-Compliance	-	2
Withdrawal By Subject	51	42
Adverse Event	1	8
Death	1	-
Pregnancy	1	-
Lost to follow-up	6	6
Reason not specified	3	4
Lack of efficacy	-	2

Baseline characteristics

Reporting groups	
Reporting group title	Overall Period

Reporting group description: -

Reporting group values	Overall Period	Total	
Number of subjects	1067	1067	
Age Categorical Units: Subjects			
Age Continuous Units: years arithmetic mean standard deviation	 50.2 ± 13.0	 -	
Gender Categorical Units: Subjects			
Female	658	658	
Male	409	409	

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 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 >/= 50 nanograms per millilitre (ng/mL) and Eosinophil counts >/= 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 >/= 50 ng/mL or Eosinophil counts >/= 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 >/= 50 ng/mL or Eosinophil counts >/= 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	247	257	251	107
Units: Exacerbation rate				
number (not applicable)	0.73	0.54	0.54	0.34

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	99	106		
Units: Exacerbation rate				
number (not applicable)	0.50	0.35		

Statistical analyses

Statistical analysis title	High: Lebrikizumab 125 mg vs Placebo

Statistical analysis description:

Adjusted exacerbation rates and 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	498
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0571
Method	Poisson regression
Parameter estimate	Rate Ratio
Point estimate	0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	1.01

Statistical analysis title	High: Lebrikizumab 37.5 mg vs Placebo

Statistical analysis description:

Adjusted exacerbation rates and 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	504
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.056
Method	Poisson regression
Parameter estimate	Rate Ratio
Point estimate	0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	1.01

Statistical analysis title	Low: Lebrikizumab 125 mg vs Placebo

Statistical analysis description:

Adjusted exacerbation rates and 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

Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9099
Method	Poisson regression
Parameter estimate	Rate Ratio
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	1.78

Statistical analysis title	Low: Lebrikizumab 37.5 mg vs Placebo

Statistical analysis description:

Adjusted exacerbation rates and 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	206
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1462
Method	Poisson regression
Parameter estimate	Rate Ratio
Point estimate	1.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	2.45

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

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.

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	226	241	231	94
Units: millilitre (mL)				
arithmetic mean (standard deviation)				
Baseline (n=247,257,251,107,99,106)	1839 (± 573)	1809 (± 515)	1836 (± 599)	1995 (± 577)
Change at Week 52 (n=226,241,231,94,88,96)	91 (± 383)	184 (± 387)	183 (± 424)	85 (± 422)

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	88	96		
Units: millilitre (mL)				
arithmetic mean (standard deviation)				
Baseline (n=247,257,251,107,99,106)	1954 (± 593)	1862 (± 537)		
Change at Week 52 (n=226,241,231,94,88,96)	98 (± 435)	103 (± 383)		

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	457
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0216
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Difference in Adjusted Means
Point estimate	82
Confidence interval	
level	95 %
sides	2-sided
lower limit	12
upper limit	152
Variability estimate	Standard error of the mean
Dispersion value	36

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	467
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0143
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Difference in Adjusted Means
Point estimate	87
Confidence interval	
level	95 %
sides	2-sided
lower limit	18
upper limit	157
Variability estimate	Standard error of the mean
Dispersion value	36

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	190
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7456
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Difference in Adjusted Means
Point estimate	19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-97
upper limit	135
Variability estimate	Standard error of the mean
Dispersion value	59

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	182
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9907
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Difference in Adjusted Means
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-117
upper limit	118
Variability estimate	Standard error of the mean
Dispersion value	60

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	247	257	251	107
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	99	106		
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	498
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0466
Method	Cox regression
Parameter estimate	Hazard ratio (HR)
Point estimate	0.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	1

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	504
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0987
Method	Cox regression
Parameter estimate	Hazard ratio (HR)
Point estimate	0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.56
upper limit	1.05

Statistical analysis title	Low: 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 and geographic region.

Comparison groups	Biomarker-Low, Placebo v Biomarker-Low, Lebrikizumab 125 mg
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8502
Method	Cox regression
Parameter estimate	Hazard ratio (HR)
Point estimate	0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	1.65

Statistical analysis title	Low: 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 and geographic region.

Comparison groups	Biomarker-Low, Placebo v Biomarker-Low, Lebrikizumab 37.5 mg
Number of subjects included in analysis	206
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2558
Method	Cox regression
Parameter estimate	Hazard ratio (HR)
Point estimate	1.37

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	2.36

Secondary: Rate of Urgent Asthma-Related Health Care Utilization (HCU) During the Placebo-Controlled Period

End point title	Rate of Urgent Asthma-Related Health Care Utilization (HCU) During the Placebo-Controlled Period

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	247	257	251	107
Units: HCU event rate				
number (not applicable)	0.45	0.35	0.42	0.30

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	99	106		
Units: HCU event rate				
number (not applicable)	0.56	0.40		

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	498
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7394
Method	Poisson regression
Parameter estimate	Rate Ratio
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	1.41

Statistical analysis title	High: Lebrikizumab 37.5 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 37.5 mg
Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2612
Method	Poisson regression
Parameter estimate	Rate Ratio
Point estimate	0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	1.21

Statistical analysis title	Low: 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 and geographic region.

Comparison groups	Biomarker-Low, Placebo v Biomarker-Low, Lebrikizumab 125 mg

Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4049
Method	Poisson regression
Parameter estimate	Rate Ratio
Point estimate	1.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	2.71

Statistical analysis title	Low: Lebrikizumab 37.5 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 and geographic region.

Comparison groups	Biomarker-Low, Placebo v Biomarker-Low, Lebrikizumab 37.5 mg
Number of subjects included in analysis	206
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0553
Method	Poisson regression
Parameter estimate	Rate Ratio
Point estimate	1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.99
upper limit	3.65

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

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 1to 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.

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	226	240	229	93
Units: Score on scale				
arithmetic mean (standard deviation)				
Baseline (n=246,256,249,106,99,106)	4.06 (± 0.98)	4.13 (± 0.98)	4.09 (± 0.94)	4.21 (± 1.07)
Change at Week 52 (n=226,240,229,93,87,96)	0.83 (± 1.03)	0.81 (± 1.06)	1.06 (± 1.11)	0.63 (± 1.07)

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	87	96		
Units: Score on scale				
arithmetic mean (standard deviation)				
Baseline (n=246,256,249,106,99,106)	4.08 (± 1.02)	3.98 (± 0.98)		
Change at Week 52 (n=226,240,229,93,87,96)	0.80 (± 1.11)	0.68 (± 1.00)		

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	455
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0057
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Difference in Adjusted Mean
Point estimate	0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.07
upper limit	0.43

Variability estimate	Standard error of the mean
Dispersion value	0.091

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 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	= 0.9227
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	-0.17
upper limit	0.19
Variability estimate	Standard error of the mean
Dispersion value	0.091

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 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	189
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5859
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Difference in Adjusted Mean
Point estimate	-0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.36
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.143

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 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	180
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4807
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	-0.18
upper limit	0.39
Variability estimate	Standard error of the mean
Dispersion value	0.146

Secondary: Change from Baseline In Asthma Rescue Medication at Week 52	
End point title	Change from Baseline In Asthma Rescue Medication at Week 52
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.	
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	222	238	225	90
Units: Puffs per day				
arithmetic mean (standard deviation)				
Baseline (n=247,256,250,107,99,105)	3.0 (± 3.0)	3.0 (± 3.5)	3.5 (± 4.5)	3.0 (± 3.0)
Change at Week 52 (n=222,238,225,90,83,93)	-0.4 (± 2.8)	-1.0 (± 2.4)	-1.2 (± 3.0)	-0.3 (± 2.0)

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	83	93		
Units: Puffs per day				
arithmetic mean (standard deviation)				
Baseline (n=247,256,250,107,99,105)	2.9 (± 2.4)	2.7 (± 2.3)		
Change at Week 52 (n=222,238,225,90,83,93)	-0.7 (± 1.6)	-0.5 (± 1.5)		

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	447
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0099
Method	Mixed Model Repeated Measures
Parameter estimate	Difference in Adjusted Means
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
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	460
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0451
Method	Mixed Model Repeated Measures
Parameter estimate	Difference in Adjusted Means
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	0
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	183
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5236
Method	Mixed Model Repeated Measures
Parameter estimate	Difference in Adjusted Means
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0.3
Variability estimate	Standard error of the mean
Dispersion value	0.2

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	173
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1851
Method	Mixed Model Repeated Measures
Parameter estimate	Difference in Adjusted Means
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.2

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.

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	224	240	230	93
Units: Score on scale				
arithmetic mean (standard deviation)				
Baseline (n=246,256,250,106,99,106)	2.8 (± 0.7)	2.7 (± 0.7)	2.7 (± 0.7)	2.7 (± 0.7)
Change at Week 52 (n=224,240,230,93,87,96)	-0.8 (± 1.0)	-0.8 (± 1.0)	-1.0 (± 1.1)	-0.7 (± 0.9)

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	87	96		
Units: Score on scale				

arithmetic mean (standard deviation)				
Baseline (n=246,256,250,106,99,106)	2.8 (± 0.8)	2.8 (± 0.7)		
Change at Week 52 (n=224,240,230,93,87,96)	-0.8 (± 1.0)	-0.7 (± 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	454
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.097
Method	Mixed Model Repeated Measures
Parameter estimate	Difference in Adjusted Mean
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	0.09

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 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	= 0.9071
Method	Mixed Model Repeated Measures
Parameter estimate	Difference in Adjusted Mean
Point estimate	0

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.09

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 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	189
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8885
Method	Mixed Model Repeated Measures
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

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	180
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3466
Method	Mixed Model Repeated Measures
Parameter estimate	Difference in Adjusted Mean
Point estimate	-0.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.14

Secondary: Percentage of Subjects With Adverse Events

End point title	Percentage of Subjects With Adverse Events

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	Secondary

End point timeframe:

Baseline, Week 124

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	44[1]	155	154	356
Units: Percentage of subjects				
number (not applicable)	71.1	90.3	85.1	82.0

Notes:

[1] - Safety population actual n=45 due to transfer of subject from other arm.

End point values	Lebrikizumab (125 mg)			
Subject group type	Reporting group			
Number of subjects analysed	357			
Units: Percentage of subjects				
number (not applicable)	83.2			

Statistical analyses

No statistical analyses for this end point

Secondary: 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	Secondary

End point timeframe:

Baseline up to Week 124 (assessed at Baseline, Weeks 4, 12, 24, 36, 52 and Safety Follow-up Week 20 [or end of the 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	44[2]	155	154	354
Units: Percentage of subjects				
number (not applicable)	0	11.6	8.4	16.1

Notes:

[2] - Safety population n=45 for this arm due to transfer from other arm.

End point values	Lebrikizumab (125 mg)			
Subject group type	Reporting group			
Number of subjects analysed	356			
Units: Percentage of subjects				
number (not applicable)	14.0			

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum Serum Concentration (Cmin) of Lebrikizumab

End point title	Minimum Serum Concentration (Cmin) of Lebrikizumab[3]

End point description:

ITT population included all subjects randomised in the study. 9999 = not reportable (when more than one third of values were lower than reportable, which was set to 0.045 mcg/mL).

End point type	Secondary

End point timeframe:

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

Notes:

[3] - 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	348	344		
Units: microgram per millilitre (mcg/mL)				
arithmetic mean (standard deviation)				
Week 4 (n=1, 0, 348, 344)	2.74 (± 2.25)	8.67 (± 3.82)		
Week 12 (n=0, 1, 339, 342)	4.44 (± 2.96)	15.5 (± 6.60)		
Week 24 (n=0, 0, 327, 335)	4.28 (± 3.06)	16.0 (± 7.73)		
Week 36 (n=0, 2, 325, 322)	4.51 (± 2.81)	17.0 (± 8.86)		
Week 52 (n=0, 0, 320, 314)	4.59 (± 3.15)	17.3 (± 8.80)		

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

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.1

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 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)
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)
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.	

Serious adverse events	Placebo	Placebo/Lebrikizumab (37.5 mg)	Placebo/Lebrikizumab (125 mg)
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 45 (24.44%)	22 / 155 (14.19%)	24 / 154 (15.58%)
number of deaths (all causes)	0	0	1
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 / 45 (0.00%)	1 / 155 (0.65%)	1 / 154 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Colon cancer			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	1 / 154 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	1 / 154 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenocarcinoma gastric			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Bladder neoplasm			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Bowen's disease			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Endometrial cancer			
subjects affected / exposed	1 / 45 (2.22%)	0 / 155 (0.00%)	0 / 154 (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
Gastric cancer			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Lipoma			

subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Lung adenocarcinoma			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	1 / 154 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to lung			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Prostate cancer			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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 cancer			
subjects affected / exposed	1 / 45 (2.22%)	0 / 155 (0.00%)	0 / 154 (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
Vocal cord neoplasm			
subjects affected / exposed	1 / 45 (2.22%)	0 / 155 (0.00%)	0 / 154 (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
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Jugular vein thrombosis			

subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Subclavian vein thrombosis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Varicose vein			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	1 / 154 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Abortion induced			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Abortion threatened			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Ectopic pregnancy			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Imminent abortion			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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	1 / 45 (2.22%)	1 / 155 (0.65%)	1 / 154 (0.65%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			
subjects affected / exposed	1 / 45 (2.22%)	0 / 155 (0.00%)	0 / 154 (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
Cyst			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Drug hypersensitivity			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Sarcoidosis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Reproductive system and breast disorders			
Uterine prolapse			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	1 / 154 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometrial hyperplasia			

subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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 cyst			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	5 / 45 (11.11%)	8 / 155 (5.16%)	4 / 154 (2.60%)
occurrences causally related to treatment / all	0 / 5	0 / 15	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	2 / 45 (4.44%)	0 / 155 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 155 (0.65%)	0 / 154 (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
Dysphonia			
subjects affected / exposed	1 / 45 (2.22%)	0 / 155 (0.00%)	0 / 154 (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
Eosinophilic pneumonia			
subjects affected / exposed	1 / 45 (2.22%)	0 / 155 (0.00%)	0 / 154 (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
Hydrothorax			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	1 / 154 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasal polyps			

subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Pharyngeal inflammation			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Pleural effusion			
subjects affected / exposed	1 / 45 (2.22%)	0 / 155 (0.00%)	0 / 154 (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
Pulmonary fibrosis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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 hilar enlargement			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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 failure			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Status asthmaticus			
subjects affected / exposed	0 / 45 (0.00%)	1 / 155 (0.65%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Acute psychosis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Completed suicide			

subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	1 / 154 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Depression suicidal			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Hallucination			
subjects affected / exposed	1 / 45 (2.22%)	0 / 155 (0.00%)	0 / 154 (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
Product issues			
Device dislocation			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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			
Blood pressure increased			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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			
Foot fracture			
subjects affected / exposed	0 / 45 (0.00%)	1 / 155 (0.65%)	0 / 154 (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
Humerus fracture			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Rib fracture			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	1 / 154 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Upper limb fracture			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Chest injury			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	1 / 154 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	1 / 154 (0.65%)
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 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Hand fracture			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Head injury			
subjects affected / exposed	0 / 45 (0.00%)	1 / 155 (0.65%)	0 / 154 (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
Overdose			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	1 / 154 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Patella fracture			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Scapula fracture			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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			
subjects affected / exposed	0 / 45 (0.00%)	1 / 155 (0.65%)	0 / 154 (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			
Atrial fibrillation			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	1 / 154 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	1 / 154 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	1 / 154 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	1 / 45 (2.22%)	0 / 155 (0.00%)	0 / 154 (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
Cardiac failure congestive			

subjects affected / exposed	1 / 45 (2.22%)	0 / 155 (0.00%)	0 / 154 (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
Cardio-respiratory arrest			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Cardiomyopathy			
subjects affected / exposed	1 / 45 (2.22%)	0 / 155 (0.00%)	0 / 154 (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
Coronary artery disease			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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 insufficiency			
subjects affected / exposed	0 / 45 (0.00%)	1 / 155 (0.65%)	0 / 154 (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
Coronary artery occlusion			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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 / 45 (0.00%)	0 / 155 (0.00%)	1 / 154 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	1 / 154 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Palpitations			

subjects affected / exposed	0 / 45 (0.00%)	1 / 155 (0.65%)	0 / 154 (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
Tachycardia			
subjects affected / exposed	1 / 45 (2.22%)	0 / 155 (0.00%)	0 / 154 (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
Nervous system disorders			
Transient ischaemic attack			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Cerebrovascular accident			
subjects affected / exposed	1 / 45 (2.22%)	0 / 155 (0.00%)	0 / 154 (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
Carotid artery stenosis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	1 / 154 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Memory impairment			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Myoclonus			
subjects affected / exposed	1 / 45 (2.22%)	0 / 155 (0.00%)	0 / 154 (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
Neuropathy peripheral			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Pschyogenic pseudosyncope			

subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Seizure			
subjects affected / exposed	1 / 45 (2.22%)	0 / 155 (0.00%)	0 / 154 (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
Syncope			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Aplastic anaemia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Eosinophilia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Leukocytosis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	1 / 154 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Inguinal hernia			
subjects affected / exposed	0 / 45 (0.00%)	2 / 155 (1.29%)	1 / 154 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Abdominal pain			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Abdominal hernia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Dental cyst			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Dysphagia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	1 / 154 (0.65%)
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 perforation			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Gastritis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	1 / 154 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 45 (0.00%)	1 / 155 (0.65%)	0 / 154 (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
Inguinal hernia strangulated			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Large intestine polyp			

subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Obstruction gastric			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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			
Bile duct stone			
subjects affected / exposed	0 / 45 (0.00%)	1 / 155 (0.65%)	0 / 154 (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
Biliary colic			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	1 / 154 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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			
Angioedema			
subjects affected / exposed	1 / 45 (2.22%)	0 / 155 (0.00%)	0 / 154 (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
Pyoderma gangrenosum			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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

Nephrolithiasis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Renal colic			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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			
Intervertebral disc degeneration			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Intervertebral disc displacement			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Intervertebral disc protrusion			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	1 / 154 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 45 (0.00%)	2 / 155 (1.29%)	0 / 154 (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
Influenza			
subjects affected / exposed	1 / 45 (2.22%)	0 / 155 (0.00%)	0 / 154 (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
Pyelonephritis acute			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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 / 45 (0.00%)	0 / 155 (0.00%)	1 / 154 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 155 (0.65%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Rhinovirus infection			
subjects affected / exposed	1 / 45 (2.22%)	0 / 155 (0.00%)	0 / 154 (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
Tuberculosis			
subjects affected / exposed	1 / 45 (2.22%)	0 / 155 (0.00%)	0 / 154 (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
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	1 / 154 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (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
Glucose tolerance impaired			
subjects affected / exposed	0 / 45 (0.00%)	0 / 155 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Lebrikizumab (37.5 mg)	Lebrikizumab (125 mg)	
Total subjects affected by serious adverse events			
subjects affected / exposed	56 / 356 (15.73%)	57 / 357 (15.97%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 356 (0.00%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer			
subjects affected / exposed	1 / 356 (0.28%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine leiomyoma			
subjects affected / exposed	0 / 356 (0.00%)	1 / 357 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma gastric			
subjects affected / exposed	1 / 356 (0.28%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			
subjects affected / exposed	1 / 356 (0.28%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder neoplasm			
subjects affected / exposed	1 / 356 (0.28%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bowen's disease			
subjects affected / exposed	1 / 356 (0.28%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Endometrial cancer			
subjects affected / exposed	0 / 356 (0.00%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric cancer			
subjects affected / exposed	0 / 356 (0.00%)	1 / 357 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lipoma			
subjects affected / exposed	1 / 356 (0.28%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma			
subjects affected / exposed	0 / 356 (0.00%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to lung			
subjects affected / exposed	1 / 356 (0.28%)	0 / 357 (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	0 / 356 (0.00%)	1 / 357 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine cancer			
subjects affected / exposed	0 / 356 (0.00%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vocal cord neoplasm			
subjects affected / exposed	0 / 356 (0.00%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			

Hypertensive crisis			
subjects affected / exposed	0 / 356 (0.00%)	2 / 357 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	0 / 356 (0.00%)	1 / 357 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jugular vein thrombosis			
subjects affected / exposed	1 / 356 (0.28%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subclavian vein thrombosis			
subjects affected / exposed	1 / 356 (0.28%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicose vein			
subjects affected / exposed	0 / 356 (0.00%)	0 / 357 (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			
Abortion induced			
subjects affected / exposed	1 / 356 (0.28%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	2 / 356 (0.56%)	1 / 357 (0.28%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abortion threatened			
subjects affected / exposed	0 / 356 (0.00%)	1 / 357 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Ectopic pregnancy			
subjects affected / exposed	0 / 356 (0.00%)	1 / 357 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Imminent abortion			
subjects affected / exposed	0 / 356 (0.00%)	1 / 357 (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	1 / 356 (0.28%)	1 / 357 (0.28%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthenia			
subjects affected / exposed	0 / 356 (0.00%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cyst			
subjects affected / exposed	1 / 356 (0.28%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 356 (0.28%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug hypersensitivity			
subjects affected / exposed	1 / 356 (0.28%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sarcoidosis			
subjects affected / exposed	1 / 356 (0.28%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Reproductive system and breast disorders			
Uterine prolapse			
subjects affected / exposed	1 / 356 (0.28%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial hyperplasia			
subjects affected / exposed	0 / 356 (0.00%)	1 / 357 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst			
subjects affected / exposed	0 / 356 (0.00%)	1 / 357 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	18 / 356 (5.06%)	19 / 357 (5.32%)	
occurrences causally related to treatment / all	0 / 25	0 / 23	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	0 / 356 (0.00%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	1 / 356 (0.28%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphonia			
subjects affected / exposed	0 / 356 (0.00%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eosinophilic pneumonia			

subjects affected / exposed	0 / 356 (0.00%)	0 / 357 (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 / 356 (0.00%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasal polyps			
subjects affected / exposed	1 / 356 (0.28%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngeal inflammation			
subjects affected / exposed	1 / 356 (0.28%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 356 (0.00%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary fibrosis			
subjects affected / exposed	1 / 356 (0.28%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary hilar enlargement			
subjects affected / exposed	0 / 356 (0.00%)	1 / 357 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 356 (0.28%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status asthmaticus			

subjects affected / exposed	0 / 356 (0.00%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Acute psychosis			
subjects affected / exposed	1 / 356 (0.28%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Completed suicide			
subjects affected / exposed	0 / 356 (0.00%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression suicidal			
subjects affected / exposed	0 / 356 (0.00%)	1 / 357 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hallucination			
subjects affected / exposed	0 / 356 (0.00%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device dislocation			
subjects affected / exposed	1 / 356 (0.28%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood pressure increased			
subjects affected / exposed	0 / 356 (0.00%)	1 / 357 (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			
Foot fracture			

subjects affected / exposed	1 / 356 (0.28%)	0 / 357 (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	1 / 356 (0.28%)	1 / 357 (0.28%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	0 / 356 (0.00%)	1 / 357 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	0 / 356 (0.00%)	2 / 357 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest injury			
subjects affected / exposed	0 / 356 (0.00%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	0 / 356 (0.00%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			
subjects affected / exposed	1 / 356 (0.28%)	0 / 357 (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 / 356 (0.28%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			

subjects affected / exposed	0 / 356 (0.00%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			
subjects affected / exposed	0 / 356 (0.00%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Patella fracture			
subjects affected / exposed	0 / 356 (0.00%)	1 / 357 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	1 / 356 (0.28%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	1 / 356 (0.28%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scapula fracture			
subjects affected / exposed	0 / 356 (0.00%)	1 / 357 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound			
subjects affected / exposed	0 / 356 (0.00%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 356 (0.28%)	1 / 357 (0.28%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			

subjects affected / exposed	0 / 356 (0.00%)	1 / 357 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 356 (0.28%)	0 / 357 (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 / 356 (0.00%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	0 / 356 (0.00%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	1 / 356 (0.28%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiomyopathy			
subjects affected / exposed	0 / 356 (0.00%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	1 / 356 (0.28%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery insufficiency			
subjects affected / exposed	0 / 356 (0.00%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery occlusion			

subjects affected / exposed	0 / 356 (0.00%)	1 / 357 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve incompetence			
subjects affected / exposed	0 / 356 (0.00%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			
subjects affected / exposed	0 / 356 (0.00%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Palpitations			
subjects affected / exposed	0 / 356 (0.00%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	0 / 356 (0.00%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Transient ischaemic attack			
subjects affected / exposed	2 / 356 (0.56%)	2 / 357 (0.56%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	0 / 356 (0.00%)	1 / 357 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery stenosis			
subjects affected / exposed	0 / 356 (0.00%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Memory impairment			

subjects affected / exposed	0 / 356 (0.00%)	1 / 357 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myoclonus			
subjects affected / exposed	0 / 356 (0.00%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuropathy peripheral			
subjects affected / exposed	0 / 356 (0.00%)	1 / 357 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pschyogenic pseudosyncope			
subjects affected / exposed	0 / 356 (0.00%)	1 / 357 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	0 / 356 (0.00%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 356 (0.28%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Aplastic anaemia			
subjects affected / exposed	0 / 356 (0.00%)	1 / 357 (0.28%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eosinophilia			
subjects affected / exposed	0 / 356 (0.00%)	1 / 357 (0.28%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukocytosis			

subjects affected / exposed	0 / 356 (0.00%)	1 / 357 (0.28%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 356 (0.00%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Inguinal hernia			
subjects affected / exposed	2 / 356 (0.56%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	0 / 356 (0.00%)	2 / 357 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal hernia			
subjects affected / exposed	0 / 356 (0.00%)	1 / 357 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dental cyst			
subjects affected / exposed	0 / 356 (0.00%)	1 / 357 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	0 / 356 (0.00%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric perforation			
subjects affected / exposed	0 / 356 (0.00%)	1 / 357 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			

subjects affected / exposed	0 / 356 (0.00%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 356 (0.00%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia strangulated			
subjects affected / exposed	1 / 356 (0.28%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			
subjects affected / exposed	1 / 356 (0.28%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstruction gastric			
subjects affected / exposed	0 / 356 (0.00%)	1 / 357 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	0 / 356 (0.00%)	1 / 357 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary colic			
subjects affected / exposed	0 / 356 (0.00%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	0 / 356 (0.00%)	1 / 357 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			

Angioedema			
subjects affected / exposed	0 / 356 (0.00%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyoderma gangrenosum			
subjects affected / exposed	1 / 356 (0.28%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	1 / 356 (0.28%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	1 / 356 (0.28%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic			
subjects affected / exposed	1 / 356 (0.28%)	0 / 357 (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			
Intervertebral disc degeneration			
subjects affected / exposed	0 / 356 (0.00%)	1 / 357 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc displacement			
subjects affected / exposed	0 / 356 (0.00%)	1 / 357 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	0 / 356 (0.00%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infections and infestations			
Pneumonia			
subjects affected / exposed	5 / 356 (1.40%)	1 / 357 (0.28%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	1 / 356 (0.28%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	0 / 356 (0.00%)	2 / 357 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	0 / 356 (0.00%)	1 / 357 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 356 (0.00%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	1 / 356 (0.28%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhinovirus infection			
subjects affected / exposed	0 / 356 (0.00%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculosis			
subjects affected / exposed	0 / 356 (0.00%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			

Hyperglycaemia			
subjects affected / exposed	0 / 356 (0.00%)	1 / 357 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus			
subjects affected / exposed	1 / 356 (0.28%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glucose tolerance impaired			
subjects affected / exposed	1 / 356 (0.28%)	0 / 357 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	Placebo/Lebrikizumab (37.5 mg)	Placebo/Lebrikizumab (125 mg)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 45 (53.33%)	117 / 155 (75.48%)	118 / 154 (76.62%)
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 45 (0.00%)	13 / 155 (8.39%)	12 / 154 (7.79%)
occurrences (all)	0	19	16
General disorders and administration site conditions			
Injection site pain			
subjects affected / exposed	3 / 45 (6.67%)	7 / 155 (4.52%)	5 / 154 (3.25%)
occurrences (all)	11	44	21
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 45 (0.00%)	13 / 155 (8.39%)	3 / 154 (1.95%)
occurrences (all)	0	13	3
Nausea			
subjects affected / exposed	2 / 45 (4.44%)	8 / 155 (5.16%)	1 / 154 (0.65%)
occurrences (all)	2	12	1
Respiratory, thoracic and mediastinal disorders			

Asthma			
subjects affected / exposed	14 / 45 (31.11%)	73 / 155 (47.10%)	75 / 154 (48.70%)
occurrences (all)	23	177	211
Cough			
subjects affected / exposed	3 / 45 (6.67%)	8 / 155 (5.16%)	8 / 154 (5.19%)
occurrences (all)	5	11	10
Rhinitis allergic			
subjects affected / exposed	1 / 45 (2.22%)	6 / 155 (3.87%)	14 / 154 (9.09%)
occurrences (all)	2	7	17
Oropharyngeal pain			
subjects affected / exposed	1 / 45 (2.22%)	3 / 155 (1.94%)	8 / 154 (5.19%)
occurrences (all)	1	3	8
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 45 (2.22%)	10 / 155 (6.45%)	9 / 154 (5.84%)
occurrences (all)	1	12	10
Arthralgia			
subjects affected / exposed	1 / 45 (2.22%)	11 / 155 (7.10%)	4 / 154 (2.60%)
occurrences (all)	1	12	4
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	6 / 45 (13.33%)	30 / 155 (19.35%)	41 / 154 (26.62%)
occurrences (all)	10	47	66
Upper respiratory tract infection			
subjects affected / exposed	6 / 45 (13.33%)	23 / 155 (14.84%)	28 / 154 (18.18%)
occurrences (all)	9	35	51
Bronchitis			
subjects affected / exposed	4 / 45 (8.89%)	19 / 155 (12.26%)	22 / 154 (14.29%)
occurrences (all)	5	26	30
Sinusitis			
subjects affected / exposed	2 / 45 (4.44%)	13 / 155 (8.39%)	15 / 154 (9.74%)
occurrences (all)	4	31	34
Pharyngitis			
subjects affected / exposed	2 / 45 (4.44%)	8 / 155 (5.16%)	8 / 154 (5.19%)
occurrences (all)	2	8	12
Acute sinusitis			

subjects affected / exposed	0 / 45 (0.00%)	10 / 155 (6.45%)	7 / 154 (4.55%)
occurrences (all)	0	14	16
Urinary tract infection			
subjects affected / exposed	1 / 45 (2.22%)	4 / 155 (2.58%)	6 / 154 (3.90%)
occurrences (all)	1	5	6
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 45 (0.00%)	4 / 155 (2.58%)	5 / 154 (3.25%)
occurrences (all)	0	5	8
Influenza			
subjects affected / exposed	0 / 45 (0.00%)	6 / 155 (3.87%)	9 / 154 (5.84%)
occurrences (all)	0	6	9

Non-serious adverse events	Lebrikizumab (37.5 mg)	Lebrikizumab (125 mg)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	239 / 356 (67.13%)	249 / 357 (69.75%)	
Nervous system disorders			
Headache			
subjects affected / exposed	29 / 356 (8.15%)	39 / 357 (10.92%)	
occurrences (all)	47	77	
General disorders and administration site conditions			
Injection site pain			
subjects affected / exposed	13 / 356 (3.65%)	16 / 357 (4.48%)	
occurrences (all)	144	92	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	18 / 356 (5.06%)	13 / 357 (3.64%)	
occurrences (all)	22	14	
Nausea			
subjects affected / exposed	9 / 356 (2.53%)	12 / 357 (3.36%)	
occurrences (all)	9	13	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	148 / 356 (41.57%)	146 / 357 (40.90%)	
occurrences (all)	412	376	
Cough			

subjects affected / exposed	18 / 356 (5.06%)	21 / 357 (5.88%)	
occurrences (all)	36	23	
Rhinitis allergic			
subjects affected / exposed	9 / 356 (2.53%)	13 / 357 (3.64%)	
occurrences (all)	11	17	
Oropharyngeal pain			
subjects affected / exposed	11 / 356 (3.09%)	8 / 357 (2.24%)	
occurrences (all)	11	9	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	20 / 356 (5.62%)	19 / 357 (5.32%)	
occurrences (all)	22	21	
Arthralgia			
subjects affected / exposed	24 / 356 (6.74%)	17 / 357 (4.76%)	
occurrences (all)	27	18	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	72 / 356 (20.22%)	60 / 357 (16.81%)	
occurrences (all)	120	101	
Upper respiratory tract infection			
subjects affected / exposed	52 / 356 (14.61%)	64 / 357 (17.93%)	
occurrences (all)	81	121	
Bronchitis			
subjects affected / exposed	44 / 356 (12.36%)	33 / 357 (9.24%)	
occurrences (all)	63	47	
Sinusitis			
subjects affected / exposed	28 / 356 (7.87%)	20 / 357 (5.60%)	
occurrences (all)	36	25	
Pharyngitis			
subjects affected / exposed	21 / 356 (5.90%)	16 / 357 (4.48%)	
occurrences (all)	25	20	
Acute sinusitis			
subjects affected / exposed	14 / 356 (3.93%)	13 / 357 (3.64%)	
occurrences (all)	23	16	
Urinary tract infection			

subjects affected / exposed	18 / 356 (5.06%)	14 / 357 (3.92%)	
occurrences (all)	27	19	
Viral upper respiratory tract infection			
subjects affected / exposed	18 / 356 (5.06%)	13 / 357 (3.64%)	
occurrences (all)	27	14	
Influenza			
subjects affected / exposed	16 / 356 (4.49%)	8 / 357 (2.24%)	
occurrences (all)	16	11	

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 add fractional exhaled nitric oxygen (FeNO) as an exploratory objective, 4) To update the biomarker subgroups for analysis to include blood eosinophil count. Biomarker-high subjects will be defined as subjects with baseline periostin ≥ 50 ng/mL or blood eosinophils ≥ 300 cells/µL, and biomarker-low subjects will be defined as subjects with baseline periostin < 50 ng/mL and blood eosinophils < 300 cells/µL, 5) To update the secondary efficacy endpoints and exploratory endpoints, 6) To update the Medical Monitor to reflect the current medical monitors, 6) To update details of the statistical analyses.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported