Clinical trial results:
A Phase II, Randomized, Double-Blind, Placebo Controlled, Multicenter Trial to Assess the Oral Corticosteroid-Sparing Effect of Lebrikizumab in Patients With Severe Corticosteroid Dependent Asthma

Summary

EudraCT number	2012-000190-24
Trial protocol	GB ES CZ BE SK SI NL PL BG DK
Global end of trial date	20 December 2016

Results information

Result version number	v1 (current)
This version publication date	01 July 2017
First version publication date	01 July 2017

Trial information

Trial identification

Sponsor protocol code	WB28182

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01987492
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001053-PIP01-10
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	17 February 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 December 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objectives of this study were: 1) To evaluate the efficacy of lebrikizumab compared with placebo as measured by the ability of participants to achieve lower daily doses of oral corticosteroids (OCS; prednisone/prednisolone) while maintaining control of their asthma; 2) To evaluate periostin as a predictive biomarker to select participants most likely to receive benefit from lebrikizumab therapy; 3) To evaluate the safety and tolerability of lebrikizumab compared with placebo.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 February 2014
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	Czech Republic: 16
Country: Number of subjects enrolled	Poland: 34
Country: Number of subjects enrolled	Slovakia: 6
Country: Number of subjects enrolled	Slovenia: 5
Country: Number of subjects enrolled	United States: 6
Country: Number of subjects enrolled	Australia: 5
Country: Number of subjects enrolled	Mexico: 6
Country: Number of subjects enrolled	New Zealand: 7
Country: Number of subjects enrolled	United Kingdom: 97
Country: Number of subjects enrolled	Belgium: 5
Country: Number of subjects enrolled	Denmark: 3
Country: Number of subjects enrolled	Spain: 10
Country: Number of subjects enrolled	France: 26
Country: Number of subjects enrolled	Netherlands: 4

Worldwide total number of subjects	230
EEA total number of subjects	206

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)	12
Adults (18-64 years)	190
From 65 to 84 years	28
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 322 participants (including 21 adolescents) were screened and 230 participants (including 12 adolescent participants) were randomized.

Period 1

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

Arms

Are arms mutually exclusive?	No
Arm title	Placebo

Arm description:

Participants received subcutaneous (SC) injection of lebrikizumab matching placebo (2 placebo injections) every 4 weeks (Q4W) for 44 weeks during double-blind placebo controlled (DBPC) period. All participants were followed for safety for 24 weeks after last dose of study drug.

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

Dosage and administration details:

Participants received SC injection of lebrikizumab matching placebo (2 placebo injections) Q4W for 44 weeks during DBPC period.

Arm title	Lebrikizumab 125 mg

Arm description:

Participants received SC injection of lebrikizumab at dose level of 125 milligrams (mg) (1 injection of lebrikizumab 125 mg + 1 placebo injection) Q4W for 44 weeks during DBPC period and then for additional 32 weeks (up to Week 76) in active treatment extension (ATE) period. Following completion of the ATE period, participants who both tolerated and derived benefit from treatment, continued same treatment into optional long-term active-treatment extension (LTE) period (maximum up to 2 years and 10 months). All participants were followed for safety for 24 weeks after last dose of study drug.

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

Dosage and administration details:

Participants received SC injection of lebrikizumab (1 injection of lebrikizumab 125 mg + 1 placebo injection) Q4W for maximum up to 2 years and 10 months.

Arm title	Lebrikizumab 250 mg

Arm description:

Participants received SC injection of lebrikizumab at dose level of 250 mg (2 injections of lebrikizumab 125 mg) Q4W for 44 weeks during DBPC period and then for additional 32 weeks (up to Week 76) in ATE period. Following completion of the ATE period, participants who both tolerated and derived benefit

from treatment, continued same treatment into optional LTE period (maximum up to 2 years and 10 months). All participants were followed for safety for 24 weeks after last dose of study drug.

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

Dosage and administration details:

Participants received SC injection of lebrikizumab (2 injections of lebrikizumab 125 mg) Q4W for maximum up to 2 years and 10 months.

Arm title	Placebo/Lebrikizumab 125 mg

Arm description:

Participants who received 'Placebo' during DBPC period and who were randomized to this group after completion of DBPC period, received SC injection of lebrikizumab at dose level of 125 mg (1 injection of lebrikizumab 125 mg + 1 placebo injection) Q4W for 32 weeks (up to Week 76) in ATE period. Following completion of the ATE period, participants who both tolerated and derived benefit from treatment, continued same treatment into optional LTE period (maximum up to 2 years and 10 months). All participants were followed for safety for 24 weeks after last dose of study drug.

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

Dosage and administration details:

Participants received SC injection of lebrikizumab (1 injection of lebrikizumab 125 mg + 1 placebo injection) Q4W from Week 44 up to maximum 2 years and 10 months.

Arm title	Placebo/Lebrikizumab 250 mg

Arm description:

Participants who received 'Placebo' during DBPC period and who were randomized to this group after completion of DBPC period, received SC injection of lebrikizumab at dose level of 250 mg (2 injections of lebrikizumab 125 mg) Q4W for 32 weeks (up to Week 76) in ATE period. Following completion of the ATE period, participants who both tolerated and derived benefit from treatment, continued same treatment into optional LTE period (maximum up to 2 years and 10 months). All participants were followed for safety for 24 weeks after last dose of study drug.

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

Dosage and administration details:

Participants received SC injection of lebrikizumab (2 injections of lebrikizumab 125 mg) Q4W from Week 44 up to maximum 2 years and 10 months.

Number of subjects in period 1	Placebo	Lebrikizumab 125 mg	Lebrikizumab 250 mg
Started	102	56	72
Completed	48	39	51
Not completed	54	17	21
Consent withdrawn by subject	5	10	16
Physician decision	1	-	1
Non-Compliance	-	1	1
Adverse Event	-	1	-
Transferred to other arm	46	-	-
Unspecified	-	4	-
Study Terminated by Sponsor	1	1	3
Lost to follow-up	1	-	-

Number of subjects in period 1	Placebo/Lebrikizumab 125 mg	Placebo/Lebrikizumab 250 mg
Started	24	22
Completed	18	19
Not completed	6	3
Consent withdrawn by subject	4	2
Physician decision	-	-
Non-Compliance	-	-
Adverse Event	-	-
Transferred to other arm	-	-
Unspecified	1	1
Study Terminated by Sponsor	1	-
Lost to follow-up	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Overall Study

Reporting group description: -

Reporting group values	Overall Study	Total	
Number of subjects	230	230	
Age Categorical Units: Subjects			
Age Continuous Units: years arithmetic mean standard deviation	 50.3 ± 14.2	 -	
Gender Categorical Units: Subjects			
Female	135	135	
Male	95	95	

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

Participants received subcutaneous (SC) injection of lebrikizumab matching placebo (2 placebo injections) every 4 weeks (Q4W) for 44 weeks during double-blind placebo controlled (DBPC) period. All participants were followed for safety for 24 weeks after last dose of study drug.

Reporting group title	Lebrikizumab 125 mg

Reporting group description:

Participants received SC injection of lebrikizumab at dose level of 125 milligrams (mg) (1 injection of lebrikizumab 125 mg + 1 placebo injection) Q4W for 44 weeks during DBPC period and then for additional 32 weeks (up to Week 76) in active treatment extension (ATE) period. Following completion of the ATE period, participants who both tolerated and derived benefit from treatment, continued same treatment into optional long-term active-treatment extension (LTE) period (maximum up to 2 years and 10 months). All participants were followed for safety for 24 weeks after last dose of study drug.

Reporting group title	Lebrikizumab 250 mg

Reporting group description:

Participants received SC injection of lebrikizumab at dose level of 250 mg (2 injections of lebrikizumab 125 mg) Q4W for 44 weeks during DBPC period and then for additional 32 weeks (up to Week 76) in ATE period. Following completion of the ATE period, participants who both tolerated and derived benefit from treatment, continued same treatment into optional LTE period (maximum up to 2 years and 10 months). All participants were followed for safety for 24 weeks after last dose of study drug.

Reporting group title	Placebo/Lebrikizumab 125 mg

Reporting group description:

Participants who received 'Placebo' during DBPC period and who were randomized to this group after completion of DBPC period, received SC injection of lebrikizumab at dose level of 125 mg (1 injection of lebrikizumab 125 mg + 1 placebo injection) Q4W for 32 weeks (up to Week 76) in ATE period. Following completion of the ATE period, participants who both tolerated and derived benefit from treatment, continued same treatment into optional LTE period (maximum up to 2 years and 10 months). All participants were followed for safety for 24 weeks after last dose of study drug.

Reporting group title	Placebo/Lebrikizumab 250 mg

Reporting group description:

Participants who received 'Placebo' during DBPC period and who were randomized to this group after completion of DBPC period, received SC injection of lebrikizumab at dose level of 250 mg (2 injections of lebrikizumab 125 mg) Q4W for 32 weeks (up to Week 76) in ATE period. Following completion of the ATE period, participants who both tolerated and derived benefit from treatment, continued same treatment into optional LTE period (maximum up to 2 years and 10 months). All participants were followed for safety for 24 weeks after last dose of study drug.

Primary: Percent Change From Baseline in Daily OCS Dose at Week 44

End point title	Percent Change From Baseline in Daily OCS Dose at Week 44[1]

End point description:

OCS used in study: prednisone/prednisolone. Participants entered their total daily use of OCS into an electronic diary (eDiary) on a daily basis. The OCS intake since the previous study visit and the prescribed OCS dose for the next 28 days was captured by physician on a dedicated page in the electronic Case Report Form (eCRF). Baseline OCS dose was calculated using the eDiary as average daily dose over 28 days prior to randomization. Post-baseline OCS dose was obtained from the eCRF and calculated as average daily dose over the 28 days preceding the timepoint. Percent change = (post-baseline value - baseline value)/baseline value * 100. Modified intent-to-treat (mITT) adult participant population included all randomized adult participants who received at least one dose of study drug. Here, 'Number of Subjects Analysed'=participants with a valid baseline value and at least one non-missing value at Week 44.

End point type	Primary

End point timeframe:

Baseline (including 28 days prior to Day 1), Week 44 (including 28 days prior to Week 44)

Notes:

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

End point values	Placebo	Lebrikizumab 125 mg	Lebrikizumab 250 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	61	28	44	
Units: percent change				
arithmetic mean (standard deviation)	-43.17 (± 49.2)	-55.78 (± 33.33)	-39.63 (± 51.35)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Mixed model of repeated measures (MMRM) was utilized for analysis. The model used percent change from baseline in daily OCS dose as response and the following covariates: Treatment arm, Mean baseline OCS dose, Baseline 7-item Asthma Control Questionnaire (ACQ-7) score, British Thoracic Society (BTS) with 2 levels (yes/no), Study Week, and a 4-level categorical variable using Periostin and Eosinophil levels as (High/High, High/ Low, Low/High, and Low/Low).

Comparison groups	Placebo v Lebrikizumab 125 mg
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in Adjusted Means
Point estimate	-6.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-27.2
upper limit	14.3
Variability estimate	Standard error of the mean
Dispersion value	10.5

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

MMRM was utilized for analysis. The model used percent change from baseline in daily OCS dose as response and the following covariates: Treatment arm, Mean baseline OCS dose, Baseline ACQ-7 score, BTS with 2 levels (yes/no), Study Week, and a 4-level categorical variable using Periostin and Eosinophil levels as (High/High, High/ Low, Low/High, and Low/Low).

Comparison groups	Placebo v Lebrikizumab 250 mg
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in Adjusted Means
Point estimate	-2.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.7
upper limit	16.3
Variability estimate	Standard error of the mean
Dispersion value	9.34

Secondary: Change From Baseline in Daily OCS Dose at Week 44

End point title	Change From Baseline in Daily OCS Dose at Week 44[2]

End point description:

OCS used in study: prednisone/prednisolone. Participants entered their total daily use of OCS into an eDiary on a daily basis. The OCS intake since the previous study visit and the prescribed OCS dose for the next 28 days was captured by physician on a dedicated page in the eCRF. Baseline OCS dose was calculated using the eDiary as average daily dose over 28 days prior to randomization. Post baseline OCS dose was obtained from the eCRF and calculated as average daily dose over the 28 days preceding the timepoint. Analysis was performed on mITT adult participant population. Here, 'Number of Subjects Analysed' signifies participants with a valid baseline value and 'n' signifies participants with a valid non-missing value at indicated time point, per arm, respectively.

End point type	Secondary

End point timeframe:

Baseline (including 28 days prior to Day 1), Week 44 (including 28 days prior to Week 44)

Notes:

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

End point values	Placebo	Lebrikizumab 125 mg	Lebrikizumab 250 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	96	56	66	
Units: mg				
arithmetic mean (standard deviation)				
Baseline (n=96,56,66)	16.13 (± 7.89)	14.75 (± 6.4)	15.01 (± 7.04)	
Change at Week 44 (n=61,28,44)	-5.89 (± 7.36)	-7.2 (± 5.37)	-5.27 (± 5.95)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

MMRM was utilized for analysis. The model used absolute change from baseline in daily OCS dose as response and the following covariates: Treatment arm, Mean baseline OCS dose, Baseline ACQ-7 score, BTS with 2 levels (yes/no), Study Week, and a 4-level categorical variable using Periostin and Eosinophil levels as (High/High, High/ Low, Low/High, and Low/Low). Actual subjects included in analysis (at Week 44) = 89.

Comparison groups	Placebo v Lebrikizumab 125 mg

Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in Adjusted Means
Point estimate	-1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.3
upper limit	1.4
Variability estimate	Standard error of the mean
Dispersion value	1.43

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

MMRM was utilized for analysis. The model used absolute change from baseline in daily OCS dose as response and the following covariates: Treatment arm, Mean baseline OCS dose, Baseline ACQ-7 score, BTS with 2 levels (yes/no), Study Week, and a 4-level categorical variable using Periostin and Eosinophil levels as (High/High, High/ Low, Low/High, and Low/Low). Actual subjects included in analysis (at Week 44) = 105.

Comparison groups	Placebo v Lebrikizumab 250 mg
Number of subjects included in analysis	162
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in Adjusted Means
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.1
upper limit	1.9
Variability estimate	Standard error of the mean
Dispersion value	1.28

Secondary: Percent Change From Week 12 in Daily OCS Dose at Week 44

End point title	Percent Change From Week 12 in Daily OCS Dose at Week 44[3]

End point description:

OCS used in study: prednisone/prednisolone. Participants entered their total daily use of OCS into an eDiary on a daily basis. The OCS intake since the previous study visit and the prescribed OCS dose for the next 28 days was captured by physician on a dedicated page in the eCRF. OCS dose at a timepoint was obtained from the eCRF and calculated as average daily dose over the 28 days preceding the timepoint. Percent change = (value at Week 44 - value at Week 12)/value at Week 12 * 100. Reported values are adjusted mean values obtained from MMRM analysis. The analysis was performed on mITT adult participant population. Here, 'Number of Subjects Analysed' signifies participants with a valid non-missing value at Week 12 and at Week 44.

End point type	Secondary

End point timeframe:

Week 12 (including 28 days prior to Week 12), Week 44 (including 28 days prior to Week 44)

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: Analysis was planned to be carried out in the indicated arms only

End point values	Placebo	Lebrikizumab 125 mg	Lebrikizumab 250 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	61	28	43	
Units: percent change				
least squares mean (standard error)	-36.3 (± 5.69)	-44 (± 8.47)	-37.8 (± 6.97)	

Statistical analyses

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

MMRM was utilized for analysis. The model used percent change from baseline in daily OCS dose as response and the following covariates: Treatment arm, Mean baseline OCS dose, Baseline ACQ-7 score, BTS with 2 levels (yes/no), Study Week, and a 4-level categorical variable using Periostin and Eosinophil levels as (High/High, High/ Low, Low/High, and Low/Low).

Comparison groups	Placebo v Lebrikizumab 250 mg
Number of subjects included in analysis	104
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in Adjusted Means
Point estimate	-1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.6
upper limit	15.7
Variability estimate	Standard error of the mean
Dispersion value	8.68

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

MMRM was utilized for analysis. The model used percent change from baseline in daily OCS dose as response and the following covariates: Treatment arm, Mean baseline OCS dose, Baseline ACQ-7 score, BTS with 2 levels (yes/no), Study Week, and a 4-level categorical variable using Periostin and Eosinophil levels as (High/High, High/ Low, Low/High, and Low/Low).

Comparison groups	Placebo v Lebrikizumab 125 mg
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in Adjusted Means
Point estimate	-7.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	-27.3
upper limit	11.9
Variability estimate	Standard error of the mean
Dispersion value	9.95

Secondary: Percentage of Participants Who Achieved at Least a 50 Percent (%) Reduction in Their Daily OCS Dose at Week 44 Relative to Baseline

End point title	Percentage of Participants Who Achieved at Least a 50 Percent (%) Reduction in Their Daily OCS Dose at Week 44 Relative to Baseline[4]

End point description:

OCS used in study: prednisone/prednisolone. Participants entered their total daily use of OCS into an eDiary on a daily basis. The OCS intake since the previous study visit and the prescribed OCS dose for the next 28 days was captured by physician on a dedicated page in the eCRF. Baseline OCS dose was calculated using the eDiary as average daily dose over 28 days prior to randomization. Post baseline OCS dose was obtained from the eCRF and calculated as average daily dose over the 28 days preceding the timepoint. The 95% confidence interval (CI) for the percentage was based on normal approximation for binomial proportion. Analysis was performed on mITT adult participant population. Here, 'Number of Subjects Analysed' signifies participants with a valid non-missing baseline value.

End point type	Secondary

End point timeframe:

Baseline (including 28 days prior to Day 1), Week 44 (including 28 days prior to Week 44)

Notes:

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

End point values	Placebo	Lebrikizumab 125 mg	Lebrikizumab 250 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	96	56	66	
Units: percentage of participants				
number (confidence interval 95%)	39.6 (29.8 to 49.4)	30.4 (18.3 to 42.4)	40.9 (29 to 52.8)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The 95% CI for the difference in percentage was based on normal approximation for binomial proportion.

Comparison groups	Placebo v Lebrikizumab 125 mg

Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in Percentage
Point estimate	-9.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.7
upper limit	6.3

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

The 95% CI for the difference in percentage was based on normal approximation for binomial proportion.

Comparison groups	Placebo v Lebrikizumab 250 mg
Number of subjects included in analysis	162
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in Percentage
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14
upper limit	16.7

Secondary: Percentage of Participants Who Either Discontinued OCS Therapy or Achieved an Adrenal Maintenance Dose at Week 44

End point title	Percentage of Participants Who Either Discontinued OCS Therapy or Achieved an Adrenal Maintenance Dose at Week 44[5]

End point description:

Percentage of participants who either discontinued OCS therapy or have achieved an adrenal maintenance dose is reported. Identification of participants achieving adrenal maintenance dose was based on physician assessment recorded in eCRF in the presence of cortisol = 100 nanomoles per liter (nmol/L). The 95% CI for the percentage was based on normal approximation for binomial proportion. Analysis was performed on mITT adult participant population. Here, 'Number of Subjects Analysed' signifies participants with a valid baseline value.

End point type	Secondary

End point timeframe:

Week 44

Notes:

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

End point values	Placebo	Lebrikizumab 125 mg	Lebrikizumab 250 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	96	56	66	
Units: percentage of participants				
number (confidence interval 95%)	11.5 (5.1 to 17.8)	10.7 (2.6 to 18.8)	9.1 (2.2 to 16)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
The 95% CI for the difference in percentage was based on normal approximation for binomial proportion.	
Comparison groups	Placebo v Lebrikizumab 125 mg
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in Percentage
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.1
upper limit	9.6

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
The 95% CI for the difference in percentage was based on normal approximation for binomial proportion.	
Comparison groups	Placebo v Lebrikizumab 250 mg
Number of subjects included in analysis	162
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in Percentage
Point estimate	-2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.8
upper limit	7.1

Secondary: Rate of Asthma Exacerbations During the 44-Week Double-Blind Placebo Controlled (DBPC) Period

End point title	Rate of Asthma Exacerbations During the 44-Week Double-Blind Placebo Controlled (DBPC) Period[6]

End point description:

An asthma exacerbation is defined as new or increased asthma symptoms (including wheeze, cough, dyspnea, chest tightness, and/or night-time awakening due to these symptoms) that lead to treatment with systemic corticosteroids or to hospitalization. Treatment with systemic corticosteroids is defined as treatment with oral, intravenous (IV), or intramuscular (IM) corticosteroids for at least 3 days or an emergency department visit with at least 1 dose of IV or IM corticosteroids. Rate of asthma exacerbation = total number of exacerbation events divided by total follow-up time in patient years. Analysis was performed on mITT adult participant population. Here, 'Number of Subjects Analysed' signifies participants with a valid baseline value.

End point type	Secondary

End point timeframe:

Baseline up to Week 44

Notes:

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

End point values	Placebo	Lebrikizumab 125 mg	Lebrikizumab 250 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	96	56	66	
Units: events per patient year				
number (not applicable)	1.93	1.26	1.58	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Adjusted exacerbation rates and rate ratios were estimated from a Poisson regression model with over-dispersion adjusted for the following covariates in addition to log(patient years) as an offset: Treatment arm, Mean baseline OCS dose, Baseline ACQ-7 score, BTS with 2 levels (yes/no), and a 4-level categorical variable using Periostin and Eosinophil levels as (High/High, High/ Low, Low/High, and Low/Low).

Comparison groups	Placebo v Lebrikizumab 125 mg
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Adjusted Rate Ratio
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	1.36

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Adjusted exacerbation rates and rate ratios were estimated from a Poisson regression model with over-dispersion adjusted for the following covariates in addition to log(patient years) as an offset: Treatment arm, Mean baseline OCS dose, Baseline ACQ-7 score, BTS with 2 levels (yes/no), and a 4-level categorical variable using Periostin and Eosinophil levels as (High/High, High/ Low, Low/High, and

Low/Low).

Comparison groups	Placebo v Lebrikizumab 250 mg
Number of subjects included in analysis	162
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Adjusted Rate Ratio
Point estimate	0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	1.21

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Baseline up to 24 weeks after last dose (up to approximately 2 years and 10 months)

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	Placebo

Reporting group description:

Participants received SC injection of lebrikizumab matching placebo (2 placebo injections) Q4W for 44 weeks during DBPC period. All participants were followed for safety for 24 weeks after last dose of study drug.

Reporting group title	Lebrikizumab 125 mg

Reporting group description:

Participants received SC injection of lebrikizumab at dose level of 125 mg (1 injection of lebrikizumab 125 mg + 1 placebo injection) Q4W for 44 weeks during DBPC period and then for additional 32 weeks (up to Week 76) in ATE period. Following completion of the ATE period, participants who both tolerated and derived benefit from treatment, continued same treatment into optional LTE period (maximum up to 2 years and 10 months). All participants were followed for safety for 24 weeks after last dose of study drug.

Reporting group title	Lebrikizumab 250 mg

Reporting group description:

Participants received SC injection of lebrikizumab at dose level of 250 mg (2 injections of lebrikizumab 125 mg) Q4W for 44 weeks during DBPC period and then for additional 32 weeks (up to Week 76) in ATE period. Following completion of the ATE period, participants who both tolerated and derived benefit from treatment, continued same treatment into optional LTE period (maximum up to 2 years and 10 months). All participants were followed for safety for 24 weeks after last dose of study drug.

Reporting group title	Placebo/Lebrikizumab 125 mg

Reporting group description:

Participants who received 'Placebo' during DBPC period and who were randomized to this group after completion of DBPC period, received SC injection of lebrikizumab at dose level of 125 mg (1 injection of lebrikizumab 125 mg + 1 placebo injection) Q4W for 32 weeks (up to Week 76) in ATE period. Following completion of the ATE period, participants who both tolerated and derived benefit from treatment, continued same treatment into optional LTE period (maximum up to 2 years and 10 months). All participants were followed for safety for 24 weeks after last dose of study drug.

Reporting group title	Placebo/Lebrikizumab 250 mg

Reporting group description:

Participants who received 'Placebo' during DBPC period and who were randomized to this group after completion of DBPC period, received SC injection of lebrikizumab at dose level of 250 mg (2 injections of lebrikizumab 125 mg) Q4W for 32 weeks (up to Week 76) in ATE period. Following completion of the ATE period, participants who both tolerated and derived benefit from treatment, continued same treatment into optional LTE period (maximum up to 2 years and 10 months). All participants were followed for safety for 24 weeks after last dose of study drug.

Serious adverse events	Placebo	Lebrikizumab 125 mg	Lebrikizumab 250 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 56 (25.00%)	6 / 56 (10.71%)	27 / 72 (37.50%)
number of deaths (all causes)	0	1	0
number of deaths resulting from			

adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	0 / 72 (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
Colon adenoma			
subjects affected / exposed	0 / 56 (0.00%)	0 / 56 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemangioma			
subjects affected / exposed	0 / 56 (0.00%)	0 / 56 (0.00%)	0 / 72 (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
Invasive ductal breast carcinoma			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	0 / 72 (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
Invasive lobular breast carcinoma			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	0 / 72 (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
Prostate cancer			
subjects affected / exposed	0 / 56 (0.00%)	0 / 56 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	0 / 72 (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
Temporal arteritis			

subjects affected / exposed	0 / 56 (0.00%)	0 / 56 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	0 / 72 (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
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 56 (0.00%)	1 / 56 (1.79%)	0 / 72 (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
Anaphylactic shock			
subjects affected / exposed	0 / 56 (0.00%)	1 / 56 (1.79%)	0 / 72 (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
Eosinophilic granulomatosis with polyangiitis			
subjects affected / exposed	0 / 56 (0.00%)	1 / 56 (1.79%)	0 / 72 (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
Hypersensitivity			
subjects affected / exposed	0 / 56 (0.00%)	0 / 56 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	7 / 56 (12.50%)	0 / 56 (0.00%)	10 / 72 (13.89%)
occurrences causally related to treatment / all	2 / 17	0 / 0	0 / 18
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vocal cord disorder			

subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	0 / 72 (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	0 / 56 (0.00%)	0 / 56 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 56 (0.00%)	1 / 56 (1.79%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Stridor			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	0 / 72 (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
Psychiatric disorders			
Mania			
subjects affected / exposed	0 / 56 (0.00%)	0 / 56 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Panic attack			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	0 / 72 (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
Injury, poisoning and procedural complications			
Hip fracture			
subjects affected / exposed	0 / 56 (0.00%)	0 / 56 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Humerus fracture			
subjects affected / exposed	0 / 56 (0.00%)	1 / 56 (1.79%)	0 / 72 (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
Meniscus injury			
subjects affected / exposed	0 / 56 (0.00%)	0 / 56 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative renal failure			
subjects affected / exposed	0 / 56 (0.00%)	0 / 56 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	0 / 56 (0.00%)	1 / 56 (1.79%)	0 / 72 (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
Skeletal injury			
subjects affected / exposed	0 / 56 (0.00%)	0 / 56 (0.00%)	0 / 72 (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
Femur fracture			
subjects affected / exposed	0 / 56 (0.00%)	0 / 56 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 56 (0.00%)	0 / 56 (0.00%)	0 / 72 (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
Dysarthria			
subjects affected / exposed	0 / 56 (0.00%)	0 / 56 (0.00%)	0 / 72 (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
Headache			

subjects affected / exposed	0 / 56 (0.00%)	0 / 56 (0.00%)	0 / 72 (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
Migraine			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	0 / 72 (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
Migraine with aura			
subjects affected / exposed	0 / 56 (0.00%)	0 / 56 (0.00%)	0 / 72 (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
Paraesthesia			
subjects affected / exposed	0 / 56 (0.00%)	0 / 56 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 56 (0.00%)	0 / 56 (0.00%)	2 / 72 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 56 (0.00%)	0 / 56 (0.00%)	0 / 72 (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
Intestinal perforation			
subjects affected / exposed	0 / 56 (0.00%)	0 / 56 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Strangulated umbilical hernia			
subjects affected / exposed	0 / 56 (0.00%)	0 / 56 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Umbilical hernia			

subjects affected / exposed	0 / 56 (0.00%)	0 / 56 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 56 (0.00%)	0 / 56 (0.00%)	0 / 72 (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			
Erythema nodosum			
subjects affected / exposed	0 / 56 (0.00%)	0 / 56 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin necrosis			
subjects affected / exposed	0 / 56 (0.00%)	1 / 56 (1.79%)	0 / 72 (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
Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			
subjects affected / exposed	0 / 56 (0.00%)	0 / 56 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spondylolisthesis			
subjects affected / exposed	0 / 56 (0.00%)	0 / 56 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Lower respiratory tract infection			
subjects affected / exposed	0 / 56 (0.00%)	0 / 56 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 56 (0.00%)	0 / 56 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pneumonia			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	0 / 72 (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
Gastroenteritis			
subjects affected / exposed	0 / 56 (0.00%)	0 / 56 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	0 / 72 (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
Meningitis bacterial			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	0 / 72 (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
Wound infection			
subjects affected / exposed	0 / 56 (0.00%)	0 / 56 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 56 (0.00%)	1 / 56 (1.79%)	0 / 72 (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

Serious adverse events	Placebo/Lebrikizumab 125 mg	Placebo/Lebrikizumab 250 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 24 (33.33%)	3 / 22 (13.64%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			

subjects affected / exposed	0 / 24 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon adenoma			
subjects affected / exposed	0 / 24 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemangioma			
subjects affected / exposed	1 / 24 (4.17%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 24 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive lobular breast carcinoma			
subjects affected / exposed	0 / 24 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	0 / 24 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Temporal arteritis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			

Non-cardiac chest pain			
subjects affected / exposed	0 / 24 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 24 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaphylactic shock			
subjects affected / exposed	0 / 24 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eosinophilic granulomatosis with polyangiitis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity			
subjects affected / exposed	0 / 24 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	4 / 24 (16.67%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vocal cord disorder			
subjects affected / exposed	0 / 24 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			

subjects affected / exposed	0 / 24 (0.00%)	0 / 22 (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 / 24 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 24 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stridor			
subjects affected / exposed	0 / 24 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Mania			
subjects affected / exposed	0 / 24 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Panic attack			
subjects affected / exposed	0 / 24 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Hip fracture			
subjects affected / exposed	0 / 24 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	0 / 24 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Meniscus injury			
subjects affected / exposed	0 / 24 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative renal failure			
subjects affected / exposed	1 / 24 (4.17%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	0 / 24 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skeletal injury			
subjects affected / exposed	1 / 24 (4.17%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	0 / 24 (0.00%)	0 / 22 (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			
Dizziness			
subjects affected / exposed	1 / 24 (4.17%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysarthria			
subjects affected / exposed	1 / 24 (4.17%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	1 / 24 (4.17%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine			

subjects affected / exposed	0 / 24 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine with aura			
subjects affected / exposed	0 / 24 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraesthesia			
subjects affected / exposed	1 / 24 (4.17%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	1 / 24 (4.17%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal perforation			
subjects affected / exposed	0 / 24 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Strangulated umbilical hernia			
subjects affected / exposed	1 / 24 (4.17%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			

subjects affected / exposed	1 / 24 (4.17%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Erythema nodosum			
subjects affected / exposed	0 / 24 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin necrosis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			
subjects affected / exposed	0 / 24 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spondylolisthesis			
subjects affected / exposed	1 / 24 (4.17%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Lower respiratory tract infection			
subjects affected / exposed	1 / 24 (4.17%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 24 (4.17%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastroenteritis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	0 / 24 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis bacterial			
subjects affected / exposed	0 / 24 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	0 / 24 (0.00%)	0 / 22 (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 / 24 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	Lebrikizumab 125 mg	Lebrikizumab 250 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	43 / 56 (76.79%)	48 / 56 (85.71%)	62 / 72 (86.11%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 56 (0.00%)	1 / 56 (1.79%)	1 / 72 (1.39%)
occurrences (all)	0	1	1
General disorders and administration site conditions			
Injection site pain			

subjects affected / exposed	1 / 56 (1.79%)	2 / 56 (3.57%)	4 / 72 (5.56%)
occurrences (all)	2	7	7
Fatigue			
subjects affected / exposed	2 / 56 (3.57%)	2 / 56 (3.57%)	4 / 72 (5.56%)
occurrences (all)	3	2	5
Injection site erythema			
subjects affected / exposed	0 / 56 (0.00%)	2 / 56 (3.57%)	3 / 72 (4.17%)
occurrences (all)	0	6	6
Peripheral swelling			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	3 / 72 (4.17%)
occurrences (all)	2	0	3
Oedema peripheral			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	2 / 72 (2.78%)
occurrences (all)	1	0	2
Injection site pruritus			
subjects affected / exposed	0 / 56 (0.00%)	3 / 56 (5.36%)	0 / 72 (0.00%)
occurrences (all)	0	12	0
Administration site pain			
subjects affected / exposed	0 / 56 (0.00%)	0 / 56 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	31 / 56 (55.36%)	38 / 56 (67.86%)	47 / 72 (65.28%)
occurrences (all)	68	104	226
Cough			
subjects affected / exposed	2 / 56 (3.57%)	2 / 56 (3.57%)	6 / 72 (8.33%)
occurrences (all)	2	2	6
Dyspnoea			
subjects affected / exposed	2 / 56 (3.57%)	2 / 56 (3.57%)	1 / 72 (1.39%)
occurrences (all)	2	2	1
Oropharyngeal pain			
subjects affected / exposed	2 / 56 (3.57%)	0 / 56 (0.00%)	2 / 72 (2.78%)
occurrences (all)	2	0	2
Sputum increased			

subjects affected / exposed	2 / 56 (3.57%)	1 / 56 (1.79%)	0 / 72 (0.00%)
occurrences (all)	2	1	0
Dyspnoea exertional			
subjects affected / exposed	0 / 56 (0.00%)	0 / 56 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 56 (1.79%)	1 / 56 (1.79%)	1 / 72 (1.39%)
occurrences (all)	1	1	1
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 56 (0.00%)	0 / 56 (0.00%)	5 / 72 (6.94%)
occurrences (all)	0	0	7
Contusion			
subjects affected / exposed	1 / 56 (1.79%)	1 / 56 (1.79%)	3 / 72 (4.17%)
occurrences (all)	1	1	3
Limb injury			
subjects affected / exposed	0 / 56 (0.00%)	1 / 56 (1.79%)	2 / 72 (2.78%)
occurrences (all)	0	1	2
Muscle strain			
subjects affected / exposed	0 / 56 (0.00%)	0 / 56 (0.00%)	4 / 72 (5.56%)
occurrences (all)	0	0	4
Skin abrasion			
subjects affected / exposed	0 / 56 (0.00%)	0 / 56 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 56 (1.79%)	3 / 56 (5.36%)	1 / 72 (1.39%)
occurrences (all)	1	3	1
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 56 (12.50%)	6 / 56 (10.71%)	13 / 72 (18.06%)
occurrences (all)	8	9	19
Paraesthesia			
subjects affected / exposed	2 / 56 (3.57%)	3 / 56 (5.36%)	2 / 72 (2.78%)
occurrences (all)	3	3	2

Dizziness			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	3 / 72 (4.17%)
occurrences (all)	1	0	7
Lethargy			
subjects affected / exposed	1 / 56 (1.79%)	1 / 56 (1.79%)	1 / 72 (1.39%)
occurrences (all)	1	1	1
Neuralgia			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	0 / 72 (0.00%)
occurrences (all)	1	0	0
Sciatica			
subjects affected / exposed	0 / 56 (0.00%)	1 / 56 (1.79%)	0 / 72 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 56 (1.79%)	1 / 56 (1.79%)	1 / 72 (1.39%)
occurrences (all)	1	1	1
Eye disorders			
Cataract			
subjects affected / exposed	0 / 56 (0.00%)	0 / 56 (0.00%)	4 / 72 (5.56%)
occurrences (all)	0	0	6
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 56 (1.79%)	1 / 56 (1.79%)	5 / 72 (6.94%)
occurrences (all)	1	1	6
Vomiting			
subjects affected / exposed	2 / 56 (3.57%)	1 / 56 (1.79%)	5 / 72 (6.94%)
occurrences (all)	2	1	6
Nausea			
subjects affected / exposed	1 / 56 (1.79%)	2 / 56 (3.57%)	2 / 72 (2.78%)
occurrences (all)	1	2	2
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 56 (0.00%)	2 / 56 (3.57%)	3 / 72 (4.17%)
occurrences (all)	0	2	3
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	2 / 56 (3.57%)	2 / 56 (3.57%)	3 / 72 (4.17%)
occurrences (all)	2	2	8

Erythema			
subjects affected / exposed	0 / 56 (0.00%)	2 / 56 (3.57%)	2 / 72 (2.78%)
occurrences (all)	0	4	2
Pruritus			
subjects affected / exposed	1 / 56 (1.79%)	1 / 56 (1.79%)	1 / 72 (1.39%)
occurrences (all)	7	1	2
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 56 (7.14%)	3 / 56 (5.36%)	10 / 72 (13.89%)
occurrences (all)	5	3	12
Back pain			
subjects affected / exposed	2 / 56 (3.57%)	5 / 56 (8.93%)	6 / 72 (8.33%)
occurrences (all)	2	5	7
Pain in extremity			
subjects affected / exposed	2 / 56 (3.57%)	3 / 56 (5.36%)	3 / 72 (4.17%)
occurrences (all)	3	3	3
Myalgia			
subjects affected / exposed	0 / 56 (0.00%)	1 / 56 (1.79%)	5 / 72 (6.94%)
occurrences (all)	0	1	6
Muscle spasms			
subjects affected / exposed	1 / 56 (1.79%)	1 / 56 (1.79%)	4 / 72 (5.56%)
occurrences (all)	1	1	4
Musculoskeletal chest pain			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	3 / 72 (4.17%)
occurrences (all)	1	0	3
Musculoskeletal pain			
subjects affected / exposed	1 / 56 (1.79%)	0 / 56 (0.00%)	2 / 72 (2.78%)
occurrences (all)	1	0	2
Infections and infestations			
Lower respiratory tract infection			
subjects affected / exposed	6 / 56 (10.71%)	7 / 56 (12.50%)	27 / 72 (37.50%)
occurrences (all)	17	18	65
Nasopharyngitis			
subjects affected / exposed	3 / 56 (5.36%)	8 / 56 (14.29%)	8 / 72 (11.11%)
occurrences (all)	3	8	10
Upper respiratory tract infection			

subjects affected / exposed	4 / 56 (7.14%)	1 / 56 (1.79%)	9 / 72 (12.50%)
occurrences (all)	4	1	15
Sinusitis			
subjects affected / exposed	6 / 56 (10.71%)	5 / 56 (8.93%)	5 / 72 (6.94%)
occurrences (all)	6	5	7
Pharyngitis			
subjects affected / exposed	4 / 56 (7.14%)	4 / 56 (7.14%)	6 / 72 (8.33%)
occurrences (all)	5	4	6
Urinary tract infection			
subjects affected / exposed	1 / 56 (1.79%)	4 / 56 (7.14%)	7 / 72 (9.72%)
occurrences (all)	1	4	8
Bronchitis			
subjects affected / exposed	4 / 56 (7.14%)	9 / 56 (16.07%)	1 / 72 (1.39%)
occurrences (all)	9	17	1
Oral candidiasis			
subjects affected / exposed	4 / 56 (7.14%)	1 / 56 (1.79%)	5 / 72 (6.94%)
occurrences (all)	4	1	5
Viral upper respiratory tract infection			
subjects affected / exposed	2 / 56 (3.57%)	1 / 56 (1.79%)	6 / 72 (8.33%)
occurrences (all)	2	1	8
Gastroenteritis			
subjects affected / exposed	1 / 56 (1.79%)	1 / 56 (1.79%)	1 / 72 (1.39%)
occurrences (all)	1	1	1
Cellulitis			
subjects affected / exposed	0 / 56 (0.00%)	1 / 56 (1.79%)	1 / 72 (1.39%)
occurrences (all)	0	1	1
Tooth abscess			
subjects affected / exposed	0 / 56 (0.00%)	0 / 56 (0.00%)	1 / 72 (1.39%)
occurrences (all)	0	0	1
Vulvovaginal candidiasis			
subjects affected / exposed	1 / 56 (1.79%)	3 / 56 (5.36%)	0 / 72 (0.00%)
occurrences (all)	1	4	0
Conjunctivitis			
subjects affected / exposed	0 / 56 (0.00%)	1 / 56 (1.79%)	0 / 72 (0.00%)
occurrences (all)	0	1	0
Lower respiratory tract infection viral			

subjects affected / exposed	0 / 56 (0.00%)	0 / 56 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Tooth infection			
subjects affected / exposed	0 / 56 (0.00%)	0 / 56 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	3 / 56 (5.36%)	0 / 56 (0.00%)	2 / 72 (2.78%)
occurrences (all)	3	0	2
Hypokalaemia			
subjects affected / exposed	3 / 56 (5.36%)	0 / 56 (0.00%)	1 / 72 (1.39%)
occurrences (all)	4	0	1

Non-serious adverse events	Placebo/Lebrikizumab 125 mg	Placebo/Lebrikizumab 250 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 24 (100.00%)	21 / 22 (95.45%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 24 (4.17%)	3 / 22 (13.64%)	
occurrences (all)	1	3	
General disorders and administration site conditions			
Injection site pain			
subjects affected / exposed	1 / 24 (4.17%)	4 / 22 (18.18%)	
occurrences (all)	2	10	
Fatigue			
subjects affected / exposed	1 / 24 (4.17%)	2 / 22 (9.09%)	
occurrences (all)	2	2	
Injection site erythema			
subjects affected / exposed	1 / 24 (4.17%)	3 / 22 (13.64%)	
occurrences (all)	2	4	
Peripheral swelling			
subjects affected / exposed	1 / 24 (4.17%)	3 / 22 (13.64%)	
occurrences (all)	1	3	
Oedema peripheral			
subjects affected / exposed	1 / 24 (4.17%)	3 / 22 (13.64%)	
occurrences (all)	1	5	

Injection site pruritus			
subjects affected / exposed	1 / 24 (4.17%)	0 / 22 (0.00%)	
occurrences (all)	2	0	
Administration site pain			
subjects affected / exposed	0 / 24 (0.00%)	2 / 22 (9.09%)	
occurrences (all)	0	4	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	22 / 24 (91.67%)	20 / 22 (90.91%)	
occurrences (all)	92	141	
Cough			
subjects affected / exposed	6 / 24 (25.00%)	3 / 22 (13.64%)	
occurrences (all)	8	4	
Dyspnoea			
subjects affected / exposed	2 / 24 (8.33%)	2 / 22 (9.09%)	
occurrences (all)	4	2	
Oropharyngeal pain			
subjects affected / exposed	2 / 24 (8.33%)	2 / 22 (9.09%)	
occurrences (all)	2	2	
Sputum increased			
subjects affected / exposed	3 / 24 (12.50%)	0 / 22 (0.00%)	
occurrences (all)	3	0	
Dyspnoea exertional			
subjects affected / exposed	1 / 24 (4.17%)	2 / 22 (9.09%)	
occurrences (all)	1	2	
Psychiatric disorders			
Depression			
subjects affected / exposed	2 / 24 (8.33%)	0 / 22 (0.00%)	
occurrences (all)	2	0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 24 (0.00%)	5 / 22 (22.73%)	
occurrences (all)	0	7	
Contusion			
subjects affected / exposed	0 / 24 (0.00%)	3 / 22 (13.64%)	
occurrences (all)	0	4	

Limb injury			
subjects affected / exposed	1 / 24 (4.17%)	2 / 22 (9.09%)	
occurrences (all)	1	2	
Muscle strain			
subjects affected / exposed	0 / 24 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Skin abrasion			
subjects affected / exposed	0 / 24 (0.00%)	2 / 22 (9.09%)	
occurrences (all)	0	2	
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 24 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 24 (8.33%)	4 / 22 (18.18%)	
occurrences (all)	4	6	
Paraesthesia			
subjects affected / exposed	0 / 24 (0.00%)	2 / 22 (9.09%)	
occurrences (all)	0	4	
Dizziness			
subjects affected / exposed	1 / 24 (4.17%)	2 / 22 (9.09%)	
occurrences (all)	2	3	
Lethargy			
subjects affected / exposed	2 / 24 (8.33%)	1 / 22 (4.55%)	
occurrences (all)	2	1	
Neuralgia			
subjects affected / exposed	0 / 24 (0.00%)	3 / 22 (13.64%)	
occurrences (all)	0	4	
Sciatica			
subjects affected / exposed	2 / 24 (8.33%)	1 / 22 (4.55%)	
occurrences (all)	2	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 24 (12.50%)	1 / 22 (4.55%)	
occurrences (all)	3	1	
Eye disorders			

Cataract			
subjects affected / exposed	1 / 24 (4.17%)	1 / 22 (4.55%)	
occurrences (all)	1	1	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 24 (8.33%)	3 / 22 (13.64%)	
occurrences (all)	3	3	
Vomiting			
subjects affected / exposed	3 / 24 (12.50%)	1 / 22 (4.55%)	
occurrences (all)	4	1	
Nausea			
subjects affected / exposed	2 / 24 (8.33%)	2 / 22 (9.09%)	
occurrences (all)	2	2	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 24 (0.00%)	2 / 22 (9.09%)	
occurrences (all)	0	2	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 24 (4.17%)	2 / 22 (9.09%)	
occurrences (all)	2	5	
Erythema			
subjects affected / exposed	0 / 24 (0.00%)	2 / 22 (9.09%)	
occurrences (all)	0	2	
Pruritus			
subjects affected / exposed	0 / 24 (0.00%)	3 / 22 (13.64%)	
occurrences (all)	0	3	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 24 (20.83%)	9 / 22 (40.91%)	
occurrences (all)	5	12	
Back pain			
subjects affected / exposed	1 / 24 (4.17%)	4 / 22 (18.18%)	
occurrences (all)	1	5	
Pain in extremity			
subjects affected / exposed	1 / 24 (4.17%)	4 / 22 (18.18%)	
occurrences (all)	2	4	

Myalgia			
subjects affected / exposed	0 / 24 (0.00%)	3 / 22 (13.64%)	
occurrences (all)	0	4	
Muscle spasms			
subjects affected / exposed	1 / 24 (4.17%)	1 / 22 (4.55%)	
occurrences (all)	1	1	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 24 (4.17%)	3 / 22 (13.64%)	
occurrences (all)	1	3	
Musculoskeletal pain			
subjects affected / exposed	2 / 24 (8.33%)	2 / 22 (9.09%)	
occurrences (all)	2	2	
Infections and infestations			
Lower respiratory tract infection			
subjects affected / exposed	11 / 24 (45.83%)	15 / 22 (68.18%)	
occurrences (all)	26	40	
Nasopharyngitis			
subjects affected / exposed	6 / 24 (25.00%)	2 / 22 (9.09%)	
occurrences (all)	10	4	
Upper respiratory tract infection			
subjects affected / exposed	2 / 24 (8.33%)	5 / 22 (22.73%)	
occurrences (all)	2	9	
Sinusitis			
subjects affected / exposed	1 / 24 (4.17%)	3 / 22 (13.64%)	
occurrences (all)	1	3	
Pharyngitis			
subjects affected / exposed	3 / 24 (12.50%)	1 / 22 (4.55%)	
occurrences (all)	3	1	
Urinary tract infection			
subjects affected / exposed	3 / 24 (12.50%)	2 / 22 (9.09%)	
occurrences (all)	6	3	
Bronchitis			
subjects affected / exposed	1 / 24 (4.17%)	1 / 22 (4.55%)	
occurrences (all)	1	2	
Oral candidiasis			

subjects affected / exposed	1 / 24 (4.17%)	3 / 22 (13.64%)	
occurrences (all)	1	4	
Viral upper respiratory tract infection			
subjects affected / exposed	2 / 24 (8.33%)	2 / 22 (9.09%)	
occurrences (all)	3	3	
Gastroenteritis			
subjects affected / exposed	0 / 24 (0.00%)	2 / 22 (9.09%)	
occurrences (all)	0	2	
Cellulitis			
subjects affected / exposed	0 / 24 (0.00%)	2 / 22 (9.09%)	
occurrences (all)	0	2	
Tooth abscess			
subjects affected / exposed	1 / 24 (4.17%)	2 / 22 (9.09%)	
occurrences (all)	2	3	
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 22 (0.00%)	
occurrences (all)	0	0	
Conjunctivitis			
subjects affected / exposed	0 / 24 (0.00%)	2 / 22 (9.09%)	
occurrences (all)	0	2	
Lower respiratory tract infection viral			
subjects affected / exposed	2 / 24 (8.33%)	1 / 22 (4.55%)	
occurrences (all)	2	1	
Tooth infection			
subjects affected / exposed	2 / 24 (8.33%)	1 / 22 (4.55%)	
occurrences (all)	3	2	
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 24 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Hypokalaemia			
subjects affected / exposed	1 / 24 (4.17%)	1 / 22 (4.55%)	
occurrences (all)	2	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 December 2013	Made study objectives and endpoints consistent; reinforced the need for eDiary compliance during the screening period; provided clarity around the application of a number of inclusion criteria; clarified that optional remnant sampling extended to both serum and plasma; updated relevant sections to reflect that the protocol would be reviewed by a single IRB; updated medical monitor contact information; added clarity to the method by which the primary endpoint would be calculated; and aligned discrepancies within the schedule of assessments and the main body of the protocol.
04 August 2014	Allowed exploration of lebrikizumab 125mg SC Q4W; expanded the study from a United Kingdom-only to a global study; enrolled an additional 90 participants (60 participants into the newly added lebrikizumab 125 mg arm and an additional 30 participants into the placebo arm); replaced the Internal Monitoring Committee and Scientific Oversight Committee with an IDMC; included statistical mechanism to control Type 1 error; provided calculations of statistical power; and allowed flexibility within the screening period for technical issues should it be required (eDairy malfunction or unavailable laboratory data to confirm eligibility).
12 June 2015	Added a long-term ATE period that would have lasted until 31 March 2018; Amended the requirements for contraceptive measures in participants included into the study; clarified events to be monitored and the reporting of adverse events of special interest (AESIs) during the study periods; and removed the requirement for reporting of pregnancies in partners of male participants.
18 June 2015	Removed "non-serious" from AESIs and included minor editorial corrections that were not addressed in last protocol version.
23 September 2015	Addressed inconsistencies identified in the last protocol version; added urine pregnancy tests to the schedule of assessments of the dosing termination visit and safety follow-up (SFU) period of the LTE period; clarified the schedule of the SFU visits in relation to the last dose of study drug throughout the document; and incorporated the collection of bone mineral density data during the DBPC, ATE and corresponding SFU periods if obtained as part of the routine clinical care of the participant.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

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

Notes: