Clinical trial results:
A Phase II, Randomized, Double-Blind, Placebo-Controlled, Study to Assess the Efficacy and Safety of Lebrikizumab in Patients with Idiopathic Pulmonary Fibrosis

Summary

EudraCT number	2013-001163-24
Trial protocol	DE IT ES PL GB BE FR
Global end of trial date	06 November 2017

Results information

Result version number	v1 (current)
This version publication date	09 August 2018
First version publication date	09 August 2018

Trial information

Trial identification

Sponsor protocol code	GB28547

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01872689
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)	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	06 November 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 November 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate lebrikizumab compared with placebo as monotherapy or as combination therapy with pirfenidone background compared with placebo in participants with idiopathic pulmonary fibrosis (IPF), as measured by the annualized rate of decline in percentage of predicted forced vital capacity (FVC) over 52 weeks.

Protection of trial subjects:

The study was conducted in accordance with the principles of the "Declaration of Helsinki" and Good Clinical Practice (GCP) according to the regulations and procedures described in the protocol. Approval from the Independent Ethics Committee/Institutional Review Board (IEC/IRB) was obtained before study start and was documented in a letter to the Investigator specifying the date on which the committee met and granted the approval. The Sponsor also obtained approval from the relevant Competent Authority prior to starting the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 October 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 222
Country: Number of subjects enrolled	Belgium: 15
Country: Number of subjects enrolled	Canada: 15
Country: Number of subjects enrolled	Spain: 12
Country: Number of subjects enrolled	France: 17
Country: Number of subjects enrolled	United Kingdom: 25
Country: Number of subjects enrolled	Germany: 31
Country: Number of subjects enrolled	Italy: 12
Country: Number of subjects enrolled	Poland: 43
Country: Number of subjects enrolled	Australia: 44
Country: Number of subjects enrolled	Japan: 49
Country: Number of subjects enrolled	Mexico: 13
Country: Number of subjects enrolled	Peru: 7
Worldwide total number of subjects	505
EEA total number of subjects	155

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)	120
From 65 to 84 years	382
85 years and over	3

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 505 participants (154 participants in Monotherapy Cohort and 351 participants in Combination Therapy Cohort) were enrolled in the study. Of the monotherapy cohort, 114 participants completed the double-blind period and only 108 of these participants continued into the 52-week open-label lebrikizumab treatment period.

Period 1

Period 1 title	Double-Blind/Placebo-Controlled 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	Monotherapy (Cohort A): Placebo

Arm description:

Participants received monotherapy with placebo matched to lebrikizumab administered via subcutaneous (SC) injection once every 4 weeks up to 52 weeks during the placebo-controlled treatment period. Participants were allowed to receive treatment with lebrikizumab at a dose of 250 milligrams (mg) administered via SC injection once every 4 weeks up to additional 52 weeks (that is, up to Week 104) in the open-label period.

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:

Placebo matched to lebrikizumab was administered via SC injection once every 4 weeks.

Arm title	Monotherapy (Cohort A): Lebrikizumab

Arm description:

Participants received monotherapy with lebrikizumab at a dose of 250 mg administered via SC injection once every 4 weeks up to 52 weeks during the placebo-controlled treatment period. Participants were allowed to receive treatment with lebrikizumab at a dose of 250 mg administered via SC injection once every 4 weeks up to additional 52 weeks (that is, up to Week 104) in the open-label period.

Arm type	Experimental
Investigational medicinal product name	Lebrikizumab
Investigational medicinal product code	
Other name	RO5490255
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Lebrikizumab was administered at a dose of 250 mg via SC injection once every 4 weeks.

Arm title	Combination Therapy (Cohort B): Placebo + Pirfenidone

Arm description:

Participants received pirfenidone at a stable dose of 2403 mg per day (three 267 mg capsules three times a day [9 capsules daily] for a total of 2403 mg/day) or at maximum tolerated dose (MTD) administered orally along with placebo matched to lebrikizumab administered via SC injection once

every 4 weeks up to 52 weeks during the placebo-controlled treatment period.

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:

Placebo matched to lebrikizumab was administered via SC injection once every 4 weeks.

Investigational medicinal product name	Pirfenidone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Pirfenidone was administered orally at a stable dose of 2403 mg per day or at MTD.

Arm title	Combination Therapy (Cohort B): Lebrikizumab + Pirfenidone

Arm description:

Participants received pirfenidone at a stable dose of 2403 mg per day (three 267 mg capsules three times a day [9 capsules daily] for a total of 2403 mg/day) or at MTD administered orally along with lebrikizumab at a dose of 250 mg administered via SC injection once every 4 weeks up to 52 weeks during the placebo-controlled treatment period.

Arm type	Experimental
Investigational medicinal product name	Lebrikizumab
Investigational medicinal product code	
Other name	RO5490255
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Lebrikizumab was administered at a dose of 250 mg via SC injection once every 4 weeks.

Investigational medicinal product name	Pirfenidone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Pirfenidone was administered orally at a stable dose of 2403 mg per day or at MTD.

Number of subjects in period 1	Monotherapy (Cohort A): Placebo	Monotherapy (Cohort A): Lebrikizumab	Combination Therapy (Cohort B): Placebo + Pirfenidone
Started	76	78	177
Completed	56	58	129
Not completed	20	20	48
Consent withdrawn by subject	9	8	14
Physician decision	-	3	3
Adverse Event	6	3	10
Death	3	4	14

Unspecified	1	1	6
Lost to follow-up	1	-	-
Lack of efficacy	-	1	-
Protocol deviation	-	-	1

Number of subjects in period 1	Combination Therapy (Cohort B): Lebrikizumab + Pirfenidone
Started	174
Completed	136
Not completed	38
Consent withdrawn by subject	16
Physician decision	1
Adverse Event	7
Death	9
Unspecified	3
Lost to follow-up	1
Lack of efficacy	-
Protocol deviation	1

Period 2

Period 2 title	Open-Label Period (Only For Monotherapy)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Monotherapy (Cohort A): Placebo

Arm description:

Participants received monotherapy with placebo matched to lebrikizumab administered via SC injection once every 4 weeks up to 52 weeks during the placebo-controlled treatment period. Participants were allowed to receive treatment with lebrikizumab at a dose of 250 mg administered via SC injection once every 4 weeks up to additional 52 weeks (that is, up to Week 104) in the open-label period.

Arm type	Placebo
Investigational medicinal product name	Lebrikizumab
Investigational medicinal product code	
Other name	RO5490255
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Lebrikizumab was administered at a dose of 250 mg via SC injection once every 4 weeks.

Arm title	Monotherapy (Cohort A): Lebrikizumab

Arm description:

Participants received monotherapy with lebrikizumab at a dose of 250 mg administered via SC injection once every 4 weeks up to 52 weeks during the placebo-controlled treatment period. Participants were allowed to receive treatment with lebrikizumab at a dose of 250 mg administered via SC injection once every 4 weeks up to additional 52 weeks (that is, up to Week 104) in the open-label period.

Arm type	Experimental
Investigational medicinal product name	Lebrikizumab
Investigational medicinal product code	
Other name	RO5490255
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Lebrikizumab was administered at a dose of 250 mg via SC injection once every 4 weeks.

Number of subjects in period 2[1]	Monotherapy (Cohort A): Placebo	Monotherapy (Cohort A): Lebrikizumab
Started	52	56
Completed	31	33
Not completed	21	23
Consent withdrawn by subject	11	12
Physician decision	-	1
Adverse Event	2	1
Death	5	3
Unspecified	2	3
Lost to follow-up	1	3

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: All participants who completed double-blind placebo-controlled period did not require to continue in the open-label period, so numbers may not match.

Baseline characteristics

Reporting groups

Reporting group title	Monotherapy (Cohort A): Placebo

Reporting group description:

Participants received monotherapy with placebo matched to lebrikizumab administered via subcutaneous (SC) injection once every 4 weeks up to 52 weeks during the placebo-controlled treatment period. Participants were allowed to receive treatment with lebrikizumab at a dose of 250 milligrams (mg) administered via SC injection once every 4 weeks up to additional 52 weeks (that is, up to Week 104) in the open-label period.

Reporting group title	Monotherapy (Cohort A): Lebrikizumab

Reporting group description:

Participants received monotherapy with lebrikizumab at a dose of 250 mg administered via SC injection once every 4 weeks up to 52 weeks during the placebo-controlled treatment period. Participants were allowed to receive treatment with lebrikizumab at a dose of 250 mg administered via SC injection once every 4 weeks up to additional 52 weeks (that is, up to Week 104) in the open-label period.

Reporting group title	Combination Therapy (Cohort B): Placebo + Pirfenidone

Reporting group description:

Participants received pirfenidone at a stable dose of 2403 mg per day (three 267 mg capsules three times a day [9 capsules daily] for a total of 2403 mg/day) or at maximum tolerated dose (MTD) administered orally along with placebo matched to lebrikizumab administered via SC injection once every 4 weeks up to 52 weeks during the placebo-controlled treatment period.

Reporting group title	Combination Therapy (Cohort B): Lebrikizumab + Pirfenidone

Reporting group description:

Participants received pirfenidone at a stable dose of 2403 mg per day (three 267 mg capsules three times a day [9 capsules daily] for a total of 2403 mg/day) or at MTD administered orally along with lebrikizumab at a dose of 250 mg administered via SC injection once every 4 weeks up to 52 weeks during the placebo-controlled treatment period.

Reporting group values	Monotherapy (Cohort A): Placebo	Monotherapy (Cohort A): Lebrikizumab	Combination Therapy (Cohort B): Placebo + Pirfenidone
Number of subjects	76	78	177
Age, Customized Units: Subjects			
From 40 to <55 years	2	1	6
From 55 to <65 years	18	10	40
From 65 to <75 years	38	44	99
>/=75 years	18	23	32
Sex: Female, Male Units: Subjects			
Female	13	13	30
Male	63	65	147
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	1	1	0
Asian	11	8	19
Native Hawaiian or Other Pacific Islander	1	0	1
Black or African American	0	0	1
White	60	66	149
More than one race	0	1	0
Unknown or Not Reported	3	2	7

Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	9	6	13
Not Hispanic or Latino	64	68	160
Unknown or Not Reported	3	4	4

Reporting group values	Combination Therapy (Cohort B): Lebrikizumab + Pirfenidone	Total	
Number of subjects	174	505	
Age, Customized Units: Subjects			
From 40 to <55 years	2	11	
From 55 to <65 years	41	109	
From 65 to <75 years	92	273	
>/=75 years	39	112	
Sex: Female, Male Units: Subjects			
Female	37	93	
Male	137	412	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	1	3	
Asian	15	53	
Native Hawaiian or Other Pacific Islander	0	2	
Black or African American	1	2	
White	151	426	
More than one race	0	1	
Unknown or Not Reported	6	18	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	15	43	
Not Hispanic or Latino	155	447	
Unknown or Not Reported	4	15	

End points

End points reporting groups

Reporting group title	Monotherapy (Cohort A): Placebo

Reporting group description:

Participants received monotherapy with placebo matched to lebrikizumab administered via subcutaneous (SC) injection once every 4 weeks up to 52 weeks during the placebo-controlled treatment period. Participants were allowed to receive treatment with lebrikizumab at a dose of 250 milligrams (mg) administered via SC injection once every 4 weeks up to additional 52 weeks (that is, up to Week 104) in the open-label period.

Reporting group title	Monotherapy (Cohort A): Lebrikizumab

Reporting group description:

Participants received monotherapy with lebrikizumab at a dose of 250 mg administered via SC injection once every 4 weeks up to 52 weeks during the placebo-controlled treatment period. Participants were allowed to receive treatment with lebrikizumab at a dose of 250 mg administered via SC injection once every 4 weeks up to additional 52 weeks (that is, up to Week 104) in the open-label period.

Reporting group title	Combination Therapy (Cohort B): Placebo + Pirfenidone

Reporting group description:

Participants received pirfenidone at a stable dose of 2403 mg per day (three 267 mg capsules three times a day [9 capsules daily] for a total of 2403 mg/day) or at maximum tolerated dose (MTD) administered orally along with placebo matched to lebrikizumab administered via SC injection once every 4 weeks up to 52 weeks during the placebo-controlled treatment period.

Reporting group title	Combination Therapy (Cohort B): Lebrikizumab + Pirfenidone

Reporting group description:

Participants received pirfenidone at a stable dose of 2403 mg per day (three 267 mg capsules three times a day [9 capsules daily] for a total of 2403 mg/day) or at MTD administered orally along with lebrikizumab at a dose of 250 mg administered via SC injection once every 4 weeks up to 52 weeks during the placebo-controlled treatment period.

Reporting group title	Monotherapy (Cohort A): Placebo

Reporting group description:

Participants received monotherapy with placebo matched to lebrikizumab administered via SC injection once every 4 weeks up to 52 weeks during the placebo-controlled treatment period. Participants were allowed to receive treatment with lebrikizumab at a dose of 250 mg administered via SC injection once every 4 weeks up to additional 52 weeks (that is, up to Week 104) in the open-label period.

Reporting group title	Monotherapy (Cohort A): Lebrikizumab

Reporting group description:

Participants received monotherapy with lebrikizumab at a dose of 250 mg administered via SC injection once every 4 weeks up to 52 weeks during the placebo-controlled treatment period. Participants were allowed to receive treatment with lebrikizumab at a dose of 250 mg administered via SC injection once every 4 weeks up to additional 52 weeks (that is, up to Week 104) in the open-label period.

Primary: Annualized Rate of Decrease in Percent Predicted Forced Vital Capacity (FVC) Over 52 Weeks

End point title	Annualized Rate of Decrease in Percent Predicted Forced Vital Capacity (FVC) Over 52 Weeks

End point description:

Annualized rates of decrease (slope throughout time from baseline to Week 52) for percent predicted FVC was assessed and reported. FVC is a standard pulmonary function test. FVC is defined as the volume of air that can forcibly be blown out after full inspiration in the upright position, measured in liters. Predicted FVC is based on sex, age, and height of a person. Percent predicted FVC (in %) = [(observed FVC)/(predicted FVC)]*100. Analysis was performed on Intent-to-Treat (ITT) Population, which included all participants who were randomized in the study, with participants grouped according to the treatment assignment at randomization. Here 'Number of Subjects Analysed' signifies number of participants evaluable for this outcome measure at Week 52.

End point type	Primary

End point timeframe:

Baseline up to Week 52 (assessed at Baseline, Weeks 1, 4, 12, 24, 36, 44, and 52)

End point values	Monotherapy (Cohort A): Placebo	Monotherapy (Cohort A): Lebrikizumab	Combination Therapy (Cohort B): Placebo + Pirfenidone	Combination Therapy (Cohort B): Lebrikizumab + Pirfenidone
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	56	120	134
Units: Percent predicted FVC/year				
arithmetic mean (standard error)	-6.1876 (± 0.92597)	-5.2065 (± 0.92758)	-6.0430 (± 0.60633)	-5.5430 (± 0.59507)

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Mixed Linear model comparing Lebrikizumab to Placebo, with assessment as the outcome variable; assessment time by treatment as fixed effects; and participant baseline FVC (<50%, 50 to 75%, >75%) and participant by assessment time as random effects with unstructured covariance.

Comparison groups	Monotherapy (Cohort A): Placebo v Monotherapy (Cohort A): Lebrikizumab
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4555
Method	Mixed models analysis
Parameter estimate	Median difference (final values)
Point estimate	0.98111
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.61
upper limit	3.57
Variability estimate	Standard error of the mean
Dispersion value	1.31064

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Mixed Linear model comparing Lebrikizumab to Placebo, with assessment as the outcome variable; assessment time by treatment as fixed effects; and participant baseline FVC (<50%, 50 to 75%, >75%) and participant by assessment time as random effects with unstructured covariance.

Comparison groups	Combination Therapy (Cohort B): Placebo + Pirfenidone v Combination Therapy (Cohort B): Lebrikizumab + Pirfenidone

Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5566
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.49998
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.17
upper limit	2.17
Variability estimate	Standard error of the mean
Dispersion value	0.84946

Secondary: Annualized Rate of Decline in 6-Minute Walk Test (6MWT) Distance Over 52 Weeks

End point title	Annualized Rate of Decline in 6-Minute Walk Test (6MWT) Distance Over 52 Weeks

End point description:

Annualized rates of decline (slope throughout time from baseline to Week 52) in 6MWT was assessed and reported. 6MWT was the distance (in meters [m]) that a participant could walk in 6 minutes. Analysis was performed on ITT Population. Here 'Number of Subjects Analysed' signifies number of participants evaluable for this outcome measure at Week 52.

End point type	Secondary

End point timeframe:

Baseline up to Week 52 (assessed at Baseline, Weeks 1, 4, 12, 24, 36, 44, and 52)

End point values	Monotherapy (Cohort A): Placebo	Monotherapy (Cohort A): Lebrikizumab	Combination Therapy (Cohort B): Placebo + Pirfenidone	Combination Therapy (Cohort B): Lebrikizumab + Pirfenidone
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	59	120	129
Units: m/year				
arithmetic mean (standard error)	-44.6512 (± 15.97862)	-22.7209 (± 15.34753)	-25.5683 (± 12.24923)	-46.9810 (± 11.84199)

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Mixed Linear model comparing Lebrikizumab to Placebo, with assessment as the outcome variable; assessment time by treatment as fixed effects; and participant baseline FVC (<50%, 50 to 75%, >75%) and participant by assessment time as random effects with unstructured covariance.

Comparison groups	Monotherapy (Cohort A): Placebo v Monotherapy (Cohort A): Lebrikizumab

Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3129
Method	Mixed models analysis
Parameter estimate	Median difference (final values)
Point estimate	21.93023
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.97
upper limit	64.83
Variability estimate	Standard error of the mean
Dispersion value	21.62248

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Mixed Linear model comparing Lebrikizumab to Placebo, with assessment as the outcome variable; assessment time by treatment as fixed effects; and participant baseline FVC (<50%, 50 to 75%, >75%) and participant by assessment time as random effects with unstructured covariance.

Comparison groups	Combination Therapy (Cohort B): Placebo + Pirfenidone v Combination Therapy (Cohort B): Lebrikizumab + Pirfenidone
Number of subjects included in analysis	249
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2036
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-21.4127
Confidence interval	
level	95 %
sides	2-sided
lower limit	-54.5
upper limit	11.67
Variability estimate	Standard error of the mean
Dispersion value	16.8016

Secondary: Percentage of Participants with Event of Greater Than or Equal to (>/=) 10% Absolute Decline in Percent Predicted FVC or Death from Any Cause

End point title	Percentage of Participants with Event of Greater Than or Equal to (>/=) 10% Absolute Decline in Percent Predicted FVC or Death from Any Cause

End point description:

FVC is defined as the volume of air that can forcibly be blown out after full inspiration in the upright position, measured in liters. Predicted FVC is based on sex, age, and height of a person. Percent predicted FVC (in %) = [(observed FVC)/(predicted FVC)]*100. Analysis was performed on ITT Population. Here 'Number of Subjects Analysed' signifies number of participants evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline up to the event of >/=10% absolute decline in percent predicted FVC or death from any cause, whichever occurred first (up to Week 122)

End point values	Monotherapy (Cohort A): Placebo	Monotherapy (Cohort A): Lebrikizumab	Combination Therapy (Cohort B): Placebo + Pirfenidone	Combination Therapy (Cohort B): Lebrikizumab + Pirfenidone
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	76	76	175	173
Units: percentage of participants				
number (not applicable)	34.2	27.6	30.3	26.6

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Occurrence of a >/=10% Absolute Decline in Percent Predicted FVC or Death from Any Cause

End point title	Time to First Occurrence of a >/=10% Absolute Decline in Percent Predicted FVC or Death from Any Cause

End point description:

FVC is defined as the volume of air that can forcibly be blown out after full inspiration in the upright position, measured in liters. Predicted FVC is based on sex, age, and height of a person. Percent predicted FVC = [(observed FVC)/(predicted FVC)]*100. Time from randomization to first occurrence of an event of >/=10% absolute decline in percent predicted FVC or death from any cause was reported. Participants without an event were censored at the last assessment during the double-blind treatment period. Any participant who underwent lung transplantation was censored at the date of the transplant. The median time to event was estimated using Kaplan-Meier method and 95% confidence interval (CI) was computed using the method of Brookmeyer and Crowley. Analysis was performed on ITT Population. 'Number of Subjects Analysed' = participants evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline up to the event of >/=10% absolute decline in percent predicted FVC or death from any cause, whichever occurred first (up to Week 122)

End point values	Monotherapy (Cohort A): Placebo	Monotherapy (Cohort A): Lebrikizumab	Combination Therapy (Cohort B): Placebo + Pirfenidone	Combination Therapy (Cohort B): Lebrikizumab + Pirfenidone
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	76[1]	76[2]	175[3]	173[4]
Units: weeks				
median (confidence interval 95%)	53.1 (52.6 to 99999)	99999 (99999 to 99999)	99999 (52.9 to 99999)	99999 (99999 to 99999)

Notes:
[1] - '99999' = CI could not be estimated due to high number of censored participants.
[2] - '99999' = median and CI could not be estimated due to high number of censored participants.
[3] - '99999' = median and CI could not be estimated due to high number of censored participants.
[4] - '99999' = median and CI could not be estimated due to high number of censored participants.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Stratified Analysis: stratified by baseline FVC (<50%, 50 to 75%, >75%)	
Comparison groups	Monotherapy (Cohort A): Placebo v Monotherapy (Cohort A): Lebrikizumab
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4299
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.44
upper limit	1.41

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Stratified Analysis: stratified by baseline FVC (<50%, 50 to 75%, >75%)	
Comparison groups	Combination Therapy (Cohort B): Placebo + Pirfenidone v Combination Therapy (Cohort B): Lebrikizumab + Pirfenidone
Number of subjects included in analysis	348
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3751
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.56
upper limit	1.24

Secondary: Annualized Rate of Decrease in Diffusion Capacity of the Lung for Carbon Monoxide (DLco) Over 52 Weeks

End point title	Annualized Rate of Decrease in Diffusion Capacity of the Lung

	for Carbon Monoxide (DLco) Over 52 Weeks

End point description:

Annualized rates of decrease (slope throughout time from baseline to Week 52) in DLco was assessed and reported. DLco (in milliliters per minute/millimeters of mercury [mL/min/mmHg]) is a measure of the gas transfer. Analysis was performed on ITT Population. Here 'Number of Subjects Analysed' signifies number of participants evaluable for this outcome measure at Week 52.

End point type	Secondary

End point timeframe:

Baseline up to Week 52 (assessed at Baseline, Weeks 1, 4, 12, 24, 36, 44, and 52)

End point values	Monotherapy (Cohort A): Placebo	Monotherapy (Cohort A): Lebrikizumab	Combination Therapy (Cohort B): Placebo + Pirfenidone	Combination Therapy (Cohort B): Lebrikizumab + Pirfenidone
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	52	112	122
Units: mL/min/mmHg/year				
arithmetic mean (standard error)	-4.7818 (± 0.74479)	-4.2400 (± 0.73826)	-5.7552 (± 0.46561)	-5.5732 (± 0.45577)

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Mixed Linear model comparing Lebrikizumab to Placebo, with assessment as the outcome variable; assessment time by treatment as fixed effects; and participant baseline FVC (<50%, 50 to 75%, >75%) and participant by assessment time as random effects with unstructured covariance.

Comparison groups	Monotherapy (Cohort A): Placebo v Monotherapy (Cohort A): Lebrikizumab
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6075
Method	Mixed models analysis
Parameter estimate	Median difference (final values)
Point estimate	0.54171
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.54
upper limit	2.62
Variability estimate	Standard error of the mean
Dispersion value	1.05201

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Mixed Linear model comparing Lebrikizumab to Placebo, with assessment as the outcome variable; assessment time by treatment as fixed effects; and participant baseline FVC (<50%, 50 to 75%, >75%) and participant by assessment time as random effects with unstructured covariance.

Comparison groups	Combination Therapy (Cohort B): Placebo + Pirfenidone v Combination Therapy (Cohort B): Lebrikizumab + Pirfenidone
Number of subjects included in analysis	234
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7803
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.18203
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	1.47
Variability estimate	Standard error of the mean
Dispersion value	0.65206

Secondary: Percentage of Participants with Event of Death, All Cause Hospitalization, or a Decrease from Baseline of >/=10% in FVC

End point title	Percentage of Participants with Event of Death, All Cause Hospitalization, or a Decrease from Baseline of >/=10% in FVC

End point description:

FVC is defined as the volume of air that can forcibly be blown out after full inspiration in the upright position, measured in liters. Predicted FVC is based on sex, age, and height of a person. Percent predicted FVC = [(observed FVC)/(predicted FVC)]*100. Analysis was performed on ITT Population. Here 'Number of Subjects Analysed' signifies number of participants evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline up to the event of death from any cause, all cause hospitalization, or a decrease from baseline of >/=10% in FVC, whichever occurred first (up to Week 122)

End point values	Monotherapy (Cohort A): Placebo	Monotherapy (Cohort A): Lebrikizumab	Combination Therapy (Cohort B): Placebo + Pirfenidone	Combination Therapy (Cohort B): Lebrikizumab + Pirfenidone
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	76	76	175	173
Units: percentage of participants				
number (not applicable)	47.4	32.9	39.4	39.9

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS)

End point title	Progression-Free Survival (PFS)

End point description:

FVC is defined as the volume of air that can forcibly be blown out after full inspiration in the upright position, measured in liters. Predicted FVC is based on sex, age, and height of a person. Percent predicted FVC = [(observed FVC)/(predicted FVC)]*100. PFS was defined as time from randomization to death from any cause, all cause hospitalization, or a decrease from baseline of >/=10% in FVC, whichever occurred first. Participants without an event were censored at the last assessment during the double-blind treatment period. Any participant who underwent lung transplantation was censored at the date of the transplant. The median PFS was estimated using Kaplan-Meier method. 95% CI for median was computed using the method of Brookmeyer and Crowley. Analysis was performed on ITT Population. Here 'Number of Subjects Analysed' signifies number of participants evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline up to the event of death from any cause, all cause hospitalization, or a decrease from baseline of >/=10% in FVC, whichever occurred first (up to Week 122)

End point values	Monotherapy (Cohort A): Placebo	Monotherapy (Cohort A): Lebrikizumab	Combination Therapy (Cohort B): Placebo + Pirfenidone	Combination Therapy (Cohort B): Lebrikizumab + Pirfenidone
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	76[5]	76[6]	175[7]	173[8]
Units: weeks				
median (confidence interval 95%)	52.6 (43.9 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (52.3 to 99999)

Notes:

[5] - '99999' = CI could not be estimated due to high number of censored participants.

[6] - '99999' = median and CI could not be estimated due to high number of censored participants.

[7] - '99999' = median and CI could not be estimated due to high number of censored participants.

[8] - '99999' = median and CI could not be estimated due to high number of censored participants.

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Stratified Analysis: stratified by baseline FVC (<50%, 50 to 75%, >75%)

Comparison groups	Monotherapy (Cohort A): Placebo v Monotherapy (Cohort A): Lebrikizumab
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0972
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.65

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.39
upper limit	1.09

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Stratified Analysis: stratified by baseline FVC (<50%, 50 to 75%, >75%)	
Comparison groups	Combination Therapy (Cohort B): Placebo + Pirfenidone v Combination Therapy (Cohort B): Lebrikizumab + Pirfenidone
Number of subjects included in analysis	348
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9344
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	1.42

Secondary: Annualized Rate of Decrease in FVC Over 52 Weeks

End point title	Annualized Rate of Decrease in FVC Over 52 Weeks

End point description:

Annualized rates of decrease (slope throughout time from baseline to Week 52) in FVC (in milliliters per year [mL/year]) was assessed and reported. FVC is defined as the volume of air that can forcibly be blown out after full inspiration in the upright position. Analysis was performed on ITT Population. Here 'Number of Subjects Analysed' signifies number of participants evaluable for this outcome measure at Week 52.

End point type	Secondary

End point timeframe:

Baseline up to Week 52 (assessed at Baseline, Weeks 1, 4, 12, 24, 36, 44, and 52)

End point values	Monotherapy (Cohort A): Placebo	Monotherapy (Cohort A): Lebrikizumab	Combination Therapy (Cohort B): Placebo + Pirfenidone	Combination Therapy (Cohort B): Lebrikizumab + Pirfenidone
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	57	120	134
Units: mL/year				
arithmetic mean (standard error)	-221.029 (± 34.87511)	-192.906 (± 34.93853)	-231.167 (± 22.67786)	-209.437 (± 22.25073)

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Mixed Linear model comparing Lebrikizumab to Placebo, with assessment as the outcome variable; assessment time by treatment as fixed effects; and participant baseline FVC (<50%, 50 to 75%, >75%) and participant by assessment time as random effects with unstructured covariance.

Comparison groups	Monotherapy (Cohort A): Placebo v Monotherapy (Cohort A): Lebrikizumab
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5707
Method	Mixed models analysis
Parameter estimate	Median difference (final values)
Point estimate	28.12302
Confidence interval	
level	95 %
sides	2-sided
lower limit	-69.8
upper limit	126.04
Variability estimate	Standard error of the mean
Dispersion value	49.47253

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Mixed Linear model comparing Lebrikizumab to Placebo, with assessment as the outcome variable; assessment time by treatment as fixed effects; and participant baseline FVC (<50%, 50 to 75%, >75%) and participant by assessment time as random effects with unstructured covariance.

Comparison groups	Combination Therapy (Cohort B): Placebo + Pirfenidone v Combination Therapy (Cohort B): Lebrikizumab + Pirfenidone
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4934
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	21.72972
Confidence interval	
level	95 %
sides	2-sided
lower limit	-40.65
upper limit	84.11

Variability estimate	Standard error of the mean
Dispersion value	31.68767

Secondary: Annualized Rate of Decrease in A Tool to Assess Quality of Life in IPF (ATAQ-IPF) Questionnaire Total Score Over 52 Weeks

End point title	Annualized Rate of Decrease in A Tool to Assess Quality of Life in IPF (ATAQ-IPF) Questionnaire Total Score Over 52 Weeks

End point description:

The ATAQ-IPF Version 3 was utilized that included 31 items within 5 domains: cough (6 items), dyspnea (7 items), exhaustion (6 items), emotional well-being (6 items), and independence (6 items). Each item was assessed on a scale ranging from 1 (Strongly disagree) to 4 (Strongly agree). The ATAQ-IPF had a recall specification of 2 weeks. Simple summation scoring was used to derive individual domain scores as well as a total score. ATAQ-IPF total score ranged from 31 to 124 with lower score indicating better quality of life (QoL). Annualized rates of decrease (slope throughout time from baseline to Week 52) in ATAQ-IPF questionnaire total score was assessed and reported. Analysis was performed on ITT Population. Here 'Number of Subjects Analysed' signifies number of participants evaluable for this outcome measure at Week 52.

End point type	Secondary

End point timeframe:

Baseline up to Week 52 (assessed at Baseline, Weeks 1, 4, 12, 24, 36, 44, and 52)

End point values	Monotherapy (Cohort A): Placebo	Monotherapy (Cohort A): Lebrikizumab	Combination Therapy (Cohort B): Placebo + Pirfenidone	Combination Therapy (Cohort B): Lebrikizumab + Pirfenidone
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58	62	136	144
Units: units on a scale/year				
arithmetic mean (standard error)	6.8907 (± 1.71778)	4.7886 (± 1.70370)	5.6189 (± 0.99880)	5.4558 (± 0.97793)

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Mixed Linear model comparing Lebrikizumab to Placebo, with assessment as the outcome variable; assessment time by treatment as fixed effects; and participant baseline FVC (<50%, 50 to 75%, >75%) and participant by assessment time as random effects with unstructured covariance.

Comparison groups	Monotherapy (Cohort A): Placebo v Monotherapy (Cohort A): Lebrikizumab
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3854
Method	Mixed models analysis
Parameter estimate	Median difference (final values)
Point estimate	-2.10204

Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.88
upper limit	2.68
Variability estimate	Standard error of the mean
Dispersion value	2.41325

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Mixed Linear model comparing Lebrikizumab to Placebo, with assessment as the outcome variable; assessment time by treatment as fixed effects; and participant baseline FVC (<50%, 50 to 75%, >75%) and participant by assessment time as random effects with unstructured covariance.

Comparison groups	Combination Therapy (Cohort B): Placebo + Pirfenidone v Combination Therapy (Cohort B): Lebrikizumab + Pirfenidone
Number of subjects included in analysis	280
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9057
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.16313
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.87
upper limit	2.55
Variability estimate	Standard error of the mean
Dispersion value	1.37698

Secondary: Percentage of Participants with an Event of St. George's Respiratory Questionnaire (SGRQ) Total Score Worsening or Death from Any Cause

End point title	Percentage of Participants with an Event of St. George's Respiratory Questionnaire (SGRQ) Total Score Worsening or Death from Any Cause[9]

End point description:

The SGRQ is a 50-item health-related QoL instrument that measured health impairment. The questionnaire contains 3 domains: symptoms, activity, and impacts. Items were assessed on various response scales, including a 5-point Likert scale and True/False scale. The SGRQ had a recall specification of 4 weeks. The SGRQ total score (summed weights) ranged from 0 to 100 with a lower score denoting a better health status. Percentage of participants with an event of SGRQ total score worsening (defined as reaching minimal important difference [MID], that is, an increase in total score of >/=7) or death from any cause was reported. Analysis was performed on ITT Population for monotherapy cohort only. Here, 'Number of Subjects Analysed' signifies number of participants evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline up to the event of SGRQ total score worsening or death from any cause, whichever occurred first (up to Week 122)

Notes:

[9] - 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: Reported analysis was planned to be carried out in the indicated arms only.

End point values	Monotherapy (Cohort A): Placebo	Monotherapy (Cohort A): Lebrikizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76	76		
Units: percentage of participants				
number (not applicable)	57.9	48.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Occurrence of SGRQ Total Score Worsening or Death from Any Cause

End point title	Time to First Occurrence of SGRQ Total Score Worsening or Death from Any Cause[10]

End point description:

The SGRQ is a 50-item health-related QoL instrument that measured health impairment. The questionnaire contains 3 domains: symptoms, activity, and impacts. Items were assessed on various response scales, including a 5-point Likert scale and True/False scale. The SGRQ had a recall specification of 4 weeks. The SGRQ total score (summed weights) ranged from 0 to 100 with a lower score denoting a better health status. Time from randomization to first occurrence of an event of SGRQ total score worsening (defined as reaching minimal important difference [MID], that is, an increase in total score of >/=7) or death from any cause was reported. The median time to event was estimated using Kaplan-Meier method. 95% CI for median was computed using the method of Brookmeyer and Crowley. ITT Population for monotherapy cohort only; 'Number of Subjects Analysed' = number of participants evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline up to the event of SGRQ total score worsening or death from any cause, whichever occurred first (up to Week 122)

Notes:

[10] - 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: Reported analysis was planned to be carried out in the indicated arms only.

End point values	Monotherapy (Cohort A): Placebo	Monotherapy (Cohort A): Lebrikizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76	76[11]		
Units: weeks				
median (confidence interval 95%)	51.7 (24.1 to 54.6)	52.3 (35.7 to 99999)		

Notes:

[11] - '99999' = upper limit of CI could not be estimated due to high number of censored participants.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Stratified Analysis: stratified by baseline FVC (<50%, 50 to 75%, >75%)	
Comparison groups	Monotherapy (Cohort A): Placebo v Monotherapy (Cohort A): Lebrikizumab
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4433
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	1.31

Secondary: Percentage of Participants with an Event of Acute Idiopathic Pulmonary Fibrosis (IPF) Exacerbation

End point title	Percentage of Participants with an Event of Acute Idiopathic Pulmonary Fibrosis (IPF) Exacerbation
End point description:	
IPF exacerbation was defined as an event that met all of the following criteria as determined by the investigator: Unexplained worsening or development of dyspnea within the previous 30 days; And radiologic evidence of new bilateral ground-glass abnormality or consolidation, superimposed on a reticular or honeycomb background pattern, that is consistent with usual interstitial pneumonitis; And absence of alternative causes, such as left heart failure, pulmonary embolism, pulmonary infection (on the basis of endotracheal aspirate or bronchoalveolar lavage if available, or investigator judgment), or other events leading to acute lung injury (for example, sepsis, aspiration, trauma, reperfusion pulmonary edema). Analysis was performed on ITT Population. Here 'Number of Subjects Analysed' signifies number of participants evaluable for this outcome measure.	
End point type	Secondary
End point timeframe:	
Baseline up to the event of acute IPF exacerbation (up to Week 122)	

End point values	Monotherapy (Cohort A): Placebo	Monotherapy (Cohort A): Lebrikizumab	Combination Therapy (Cohort B): Placebo + Pirfenidone	Combination Therapy (Cohort B): Lebrikizumab + Pirfenidone
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	76	76	175	172
Units: percentage of participants				
number (not applicable)	3.9	3.9	6.3	2.9

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Event of Acute IPF Exacerbation

End point title	Time to First Event of Acute IPF Exacerbation

End point description:

Time from randomization to first occurrence of an event of IPF exacerbation was reported. IPF exacerbation was defined as an event that met all of the following criteria as determined by the investigator: Unexplained worsening or development of dyspnea within the previous 30 days; And radiologic evidence of new bilateral ground-glass abnormality or consolidation, superimposed on a reticular or honeycomb background pattern, that is consistent with usual interstitial pneumonitis; And absence of alternative causes, or other events leading to acute lung injury. The median time to event was estimated using Kaplan-Meier method. 95% CI for median was computed using the method of Brookmeyer and Crowley. Analysis was performed on ITT Population. Here 'Number of Subjects Analysed' signifies number of participants evaluable for this outcome measure. The data '99999' in the results signifies that median and corresponding CI could not be estimated due to high number of censored participants.

End point type	Secondary

End point timeframe:

Baseline up to the event of acute IPF exacerbation (up to Week 122)

End point values	Monotherapy (Cohort A): Placebo	Monotherapy (Cohort A): Lebrikizumab	Combination Therapy (Cohort B): Placebo + Pirfenidone	Combination Therapy (Cohort B): Lebrikizumab + Pirfenidone
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	76	76	175	172
Units: weeks				
median (confidence interval 95%)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Stratified Analysis: stratified by baseline FVC (<50%, 50 to 75%, >75%)

Comparison groups	Monotherapy (Cohort A): Placebo v Monotherapy (Cohort A): Lebrikizumab
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9366
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.21
upper limit	5.3

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Stratified Analysis: stratified by baseline FVC (<50%, 50 to 75%, >75%)	
Comparison groups	Combination Therapy (Cohort B): Placebo + Pirfenidone v Combination Therapy (Cohort B): Lebrikizumab + Pirfenidone
Number of subjects included in analysis	347
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1346
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.16
upper limit	1.31

Secondary: Percentage of Participants with Respiratory-Related Hospitalization

End point title	Percentage of Participants with Respiratory-Related Hospitalization[12]

End point description:

Analysis was performed on ITT Population for combination therapy cohorts only. Here, 'Number of Subjects Analysed' signifies number of participants evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline up to the event of respiratory-related hospitalization (up to Week 122)

Notes:

[12] - 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: Reported analysis was planned to be carried out in the indicated arms only.

End point values	Combination Therapy (Cohort B): Placebo + Pirfenidone	Combination Therapy (Cohort B): Lebrikizumab + Pirfenidone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	175	173		
Units: percentage of participants				
number (not applicable)	15.4	14.5		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Respiratory-Related Hospitalization

End point title	Time to Respiratory-Related Hospitalization[13]

End point description:

Time from randomization to first occurrence of an event of respiratory-related hospitalization was reported. Participants without an event were censored at the last known alive day, study Day 368, or the last date during the double-blind period. The median time to event was estimated using Kaplan-Meier method. 95% CI for median was computed using the method of Brookmeyer and Crowley. Analysis was performed on ITT Population for combination therapy cohorts only. Here 'Number of Subjects Analysed' signifies number of participants evaluable for this outcome measure. The data '99999' in the results signifies that median and corresponding CI could not be estimated due to high number of censored participants.

End point type	Secondary

End point timeframe:

Baseline up to the event of respiratory-related hospitalization (up to Week 122)

Notes:

[13] - 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: Reported analysis was planned to be carried out in the indicated arms only.

End point values	Combination Therapy (Cohort B): Placebo + Pirfenidone	Combination Therapy (Cohort B): Lebrikizumab + Pirfenidone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	175	173		
Units: weeks				
median (confidence interval 95%)	99999 (99999 to 99999)	99999 (99999 to 99999)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Stratified Analysis: stratified by baseline FVC (<50%, 50 to 75%, >75%)

Comparison groups	Combination Therapy (Cohort B): Placebo + Pirfenidone v Combination Therapy (Cohort B): Lebrikizumab + Pirfenidone
Number of subjects included in analysis	348
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6815
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.52
upper limit	1.54

Secondary: Percentage of Participants with an Event of >/=15% Absolute Decrease in Percentage of Predicted DLco or Death from Any Cause

End point title	Percentage of Participants with an Event of >/=15% Absolute Decrease in Percentage of Predicted DLco or Death from Any Cause

End point description:

DLco (in mL/min/mmHg) is a measure of the gas transfer. Predicted DLco is based on sex, age, and height of a person. Percent of predicted DLco (in %) = [(observed DLco)/(predicted DLco)]*100. Analysis was performed on ITT Population. Here 'Number of Subjects Analysed' signifies number of participants evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline up to the event of >/=15% absolute decrease in percentage of predicted DLco or death from any cause (up to Week 122)

End point values	Monotherapy (Cohort A): Placebo	Monotherapy (Cohort A): Lebrikizumab	Combination Therapy (Cohort B): Placebo + Pirfenidone	Combination Therapy (Cohort B): Lebrikizumab + Pirfenidone
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	76	76	175	173
Units: percentage of participants				
number (not applicable)	9.2	6.6	14.9	11.0

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Event of >/=15% Absolute Decrease in Percentage of Predicted DLco or Death from Any Cause

End point title	Time to First Event of >/=15% Absolute Decrease in Percentage of Predicted DLco or Death from Any Cause

End point description:

DLco is a measure of the gas transfer. Predicted DLco is based on sex, age, and height of a person. Percent of predicted DLco (in %) = [(observed DLco)/(predicted DLco)]*100. Time from randomization to first occurrence of >/=15% absolute decrease in percentage of predicted DLco or death from any cause was reported. The median time to event was estimated using Kaplan-Meier method. 95% CI for median was computed using the method of Brookmeyer and Crowley. Analysis was performed on ITT Population. Here 'Number of Subjects Analysed' signifies number of participants evaluable for this outcome measure. The data ‘99999’ in the results signifies that median and corresponding CI could not be estimated due to high number of censored participants.

End point type	Secondary

End point timeframe:

Baseline up to the event of >/=15% absolute decrease in percentage of predicted DLco or death from any cause (up to Week 122)

End point values	Monotherapy (Cohort A): Placebo	Monotherapy (Cohort A): Lebrikizumab	Combination Therapy (Cohort B): Placebo + Pirfenidone	Combination Therapy (Cohort B): Lebrikizumab + Pirfenidone
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	76	76	175	173
Units: weeks				
median (confidence interval 95%)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Stratified Analysis: stratified by baseline FVC (<50%, 50 to 75%, >75%)	
Comparison groups	Monotherapy (Cohort A): Placebo v Monotherapy (Cohort A): Lebrikizumab
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5685
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.23
upper limit	2.26

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Stratified Analysis: stratified by baseline FVC (<50%, 50 to 75%, >75%)	
Comparison groups	Combination Therapy (Cohort B): Placebo + Pirfenidone v Combination Therapy (Cohort B): Lebrikizumab + Pirfenidone
Number of subjects included in analysis	348
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1976
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.68

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.37
upper limit	1.23

Secondary: Percentage of Participants with Anti-therapeutic Antibody (ATA) to Lebrikizumab

End point title	Percentage of Participants with Anti-therapeutic Antibody (ATA) to Lebrikizumab[14]

End point description:

ATA to lebrikizumab was tested using a validated immunoassay. A positive ATA result was defined as one in which the presence of detectable ATAs could be confirmed by competitive binding with lebrikizumab. Percentage of participants with positive results for ATA at Baseline and at Post-baseline time points were reported. Only participants who received lebrikizumab were included in the analysis. Analysis was performed on Safety Population, which included all participants who received at least one dose of study drug and grouped according to the actual treatment received. Here, 'Number of Subjects Analysed' = participants evaluable for this outcome measure; ‘n’ = number of participants evaluable at indicated time points.

End point type	Secondary

End point timeframe:

Baseline and Post-Baseline (assessed at multiple time points: Weeks 4, 12, 24, 36, 52, 56, 64, 76, and at safety follow-up up to Week 122)

Notes:

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

End point values	Monotherapy (Cohort A): Lebrikizumab	Combination Therapy (Cohort B): Lebrikizumab + Pirfenidone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	75	172		
Units: percentage of participants				
number (not applicable)				
Baseline (n=75,171)	5.3	1.8		
Post-Baseline (n=75,172)	6.7	5.2		

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum Observed Serum Concentration (Cmin) of Lebrikizumab at Week 52

End point title	Minimum Observed Serum Concentration (Cmin) of Lebrikizumab at Week 52[15]

End point description:

Participants who received lebrikizumab were only included in the analysis. Analysis was performed on Pharmacokinetic (PK)-Evaluable Population, which included all participants who received at least one

dose of study drug and had at least one non-missing PK observation. Here 'Number of Subjects Analysed' signifies number of participants evaluable for this outcome measure at Week 52.

End point type	Secondary

End point timeframe:

Predose (Hour 0) at Week 52

Notes:

[15] - 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: Reported analysis was planned to be carried out in the indicated arms only.

End point values	Monotherapy (Cohort A): Lebrikizumab	Combination Therapy (Cohort B): Lebrikizumab + Pirfenidone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	137		
Units: micrograms per milliliter (mcg/mL)				
arithmetic mean (standard deviation)	29.6 (± 14.0)	25.2 (± 12.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum Observed Serum Concentration (Cmin) of Lebrikizumab

End point title	Minimum Observed Serum Concentration (Cmin) of Lebrikizumab[16]

End point description:

Participants who received lebrikizumab were only included in the analysis. Analysis was performed on PK-Evaluable Population. Here, 'Number of Subjects Analysed' signifies number of participants evaluable for this outcome measure and `n signifies number of participants evaluable at specified time points for different arms, respectively

End point type	Secondary

End point timeframe:

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

Notes:

[16] - 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: Reported analysis was planned to be carried out in the indicated arms only.

End point values	Monotherapy (Cohort A): Lebrikizumab	Combination Therapy (Cohort B): Lebrikizumab + Pirfenidone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78	174		
Units: mcg/mL				
arithmetic mean (standard deviation)				
Cmin at Week 4 (n=74,170)	14.0 (± 4.86)	14.9 (± 5.75)		
Cmin at Week 12 (n=68,165)	24.4 (± 9.86)	25.0 (± 11.0)		

Cmin at Week 24 (n=65,153)	28.5 (± 12.5)	25.7 (± 12.4)		
Cmin at Week 36 (n=61,146)	29.9 (± 14.1)	25.6 (± 13.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Elimination Half-Life (t1/2) of Lebrikizumab

End point title	Elimination Half-Life (t1/2) of Lebrikizumab[17]

End point description:

Elimination half-life is the time measured for the plasma drug concentration to decrease by one-half during the elimination phase of the drug. Analysis was performed on PK-Evaluable Population. Participants who received lebrikizumab were only included in the analysis. Analysis was performed on PK-Evaluable Population. Here, 'Number of Subjects Analysed' signifies number of participants evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Pre-dose (Hour 0) at Weeks 1, 4, 12, 24, 36, 64, 76, 88, 104; and at 4, 12, and 18 weeks post-last dose (last dose = Week 104)

Notes:

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

End point values	Monotherapy (Cohort A): Lebrikizumab	Combination Therapy (Cohort B): Lebrikizumab + Pirfenidone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	125		
Units: days				
arithmetic mean (standard deviation)	23.5 (± 5.36)	21.9 (± 4.79)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline up to Week 122	
Adverse event reporting additional description:	
Safety Population	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups	
Reporting group title	Monotherapy (Cohort A): Placebo
Reporting group description:	
Participants received monotherapy with placebo matched to lebrikizumab administered via SC injection once every 4 weeks up to 52 weeks during the placebo-controlled treatment period. Participants were allowed to receive treatment with lebrikizumab at a dose of 250 mg administered via SC injection once every 4 weeks up to additional 52 weeks (that is, up to Week 104) in the open-label period.	
Reporting group title	Monotherapy (Cohort A): Lebrikizumab
Reporting group description:	
Participants received monotherapy with lebrikizumab at a dose of 250 mg administered via SC injection once every 4 weeks up to 52 weeks during the placebo-controlled treatment period. Participants were allowed to receive treatment with lebrikizumab at a dose of 250 mg administered via SC injection once every 4 weeks up to additional 52 weeks (that is, up to Week 104) in the open-label period.	
Reporting group title	Combination Therapy (Cohort B): Placebo + Pirfenidone
Reporting group description:	
Participants received pirfenidone at a stable dose of 2403 mg per day (three 267 mg capsules three times a day [9 capsules daily] for a total of 2403 mg/day) or at MTD administered orally along with placebo matched to lebrikizumab administered via SC injection once every 4 weeks up to 52 weeks during the placebo-controlled treatment period.	
Reporting group title	Combination Therapy (Cohort B): Lebrikizumab + Pirfenidone
Reporting group description:	
Participants received pirfenidone at a stable dose of 2403 mg per day (three 267 mg capsules three times a day [9 capsules daily] for a total of 2403 mg/day) or at MTD administered orally along with lebrikizumab at a dose of 250 mg administered via SC injection once every 4 weeks up to 52 weeks during the placebo-controlled treatment period.	

Serious adverse events	Monotherapy (Cohort A): Placebo	Monotherapy (Cohort A): Lebrikizumab	Combination Therapy (Cohort B): Placebo + Pirfenidone
Total subjects affected by serious adverse events			
subjects affected / exposed	19 / 76 (25.00%)	23 / 78 (29.49%)	47 / 177 (26.55%)
number of deaths (all causes)	4	4	15
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			

subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 177 (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
Basosquamous carcinoma			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 177 (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
Chondrosarcoma			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 177 (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
Hepatic cancer			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 177 (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
Hepatocellular carcinoma			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 177 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung Adenocarcinoma Stage IV			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 177 (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 Neoplasm			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	1 / 177 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm malignant			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 177 (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
Lung squamous cell carcinoma Stage 0			

subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 177 (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
Neuroendocrine carcinoma			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 177 (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
Pancreatic carcinoma metastatic			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 177 (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
Plasma cell myeloma			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 177 (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
Squamous cell carcinoma			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	3 / 177 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 177 (0.56%)
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			
Aortic aneurysm			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 177 (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
Aortic stenosis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 177 (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
Axillary vein thrombosis			

subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 177 (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
Hypotension			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 177 (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
Orthostatic hypotension			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 177 (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 / 76 (1.32%)	0 / 78 (0.00%)	0 / 177 (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
Death			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 177 (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
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 177 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 177 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Immune system disorders			
Graft versus host disease			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 177 (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			
Acute respiratory failure			
subjects affected / exposed	2 / 76 (2.63%)	1 / 78 (1.28%)	1 / 177 (0.56%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	1 / 2	0 / 0	0 / 1
Haemoptysis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 177 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperventilation			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 177 (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
Hypoxia			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 177 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Idiopathic pulmonary fibrosis			
subjects affected / exposed	13 / 76 (17.11%)	11 / 78 (14.10%)	22 / 177 (12.43%)
occurrences causally related to treatment / all	2 / 15	0 / 15	3 / 27
deaths causally related to treatment / all	1 / 7	0 / 4	1 / 11
Oropharyngeal discomfort			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 177 (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	0 / 76 (0.00%)	1 / 78 (1.28%)	1 / 177 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pneumomediastinum			
subjects affected / exposed	2 / 76 (2.63%)	0 / 78 (0.00%)	0 / 177 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pneumothorax			
subjects affected / exposed	2 / 76 (2.63%)	2 / 78 (2.56%)	0 / 177 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary arterial hypertension			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 177 (0.56%)
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	3 / 76 (3.95%)	2 / 78 (2.56%)	1 / 177 (0.56%)
occurrences causally related to treatment / all	0 / 3	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Pulmonary fibrosis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 177 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pulmonary hypertension			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 177 (0.56%)
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 failure			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 177 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Dyspnoea			
subjects affected / exposed	2 / 76 (2.63%)	1 / 78 (1.28%)	1 / 177 (0.56%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 177 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			

Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 177 (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
Hepatic enzyme increased			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 177 (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			
Fall			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 177 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural hypotension			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 177 (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
Procedural pain			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	1 / 177 (0.56%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 177 (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
Spinal fracture			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 177 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome			

subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 177 (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
Acute myocardial infarction			
subjects affected / exposed	1 / 76 (1.32%)	1 / 78 (1.28%)	0 / 177 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Angina pectoris			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 177 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	2 / 177 (1.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 177 (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
Atrioventricular block			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 177 (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
Atrioventricular block second degree			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 177 (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
Bradycardia			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 177 (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 arrest			

subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 177 (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
Cardio-respiratory arrest			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 177 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 76 (0.00%)	2 / 78 (2.56%)	3 / 177 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiomegaly			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 177 (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 disease			
subjects affected / exposed	2 / 76 (2.63%)	0 / 78 (0.00%)	2 / 177 (1.13%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery occlusion			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 177 (0.56%)
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 / 76 (0.00%)	1 / 78 (1.28%)	3 / 177 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Right ventricular failure			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 177 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia			

subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 177 (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
Nervous system disorders			
Carotid artery stenosis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 177 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 177 (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
Epilepsy			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 177 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 177 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 177 (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	1 / 76 (1.32%)	1 / 78 (1.28%)	1 / 177 (0.56%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 177 (0.56%)
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			

Diarrhoea			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 177 (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
Diverticulum intestinal haemorrhagic			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 177 (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	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 177 (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
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 177 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 177 (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 prolapse			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 177 (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
Mesenteric vein thrombosis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 177 (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
Nausea			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 177 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			

subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 177 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	2 / 76 (2.63%)	0 / 78 (0.00%)	0 / 177 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toothache			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 177 (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
Vomiting			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 177 (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			
Drug-induced liver injury			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 177 (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	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 177 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 177 (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 chest pain			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 177 (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 pain			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 177 (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
Rheumatoid arthritis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 177 (0.56%)
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			
Bronchitis			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	1 / 177 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis bacterial			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 177 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopulmonary aspergillosis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 177 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Campylobacter infection			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 177 (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
Diverticulitis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 177 (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
Erysipelas			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 177 (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
Fungal infection			

subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 177 (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
H1N1 influenza			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 177 (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
Influenza			
subjects affected / exposed	1 / 76 (1.32%)	1 / 78 (1.28%)	0 / 177 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	1 / 76 (1.32%)	4 / 78 (5.13%)	2 / 177 (1.13%)
occurrences causally related to treatment / all	0 / 1	0 / 5	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Lung infection			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	1 / 177 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pneumonia			
subjects affected / exposed	2 / 76 (2.63%)	3 / 78 (3.85%)	7 / 177 (3.95%)
occurrences causally related to treatment / all	0 / 2	1 / 3	2 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Pneumonia bacterial			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 177 (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
Pneumonia haemophilus			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 177 (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
Pneumonia influenzal			

subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 177 (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
Pneumonia viral			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 177 (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
Postoperative wound infection			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 177 (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 syncytial virus infection			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 177 (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	1 / 76 (1.32%)	1 / 78 (1.28%)	3 / 177 (1.69%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 177 (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
Septic shock			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 177 (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
Urinary tract infection enterococcal			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 177 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection bacterial			

subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 177 (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
Mycobacterium avium complex infection			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 177 (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
Urinary tract infection			
subjects affected / exposed	0 / 76 (0.00%)	2 / 78 (2.56%)	0 / 177 (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
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 177 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 177 (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
Hypercalcaemia			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 177 (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
Hyponatraemia			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 177 (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	Combination Therapy (Cohort B): Lebrikizumab + Pirfenidone		
Total subjects affected by serious adverse events			
subjects affected / exposed	56 / 174 (32.18%)		
number of deaths (all causes)	7		

number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 174 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Basosquamous carcinoma			
subjects affected / exposed	0 / 174 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chondrosarcoma			
subjects affected / exposed	0 / 174 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatic cancer			
subjects affected / exposed	1 / 174 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatocellular carcinoma			
subjects affected / exposed	0 / 174 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lung Adenocarcinoma Stage IV			
subjects affected / exposed	1 / 174 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lung Neoplasm			
subjects affected / exposed	0 / 174 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lung neoplasm malignant			

subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung squamous cell carcinoma Stage 0				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neuroendocrine carcinoma				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatic carcinoma metastatic				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Plasma cell myeloma				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma of skin				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Aortic aneurysm				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Aortic stenosis				

subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Axillary vein thrombosis				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypotension				
subjects affected / exposed	2 / 174 (1.15%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Orthostatic hypotension				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Chest pain				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Death				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Multiple organ dysfunction syndrome				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sudden death				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				

Graft versus host disease				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Respiratory, thoracic and mediastinal disorders				
Acute respiratory failure				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Haemoptysis				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hyperventilation				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypoxia				
subjects affected / exposed	3 / 174 (1.72%)			
occurrences causally related to treatment / all	2 / 4			
deaths causally related to treatment / all	0 / 0			
Idiopathic pulmonary fibrosis				
subjects affected / exposed	17 / 174 (9.77%)			
occurrences causally related to treatment / all	0 / 21			
deaths causally related to treatment / all	0 / 6			
Oropharyngeal discomfort				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Pneumomediastinum			
subjects affected / exposed	1 / 174 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			
subjects affected / exposed	1 / 174 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary arterial hypertension			
subjects affected / exposed	0 / 174 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	2 / 174 (1.15%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pulmonary fibrosis			
subjects affected / exposed	1 / 174 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary hypertension			
subjects affected / exposed	0 / 174 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	0 / 174 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	1 / 174 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			

Delirium				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
Blood creatine phosphokinase increased				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatic enzyme increased				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Fall				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Procedural hypotension				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Procedural pain				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Radius fracture				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Spinal fracture				

subjects affected / exposed	0 / 174 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 174 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Acute myocardial infarction			
subjects affected / exposed	1 / 174 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Angina pectoris			
subjects affected / exposed	1 / 174 (0.57%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	1 / 174 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Atrial flutter			
subjects affected / exposed	1 / 174 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Atrioventricular block			
subjects affected / exposed	0 / 174 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrioventricular block second degree			
subjects affected / exposed	0 / 174 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bradycardia			

subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac arrest				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardio-respiratory arrest				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 1			
Cardiomegaly				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Coronary artery disease				
subjects affected / exposed	2 / 174 (1.15%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Coronary artery occlusion				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial ischaemia				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Right ventricular failure				

subjects affected / exposed	1 / 174 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tachycardia			
subjects affected / exposed	0 / 174 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Carotid artery stenosis			
subjects affected / exposed	0 / 174 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cerebrovascular accident			
subjects affected / exposed	1 / 174 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Epilepsy			
subjects affected / exposed	0 / 174 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ischaemic stroke			
subjects affected / exposed	0 / 174 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Presyncope			
subjects affected / exposed	0 / 174 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	1 / 174 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			

Vertigo positional			
subjects affected / exposed	0 / 174 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 174 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diverticulum intestinal haemorrhagic			
subjects affected / exposed	1 / 174 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastritis			
subjects affected / exposed	0 / 174 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 174 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia			
subjects affected / exposed	1 / 174 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intestinal prolapse			
subjects affected / exposed	0 / 174 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mesenteric vein thrombosis			
subjects affected / exposed	1 / 174 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nausea			

subjects affected / exposed	1 / 174 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pancreatitis			
subjects affected / exposed	2 / 174 (1.15%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Pancreatitis acute			
subjects affected / exposed	0 / 174 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Toothache			
subjects affected / exposed	0 / 174 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	1 / 174 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Drug-induced liver injury			
subjects affected / exposed	2 / 174 (1.15%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 174 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 174 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Musculoskeletal chest pain				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal pain				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rheumatoid arthritis				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Bronchitis				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchitis bacterial				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchopulmonary aspergillosis				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Campylobacter infection				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diverticulitis				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Erysipelas				

subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Fungal infection				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
H1N1 influenza				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lung infection				
subjects affected / exposed	2 / 174 (1.15%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	7 / 174 (4.02%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 1			
Pneumonia bacterial				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia haemophilus				

subjects affected / exposed	0 / 174 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia influenzal			
subjects affected / exposed	0 / 174 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia viral			
subjects affected / exposed	1 / 174 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Postoperative wound infection			
subjects affected / exposed	1 / 174 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 174 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection			
subjects affected / exposed	5 / 174 (2.87%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 174 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Septic shock			
subjects affected / exposed	1 / 174 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Urinary tract infection enterococcal			

subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wound infection bacterial				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Mycobacterium avium complex infection				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Decreased appetite				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dehydration				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypercalcaemia				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hyponatraemia				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

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

Non-serious adverse events	Monotherapy (Cohort A): Placebo	Monotherapy (Cohort A): Lebrikizumab	Combination Therapy (Cohort B): Placebo + Pirfenidone
Total subjects affected by non-serious adverse events			
subjects affected / exposed	70 / 76 (92.11%)	73 / 78 (93.59%)	158 / 177 (89.27%)
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 76 (5.26%)	4 / 78 (5.13%)	4 / 177 (2.26%)
occurrences (all)	4	4	4
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 76 (2.63%)	5 / 78 (6.41%)	3 / 177 (1.69%)
occurrences (all)	2	5	3
Chest discomfort			
subjects affected / exposed	5 / 76 (6.58%)	2 / 78 (2.56%)	3 / 177 (1.69%)
occurrences (all)	9	2	3
Chest pain			
subjects affected / exposed	5 / 76 (6.58%)	7 / 78 (8.97%)	7 / 177 (3.95%)
occurrences (all)	6	8	7
Fatigue			
subjects affected / exposed	12 / 76 (15.79%)	15 / 78 (19.23%)	22 / 177 (12.43%)
occurrences (all)	17	17	24
Injection site erythema			
subjects affected / exposed	1 / 76 (1.32%)	4 / 78 (5.13%)	1 / 177 (0.56%)
occurrences (all)	1	18	1
Oedema peripheral			
subjects affected / exposed	2 / 76 (2.63%)	4 / 78 (5.13%)	4 / 177 (2.26%)
occurrences (all)	2	5	4
Pain			
subjects affected / exposed	2 / 76 (2.63%)	4 / 78 (5.13%)	2 / 177 (1.13%)
occurrences (all)	3	4	2
Pyrexia			
subjects affected / exposed	2 / 76 (2.63%)	6 / 78 (7.69%)	5 / 177 (2.82%)
occurrences (all)	2	7	7
Respiratory, thoracic and mediastinal			

disorders			
Cough			
subjects affected / exposed	19 / 76 (25.00%)	21 / 78 (26.92%)	46 / 177 (25.99%)
occurrences (all)	22	33	59
Dysphonia			
subjects affected / exposed	0 / 76 (0.00%)	4 / 78 (5.13%)	1 / 177 (0.56%)
occurrences (all)	0	4	1
Dyspnoea			
subjects affected / exposed	12 / 76 (15.79%)	14 / 78 (17.95%)	18 / 177 (10.17%)
occurrences (all)	19	14	19
Dyspnoea exertional			
subjects affected / exposed	4 / 76 (5.26%)	6 / 78 (7.69%)	4 / 177 (2.26%)
occurrences (all)	4	6	4
Idiopathic pulmonary fibrosis			
subjects affected / exposed	13 / 76 (17.11%)	11 / 78 (14.10%)	10 / 177 (5.65%)
occurrences (all)	14	12	10
Oropharyngeal pain			
subjects affected / exposed	7 / 76 (9.21%)	4 / 78 (5.13%)	5 / 177 (2.82%)
occurrences (all)	7	6	5
Productive cough			
subjects affected / exposed	3 / 76 (3.95%)	8 / 78 (10.26%)	8 / 177 (4.52%)
occurrences (all)	3	12	8
Sinus congestion			
subjects affected / exposed	1 / 76 (1.32%)	5 / 78 (6.41%)	1 / 177 (0.56%)
occurrences (all)	1	5	1
Psychiatric disorders			
Anxiety			
subjects affected / exposed	5 / 76 (6.58%)	3 / 78 (3.85%)	1 / 177 (0.56%)
occurrences (all)	6	3	1
Insomnia			
subjects affected / exposed	3 / 76 (3.95%)	7 / 78 (8.97%)	4 / 177 (2.26%)
occurrences (all)	3	7	4
Investigations			
Forced vital capacity decreased			
subjects affected / exposed	4 / 76 (5.26%)	11 / 78 (14.10%)	6 / 177 (3.39%)
occurrences (all)	4	12	6
Weight decreased			

subjects affected / exposed	5 / 76 (6.58%)	2 / 78 (2.56%)	9 / 177 (5.08%)
occurrences (all)	5	2	9
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	6 / 76 (7.89%)	4 / 78 (5.13%)	3 / 177 (1.69%)
occurrences (all)	8	5	3
Nervous system disorders			
Dizziness			
subjects affected / exposed	10 / 76 (13.16%)	14 / 78 (17.95%)	14 / 177 (7.91%)
occurrences (all)	15	18	18
Headache			
subjects affected / exposed	9 / 76 (11.84%)	10 / 78 (12.82%)	17 / 177 (9.60%)
occurrences (all)	14	12	21
Eye disorders			
Cataract			
subjects affected / exposed	2 / 76 (2.63%)	4 / 78 (5.13%)	7 / 177 (3.95%)
occurrences (all)	2	5	8
Dry eye			
subjects affected / exposed	0 / 76 (0.00%)	4 / 78 (5.13%)	1 / 177 (0.56%)
occurrences (all)	0	4	1
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	2 / 76 (2.63%)	4 / 78 (5.13%)	3 / 177 (1.69%)
occurrences (all)	2	4	3
Abdominal pain			
subjects affected / exposed	3 / 76 (3.95%)	4 / 78 (5.13%)	2 / 177 (1.13%)
occurrences (all)	4	4	2
Abdominal pain upper			
subjects affected / exposed	4 / 76 (5.26%)	4 / 78 (5.13%)	4 / 177 (2.26%)
occurrences (all)	4	5	6
Constipation			
subjects affected / exposed	11 / 76 (14.47%)	11 / 78 (14.10%)	12 / 177 (6.78%)
occurrences (all)	14	14	13
Diarrhoea			
subjects affected / exposed	16 / 76 (21.05%)	17 / 78 (21.79%)	23 / 177 (12.99%)
occurrences (all)	19	25	30

Dry mouth			
subjects affected / exposed	0 / 76 (0.00%)	6 / 78 (7.69%)	2 / 177 (1.13%)
occurrences (all)	0	6	2
Dyspepsia			
subjects affected / exposed	2 / 76 (2.63%)	4 / 78 (5.13%)	5 / 177 (2.82%)
occurrences (all)	2	4	5
Flatulence			
subjects affected / exposed	0 / 76 (0.00%)	4 / 78 (5.13%)	1 / 177 (0.56%)
occurrences (all)	0	4	1
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 76 (2.63%)	3 / 78 (3.85%)	9 / 177 (5.08%)
occurrences (all)	3	4	11
Nausea			
subjects affected / exposed	10 / 76 (13.16%)	10 / 78 (12.82%)	23 / 177 (12.99%)
occurrences (all)	15	12	29
Toothache			
subjects affected / exposed	4 / 76 (5.26%)	0 / 78 (0.00%)	2 / 177 (1.13%)
occurrences (all)	4	0	2
Vomiting			
subjects affected / exposed	6 / 76 (7.89%)	3 / 78 (3.85%)	9 / 177 (5.08%)
occurrences (all)	11	4	10
Skin and subcutaneous tissue disorders			
Photosensitivity reaction			
subjects affected / exposed	6 / 76 (7.89%)	3 / 78 (3.85%)	24 / 177 (13.56%)
occurrences (all)	8	4	27
Pruritus			
subjects affected / exposed	2 / 76 (2.63%)	3 / 78 (3.85%)	12 / 177 (6.78%)
occurrences (all)	2	7	12
Rash			
subjects affected / exposed	5 / 76 (6.58%)	9 / 78 (11.54%)	21 / 177 (11.86%)
occurrences (all)	9	15	24
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	9 / 76 (11.84%)	9 / 78 (11.54%)	8 / 177 (4.52%)
occurrences (all)	15	9	10
Back pain			

subjects affected / exposed	9 / 76 (11.84%)	12 / 78 (15.38%)	11 / 177 (6.21%)
occurrences (all)	9	15	13
Muscle spasms			
subjects affected / exposed	5 / 76 (6.58%)	6 / 78 (7.69%)	4 / 177 (2.26%)
occurrences (all)	5	6	6
Musculoskeletal chest pain			
subjects affected / exposed	1 / 76 (1.32%)	5 / 78 (6.41%)	2 / 177 (1.13%)
occurrences (all)	1	5	2
Musculoskeletal pain			
subjects affected / exposed	10 / 76 (13.16%)	5 / 78 (6.41%)	8 / 177 (4.52%)
occurrences (all)	11	6	8
Infections and infestations			
Bronchitis			
subjects affected / exposed	11 / 76 (14.47%)	15 / 78 (19.23%)	11 / 177 (6.21%)
occurrences (all)	14	21	17
Influenza			
subjects affected / exposed	4 / 76 (5.26%)	5 / 78 (6.41%)	10 / 177 (5.65%)
occurrences (all)	5	5	12
Lower respiratory tract infection			
subjects affected / exposed	5 / 76 (6.58%)	11 / 78 (14.10%)	13 / 177 (7.34%)
occurrences (all)	9	23	21
Nasopharyngitis			
subjects affected / exposed	19 / 76 (25.00%)	17 / 78 (21.79%)	25 / 177 (14.12%)
occurrences (all)	33	28	35
Pneumonia			
subjects affected / exposed	3 / 76 (3.95%)	1 / 78 (1.28%)	9 / 177 (5.08%)
occurrences (all)	5	1	9
Respiratory tract infection			
subjects affected / exposed	5 / 76 (6.58%)	4 / 78 (5.13%)	9 / 177 (5.08%)
occurrences (all)	7	4	16
Rhinitis			
subjects affected / exposed	4 / 76 (5.26%)	4 / 78 (5.13%)	7 / 177 (3.95%)
occurrences (all)	4	4	9
Sinusitis			
subjects affected / exposed	5 / 76 (6.58%)	6 / 78 (7.69%)	9 / 177 (5.08%)
occurrences (all)	5	6	10

Upper respiratory tract infection			
subjects affected / exposed	13 / 76 (17.11%)	18 / 78 (23.08%)	38 / 177 (21.47%)
occurrences (all)	17	27	47
Urinary tract infection			
subjects affected / exposed	5 / 76 (6.58%)	9 / 78 (11.54%)	11 / 177 (6.21%)
occurrences (all)	7	14	14
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	5 / 76 (6.58%)	9 / 78 (11.54%)	22 / 177 (12.43%)
occurrences (all)	8	9	22

Non-serious adverse events	Combination Therapy (Cohort B): Lebrikizumab + Pirfenidone		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	142 / 174 (81.61%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	7 / 174 (4.02%)		
occurrences (all)	7		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 174 (0.00%)		
occurrences (all)	0		
Chest discomfort			
subjects affected / exposed	3 / 174 (1.72%)		
occurrences (all)	3		
Chest pain			
subjects affected / exposed	10 / 174 (5.75%)		
occurrences (all)	12		
Fatigue			
subjects affected / exposed	28 / 174 (16.09%)		
occurrences (all)	32		
Injection site erythema			
subjects affected / exposed	1 / 174 (0.57%)		
occurrences (all)	2		
Oedema peripheral			

subjects affected / exposed	3 / 174 (1.72%)		
occurrences (all)	3		
Pain			
subjects affected / exposed	1 / 174 (0.57%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	1 / 174 (0.57%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	33 / 174 (18.97%)		
occurrences (all)	38		
Dysphonia			
subjects affected / exposed	0 / 174 (0.00%)		
occurrences (all)	0		
Dyspnoea			
subjects affected / exposed	13 / 174 (7.47%)		
occurrences (all)	14		
Dyspnoea exertional			
subjects affected / exposed	5 / 174 (2.87%)		
occurrences (all)	6		
Idiopathic pulmonary fibrosis			
subjects affected / exposed	9 / 174 (5.17%)		
occurrences (all)	9		
Oropharyngeal pain			
subjects affected / exposed	2 / 174 (1.15%)		
occurrences (all)	2		
Productive cough			
subjects affected / exposed	6 / 174 (3.45%)		
occurrences (all)	6		
Sinus congestion			
subjects affected / exposed	2 / 174 (1.15%)		
occurrences (all)	2		
Psychiatric disorders			

Anxiety subjects affected / exposed occurrences (all) Insomnia subjects affected / exposed occurrences (all)	2 / 174 (1.15%) 2 8 / 174 (4.60%) 10		
Investigations Forced vital capacity decreased subjects affected / exposed occurrences (all) Weight decreased subjects affected / exposed occurrences (all)	6 / 174 (3.45%) 6 11 / 174 (6.32%) 12		
Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all)	6 / 174 (3.45%) 7		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all)	11 / 174 (6.32%) 12 11 / 174 (6.32%) 17		
Eye disorders Cataract subjects affected / exposed occurrences (all) Dry eye subjects affected / exposed occurrences (all)	4 / 174 (2.30%) 5 3 / 174 (1.72%) 3		
Gastrointestinal disorders Abdominal discomfort subjects affected / exposed occurrences (all) Abdominal pain	3 / 174 (1.72%) 3		

subjects affected / exposed	1 / 174 (0.57%)		
occurrences (all)	1		
Abdominal pain upper			
subjects affected / exposed	6 / 174 (3.45%)		
occurrences (all)	9		
Constipation			
subjects affected / exposed	14 / 174 (8.05%)		
occurrences (all)	15		
Diarrhoea			
subjects affected / exposed	18 / 174 (10.34%)		
occurrences (all)	20		
Dry mouth			
subjects affected / exposed	4 / 174 (2.30%)		
occurrences (all)	4		
Dyspepsia			
subjects affected / exposed	8 / 174 (4.60%)		
occurrences (all)	12		
Flatulence			
subjects affected / exposed	1 / 174 (0.57%)		
occurrences (all)	1		
Gastrooesophageal reflux disease			
subjects affected / exposed	9 / 174 (5.17%)		
occurrences (all)	14		
Nausea			
subjects affected / exposed	28 / 174 (16.09%)		
occurrences (all)	30		
Toothache			
subjects affected / exposed	1 / 174 (0.57%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	8 / 174 (4.60%)		
occurrences (all)	10		
Skin and subcutaneous tissue disorders			
Photosensitivity reaction			
subjects affected / exposed	7 / 174 (4.02%)		
occurrences (all)	9		

Pruritus			
subjects affected / exposed	8 / 174 (4.60%)		
occurrences (all)	8		
Rash			
subjects affected / exposed	18 / 174 (10.34%)		
occurrences (all)	24		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	10 / 174 (5.75%)		
occurrences (all)	11		
Back pain			
subjects affected / exposed	11 / 174 (6.32%)		
occurrences (all)	11		
Muscle spasms			
subjects affected / exposed	2 / 174 (1.15%)		
occurrences (all)	2		
Musculoskeletal chest pain			
subjects affected / exposed	1 / 174 (0.57%)		
occurrences (all)	1		
Musculoskeletal pain			
subjects affected / exposed	2 / 174 (1.15%)		
occurrences (all)	2		
Infections and infestations			
Bronchitis			
subjects affected / exposed	17 / 174 (9.77%)		
occurrences (all)	19		
Influenza			
subjects affected / exposed	3 / 174 (1.72%)		
occurrences (all)	3		
Lower respiratory tract infection			
subjects affected / exposed	10 / 174 (5.75%)		
occurrences (all)	11		
Nasopharyngitis			
subjects affected / exposed	31 / 174 (17.82%)		
occurrences (all)	38		
Pneumonia			

subjects affected / exposed	3 / 174 (1.72%)		
occurrences (all)	3		
Respiratory tract infection			
subjects affected / exposed	8 / 174 (4.60%)		
occurrences (all)	9		
Rhinitis			
subjects affected / exposed	2 / 174 (1.15%)		
occurrences (all)	2		
Sinusitis			
subjects affected / exposed	11 / 174 (6.32%)		
occurrences (all)	13		
Upper respiratory tract infection			
subjects affected / exposed	31 / 174 (17.82%)		
occurrences (all)	43		
Urinary tract infection			
subjects affected / exposed	6 / 174 (3.45%)		
occurrences (all)	9		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	17 / 174 (9.77%)		
occurrences (all)	17		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 May 2014	The IPF diagnostic criteria required for eligibility were expanded to include participants with a diagnosis of definite IPF, probable IPF, possible IPF, or possible high-resolution computed tomography (HRCT) with no surgical lung biopsy (SLB) based on 2011 ATS/ERS/JRS/ALAT guidelines; A Multidisciplinary Discussion of Diagnosis (MDD) based on 2011 ATS/ERS/JRS/ALAT guidelines was utilized to finalize the diagnosis in the event of initial central review outcome results for HRCT and SLB were disparate; Time period for inclusion was extended to 5 years since initial diagnosis of IPF; Historical HRCT scans performed within 12 months of screening Visit 1 were allowed to be used to confirm IPF diagnosis and eligibility; Eligibility was expanded to include participants with minimal or no limitation in lung function indicated by FVC upper limit to 100% predicted.
11 February 2015	Two cohorts were included of participants to test lebrikizumab as monotherapy (Cohort A) or as combination therapy with pirfenidone (Cohort B); The primary endpoint for each cohort was changed from PFS to the absolute change from baseline to Week 52 in percent predicted FVC; The placebo-controlled study treatment duration was changed from a maximum of 2.5 years to 52 weeks; The statistical analysis considerations and plans were changed based upon the revised target participant populations, treatment duration, and primary endpoint; Open-label treatment (with lebrikizumab) period was added for participants in Cohort A who completed the 52-week placebo-controlled study period; The biosensor substudy was limited to participants who enrolled in the study prior to this version of the protocol.
27 March 2015	Clarity was provided with respect to protocol execution to ensure high quality data was captured throughout the study periods in both cohorts.
02 December 2015	Number of sites was updated from 110 to 120; The sample size of Cohort B was increased; Stratification for Cohort B was changed to by prior pirfenidone exposure, baseline lung function, and baseline serum periostin concentration; Updates were included to reflect the statistical power of each study cohort, to clarify the time period for the efficacy analysis of Cohort A, and how the missing data was handled for the analysis of primary endpoint.
23 October 2016	The objectives, endpoints, and statistical methods were updated; The randomization for Cohort B was modified to be stratified by region, baseline lung function, and baseline serum periostin concentration; The benefit-risk profile for lebrikizumab was updated based on the totality of data from completed studies.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported