Clinical trial results:
A randomised, double-blind, placebo-controlled, parallel group, dose-finding study evaluating efficacy, safety and tolerability of BI 1291583 qd over at least 24 weeks in patients with bronchiectasis (Airleaf™)

Summary

EudraCT number	2021-003304-41
Trial protocol	BE NL ES HU FR IT LV CZ DE GR DK PL PT BG
Global end of trial date	30 May 2024

Results information

Result version number	v1 (current)
This version publication date	12 June 2025
First version publication date	12 June 2025

Trial information

Trial identification

Sponsor protocol code	1397-0012

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05238675
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Boehringer Ingelheim
Sponsor organisation address	Binger Strasse 173, Ingelheim am Rhein, Germany, 55216
Public contact	Boehringer Ingelheim, Call Center, Boehringer Ingelheim, 001 18002430127, clintriage.rdg@boehringer-ingelheim.com
Scientific contact	Boehringer Ingelheim, Call Center, Boehringer Ingelheim, 001 18002430127, clintriage.rdg@boehringer-ingelheim.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	26 June 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 May 2024
Global end of trial reached?	Yes
Global end of trial date	30 May 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to demonstrate a non-flat dose response curve and evaluate the dose-response relationship for 3 oral dosing regimens of BI 1291583 versus placebo on the primary endpoint, the time to first pulmonary exacerbation up to week 48. The secondary objective was to demonstrate superiority of BI 1291583 5 mg versus placebo on the primary endpoint, the time to first pulmonary exacerbation up to week 48, as well as on the key secondary endpoint, the rate of pulmonary exacerbations up to week 48.

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were to be entered in the study. All subjects were free to withdraw from the clinical trial at any time for any reason given. Close monitoring of all subjects was adhered to throughout the trial conduct. Rescue medication was allowed for all subjects as required.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 April 2022
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	Australia: 35
Country: Number of subjects enrolled	Belgium: 8
Country: Number of subjects enrolled	Bulgaria: 21
Country: Number of subjects enrolled	Canada: 7
Country: Number of subjects enrolled	Czechia: 9
Country: Number of subjects enrolled	Denmark: 23
Country: Number of subjects enrolled	France: 12
Country: Number of subjects enrolled	Germany: 43
Country: Number of subjects enrolled	Greece: 1
Country: Number of subjects enrolled	Hungary: 21
Country: Number of subjects enrolled	Israel: 19
Country: Number of subjects enrolled	Italy: 9
Country: Number of subjects enrolled	Japan: 51
Country: Number of subjects enrolled	Korea, Republic of: 37
Country: Number of subjects enrolled	Latvia: 31
Country: Number of subjects enrolled	Mexico: 33
Country: Number of subjects enrolled	Netherlands: 11

Country: Number of subjects enrolled	Poland: 30
Country: Number of subjects enrolled	Portugal: 2
Country: Number of subjects enrolled	Spain: 13
Country: Number of subjects enrolled	Türkiye: 13
Country: Number of subjects enrolled	United Kingdom: 9
Country: Number of subjects enrolled	United States: 67
Worldwide total number of subjects	505
EEA total number of subjects	234

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)	249
From 65 to 84 years	255
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

This was a multi-center, randomised, placebo-controlled, double-blind, parallel group clinical trial in patients with bronchiectasis to investigate the efficacy, safety and tolerability of three different doses of BI 1291583 (orally, once daily). The treatment period was at least 24 and up to 48 weeks, with a follow-up period of 4 weeks.

Pre-assignment

Screening details:

All subjects were screened for eligibility prior to participation in the trial. Subjects attended a specialist site which ensured that they (the subjects) strictly met all inclusion and none of the exclusion criteria. Subjects were not to be allocated to a treatment group if any of the entry criteria were violated.

Period 1

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

Blinding implementation details:

Patients, investigators, central reviewers, and everyone involved in trial conduct or analysis or with any other interest in this double-blind trial were to remain blinded regarding the randomised treatment assignments until after final database lock.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Patients with bronchiectasis administered placebo matching BI 1291583 as tablets orally once a day in the morning for at least 24 weeks, and up to 48 weeks or until the end of trial, whichever happens first.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo matching BI 1291583 once a day in the morning for at least 24 weeks, and up to 48 weeks or until the end of trial, whichever happens first

Arm title	BI 1291583 1 mg

Arm description:

Patients with bronchiectasis administered one 1 milligram (mg) dose of BI 1291583 as a tablet orally once a day in the morning for at least 24 weeks, and up to 48 weeks or until the end of trial, whichever happens first.

Arm type	Experimental
Investigational medicinal product name	BI 1291583
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 mg dose of BI 1291583 once a day in the morning for at least 24 weeks, and up to 48 weeks or until the end of trial, whichever happens first.

Arm title	BI 1291583 2.5 mg

Arm description:

Patients with bronchiectasis administered one 2.5 mg dose of BI 1291583 as a tablet orally once a day in the morning for at least 24 weeks, and up to 48 weeks or until the end of trial, whichever happens first.

Arm type	Experimental
Investigational medicinal product name	BI 1291583
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

One 2.5 mg dose of BI 1291583 once a day in the morning for at least 24 weeks, and up to 48 weeks or until the end of trial, whichever happens first.

Arm title	BI 1291583 5 mg

Arm description:

Patients with bronchiectasis administered one 5 mg dose of BI 1291583 as a tablet orally once a day in the morning for at least 24 weeks, and up to 48 weeks or until the end of trial, whichever happens first.

Arm type	Experimental
Investigational medicinal product name	BI 1291583
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

One 5 mg dose of BI 1291583 once a day in the morning for at least 24 weeks, and up to 48 weeks or until the end of trial, whichever happens first.

Number of subjects in period 1[1]	Placebo	BI 1291583 1 mg	BI 1291583 2.5 mg
Started	109	53	53
Treated	109	53	53
Completed	95	49	48
Not completed	14	4	5
Consent withdrawn by subject	6	3	4
Physician decision	4	1	-
Lost to follow-up	1	-	-
Other than listed	3	-	1

Number of subjects in period 1[1]	BI 1291583 5 mg
Started	107
Treated	107
Completed	91
Not completed	16
Consent withdrawn by subject	12

Physician decision	-
Lost to follow-up	3
Other than listed	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Out of the 505 enrolled subjects, only 322 were treated.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Patients with bronchiectasis administered placebo matching BI 1291583 as tablets orally once a day in the morning for at least 24 weeks, and up to 48 weeks or until the end of trial, whichever happens first.	
Reporting group title	BI 1291583 1 mg
Reporting group description:	
Patients with bronchiectasis administered one 1 milligram (mg) dose of BI 1291583 as a tablet orally once a day in the morning for at least 24 weeks, and up to 48 weeks or until the end of trial, whichever happens first.	
Reporting group title	BI 1291583 2.5 mg
Reporting group description:	
Patients with bronchiectasis administered one 2.5 mg dose of BI 1291583 as a tablet orally once a day in the morning for at least 24 weeks, and up to 48 weeks or until the end of trial, whichever happens first.	
Reporting group title	BI 1291583 5 mg
Reporting group description:	
Patients with bronchiectasis administered one 5 mg dose of BI 1291583 as a tablet orally once a day in the morning for at least 24 weeks, and up to 48 weeks or until the end of trial, whichever happens first.	

Reporting group values	Placebo	BI 1291583 1 mg	BI 1291583 2.5 mg
Number of subjects	109	53	53
Age categorical			
Treated set (TS): includes all subjects who were randomized and were documented to have taken at least one dose of investigational treatment.			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	54	31	29
From 65-84 years	55	22	24
85 years and over	0	0	0
Age Continuous			
Treated set (TS): includes all subjects who were randomized and were documented to have taken at least one dose of investigational treatment.			
Units: years			
arithmetic mean	60.1	58.1	60.9
standard deviation	± 16.5	± 15.5	± 15.1
Sex: Female, Male			
Treated set (TS): includes all subjects who were randomized and were documented to have taken at least one dose of investigational treatment.			
Units: Subjects			
Female	67	33	27
Male	42	20	26

Race (NIH/OMB)			
Treated set (TS): includes all subjects who were randomized and were documented to have taken at least one dose of investigational treatment.			
Units: Subjects			
American Indian or Alaska Native	4	1	1
Asian	23	8	14
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	0	1
White	81	44	37
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB)			
Treated set (TS): includes all subjects who were randomized and were documented to have taken at least one dose of investigational treatment.			
Units: Subjects			
Hispanic or Latino	12	4	2
Not Hispanic or Latino	97	49	51
Unknown or Not Reported	0	0	0

Reporting group values	BI 1291583 5 mg	Total	
Number of subjects	107	322	
Age categorical			
Treated set (TS): includes all subjects who were randomized and were documented to have taken at least one dose of investigational treatment.			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	55	169	
From 65-84 years	51	152	
85 years and over	1	1	
Age Continuous			
Treated set (TS): includes all subjects who were randomized and were documented to have taken at least one dose of investigational treatment.			
Units: years			
arithmetic mean	59.8		
standard deviation	± 15.5	-	
Sex: Female, Male			
Treated set (TS): includes all subjects who were randomized and were documented to have taken at least one dose of investigational treatment.			
Units: Subjects			
Female	64	191	
Male	43	131	
Race (NIH/OMB)			
Treated set (TS): includes all subjects who were randomized and were documented to have taken at least one dose of investigational treatment.			
Units: Subjects			
American Indian or Alaska Native	2	8	

Asian	16	61	
Native Hawaiian or Other Pacific Islander	1	1	
Black or African American	0	2	
White	88	250	
More than one race	0	0	
Unknown or Not Reported	0	0	
Ethnicity (NIH/OMB)			
Treated set (TS): includes all subjects who were randomized and were documented to have taken at least one dose of investigational treatment.			
Units: Subjects			
Hispanic or Latino	6	24	
Not Hispanic or Latino	101	298	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Patients with bronchiectasis administered placebo matching BI 1291583 as tablets orally once a day in the morning for at least 24 weeks, and up to 48 weeks or until the end of trial, whichever happens first.	
Reporting group title	BI 1291583 1 mg
Reporting group description:	
Patients with bronchiectasis administered one 1 milligram (mg) dose of BI 1291583 as a tablet orally once a day in the morning for at least 24 weeks, and up to 48 weeks or until the end of trial, whichever happens first.	
Reporting group title	BI 1291583 2.5 mg
Reporting group description:	
Patients with bronchiectasis administered one 2.5 mg dose of BI 1291583 as a tablet orally once a day in the morning for at least 24 weeks, and up to 48 weeks or until the end of trial, whichever happens first.	
Reporting group title	BI 1291583 5 mg
Reporting group description:	
Patients with bronchiectasis administered one 5 mg dose of BI 1291583 as a tablet orally once a day in the morning for at least 24 weeks, and up to 48 weeks or until the end of trial, whichever happens first.	

Primary: Time to first pulmonary exacerbation up to 48 weeks after first drug administration

End point title	Time to first pulmonary exacerbation up to 48 weeks after first drug administration
End point description:	
The time to first pulmonary exacerbation up to 48 weeks after first drug administration is reported. A pulmonary exacerbation was defined as having 3 or more of the following symptoms for at least 48 hours resulting in a physician's decision to prescribe antibiotics: increased cough, increased sputum volume or change in sputum consistency, increased sputum purulence, increased breathlessness and/or decreased exercise tolerance, fatigue and/or malaise, hemoptysis. Dose or frequency change of background antibiotic treatment of ≥ 2-fold when administered for ≥ 3 symptoms met the definition of exacerbation. "Onset of exacerbation" was defined by the onset of first recorded symptom. All observed data up to 48 weeks were included in the analysis. 99999 (1mg): Upper limit of 95% Confidence Interval was not estimable due to the lack of events at later time points. 99999 (2.5 and 5 mg): Median was not reached. Upper limit of 95% Confidence Interval was not estimable. TS.	
End point type	Primary
End point timeframe:	
From first drug administration, up to 48 weeks.	

End point values	Placebo	BI 1291583 1 mg	BI 1291583 2.5 mg	BI 1291583 5 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	109	53	53	107
Units: Week				
median (confidence interval 95%)	29.6 (23.0 to 37.6)	31.7 (20.0 to 99999)	99999 (23.6 to 99999)	99999 (30.3 to 99999)

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

A multiple comparison procedure with modelling technique (MCPMod) was used to test a non-flat dose response relationship for 3 doses vs placebo. Four possible dose-response patterns were simultaneously analyzed at the 1-sided α-level of 0.05. As a basis for the MCPMod analysis, a Cox regression model on the primary endpoint was used. The model included treatment and the stratification factors P. aeruginosa status (positive vs negative) and maintenance use of macrolides (yes vs no) at baseline.

Comparison groups	Placebo v BI 1291583 1 mg v BI 1291583 2.5 mg v BI 1291583 5 mg
Number of subjects included in analysis	322
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0.0448 [2]
Method	MCPMod Emax1 model

Notes:

[1] - MCPMod Emax1 model assumption: 50% of the maximum effect is achieved at 2.5 mg dose.

[2] - Adjusted p-value from multiple contrast test.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

A multiple comparison procedure with modelling technique (MCPMod) was used to test a non-flat dose response relationship for 3 doses vs placebo. Four possible dose-response patterns were simultaneously analyzed at the 1-sided α-level of 0.05. As a basis for the MCPMod analysis, a Cox regression model on the primary endpoint was used. The model included treatment and the stratification factors P. aeruginosa status (positive vs negative) and maintenance use of macrolides (yes vs no) at baseline.

Comparison groups	Placebo v BI 1291583 1 mg v BI 1291583 2.5 mg v BI 1291583 5 mg
Number of subjects included in analysis	322
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	= 0.1216 [4]
Method	MCPMod Exponential model

Notes:

[3] - MCPMod Exponential model assumption: 10% of the maximum effect is achieved at 2.5 mg dose.

[4] - Adjusted p-value from multiple contrast test.

Statistical analysis title	Statistical analysis 7

Statistical analysis description:

Ratios were obtained from a Cox regression model on the primary endpoint, time to first pulmonary exacerbation up to Week 48 was used. The model included treatment and the stratification factors P. aeruginosa status (positive vs negative) and maintenance use of macrolides (yes vs no) at baseline. As per protocol, hypothesis testing was done only on the BI 1291583 5 mg dose group.

Comparison groups	Placebo v BI 1291583 5 mg

Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	other[5]
P-value	= 0.0857
Method	Wald test
Parameter estimate	Cox proportional hazard
Point estimate	0.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.48
upper limit	1.05

Notes:

[5] - BI 1291583 5 mg/Placebo

Statistical analysis title	Statistical analysis 5

Statistical analysis description:

Ratios were obtained from a Cox regression model on the primary endpoint, time to first pulmonary exacerbation up to Week 48 was used. The model included treatment and the stratification factors P. aeruginosa status (positive vs negative) and maintenance use of macrolides (yes vs no) at baseline. As per protocol, hypothesis testing was done only on the BI 1291583 5 mg dose group.

Comparison groups	Placebo v BI 1291583 1 mg
Number of subjects included in analysis	162
Analysis specification	Pre-specified
Analysis type	other[6]
Parameter estimate	Cox proportional hazard
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	1.45

Notes:

[6] - BI 1291583 1 mg/Placebo

Statistical analysis title	Statistical analysis 6

Statistical analysis description:

Ratios were obtained from a Cox regression model on the primary endpoint, time to first pulmonary exacerbation up to Week 48 was used. The model included treatment and the stratification factors P. aeruginosa status (positive vs negative) and maintenance use of macrolides (yes vs no) at baseline. As per protocol, hypothesis testing was done only on the BI 1291583 5 mg dose group.

Comparison groups	Placebo v BI 1291583 2.5 mg
Number of subjects included in analysis	162
Analysis specification	Pre-specified
Analysis type	other[7]
Parameter estimate	Cox proportional hazard
Point estimate	0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	1.08

Notes:

[7] - BI 1291583 2.5 mg/Placebo

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

A multiple comparison procedure with modelling technique (MCPMod) was used to test a non-flat dose response relationship for 3 doses vs placebo. Four possible dose-response patterns were simultaneously analyzed at the 1-sided α-level of 0.05. As a basis for the MCPMod analysis, a Cox regression model on the primary endpoint was used. The model included treatment and the stratification factors P. aeruginosa status (positive vs negative) and maintenance use of macrolides (yes vs no) at baseline.

Comparison groups	Placebo v BI 1291583 1 mg v BI 1291583 2.5 mg v BI 1291583 5 mg
Number of subjects included in analysis	322
Analysis specification	Pre-specified
Analysis type	other[8]
P-value	= 0.0665 [9]
Method	MCPMod Emax2 model

Notes:

[8] - MCPMod Emax2 model assumption: 80% of the maximum effect is achieved at 1 mg dose.

[9] - Adjusted p-value from multiple contrast test.

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

A multiple comparison procedure with modelling technique (MCPMod) was used to test a non-flat dose response relationship for 3 doses vs placebo. Four possible dose-response patterns were simultaneously analyzed at the 1-sided α-level of 0.05. As a basis for the MCPMod analysis, a Cox regression model on the primary endpoint was used. The model included treatment and the stratification factors P. aeruginosa status (positive vs negative) and maintenance use of macrolides (yes vs no) at baseline.

Comparison groups	Placebo v BI 1291583 1 mg v BI 1291583 2.5 mg v BI 1291583 5 mg
Number of subjects included in analysis	322
Analysis specification	Pre-specified
Analysis type	other[10]
P-value	= 0.0573 [11]
Method	MCPMod Linear model

Notes:

[10] - MCPMod Linear model: no assumptions.

[11] - Adjusted p-value from multiple contrast test.

Secondary: Key secondary outcome measure: rate of pulmonary exacerbations (number of events per person-time) up to week 48 after first drug administration

End point title	Key secondary outcome measure: rate of pulmonary exacerbations (number of events per person-time) up to week 48 after first drug administration

End point description:

The rate of pulmonary exacerbations (number of events per person-time) up to week 48 after first drug administration is reported. Adjusted event rates were obtained using a negative binomial regression model adjusting for the categorical variable treatment (all 4 treatment groups), P. aeruginosa status (positive vs negative) and the maintenance use of macrolides (yes vs no) at baseline as well as the logarithm of the duration of observational time (in years) as an offset. All observed data up to 48 weeks were included in the analysis.
Treated set (TS): includes all subjects who were randomized and were documented to have taken at least one dose of investigational treatment.

End point type	Secondary

End point timeframe:

From first drug administration, up to 48 weeks.

End point values	Placebo	BI 1291583 1 mg	BI 1291583 2.5 mg	BI 1291583 5 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	109	53	53	107
Units: Events per person-year				
number (confidence interval 95%)	1.25 (0.96 to 1.63)	1.30 (0.91 to 1.86)	0.85 (0.56 to 1.28)	1.11 (0.84 to 1.47)

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Adjusted event rate ratios were obtained using a negative binomial regression model adjusting for the categorical variable treatment (all 4 treatment groups), P. aeruginosa status (positive vs negative) and the maintenance use of macrolides (yes vs no) at baseline as well as the logarithm of the duration of observational time (in years) as an offset.

Comparison groups	Placebo v BI 1291583 1 mg
Number of subjects included in analysis	162
Analysis specification	Pre-specified
Analysis type	other[12]
Parameter estimate	Adjusted event rate ratio
Point estimate	1.034
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.685
upper limit	1.563
Variability estimate	Standard error of the mean
Dispersion value	0.218

Notes:

[12] - BI 1291583 1 mg/Placebo

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Adjusted event rate ratios were obtained using a negative binomial regression model adjusting for the categorical variable treatment (all 4 treatment groups), P. aeruginosa status (positive vs negative) and the maintenance use of macrolides (yes vs no) at baseline as well as the logarithm of the duration of observational time (in years) as an offset.

Comparison groups	Placebo v BI 1291583 5 mg
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	other[13]
Parameter estimate	Adjusted event rate ratio
Point estimate	0.886

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.626
upper limit	1.256
Variability estimate	Standard error of the mean
Dispersion value	0.158

Notes:

[13] - BI 1291583 5 mg/Placebo

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Adjusted event rate ratios were obtained using a negative binomial regression model adjusting for the categorical variable treatment (all 4 treatment groups), P. aeruginosa status (positive vs negative) and the maintenance use of macrolides (yes vs no) at baseline as well as the logarithm of the duration of observational time (in years) as an offset.

Comparison groups	Placebo v BI 1291583 2.5 mg
Number of subjects included in analysis	162
Analysis specification	Pre-specified
Analysis type	other[14]
Parameter estimate	Adjusted event rate ratio
Point estimate	0.677
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.426
upper limit	1.076
Variability estimate	Standard error of the mean
Dispersion value	0.16

Notes:

[14] - BI 1291583 2.5 mg/Placebo

Secondary: Absolute change from baseline in Quality of Life Questionnaire – Bronchiectasis (QOL-B) respiratory symptoms domain score at week 24 after first drug administration

End point title	Absolute change from baseline in Quality of Life Questionnaire – Bronchiectasis (QOL-B) respiratory symptoms domain score at week 24 after first drug administration

End point description:

Absolute change from baseline in QOL-B respiratory symptoms domain score at week 24 after first drug administration is reported. The QOL-B, a self-administered, patient-reported outcome measure assessing symptoms, functioning and health-related quality of life for subjects with bronchiectasis, contains 37 items on 8 scales (Respiratory Symptoms, Physical, Role, Emotional and Social Functioning, Vitality, Health Perceptions and Treatment Burden). The score range is 0-100, a higher score indicates fewer symptoms or better health status. Adjusted means were obtained using a REML estimation for the QOL-B respiratory symptoms domain based on a ANCOVA model. This model included treatment, P. aeruginosa status (positive vs negative) and the maintenance use of macrolides (yes vs no) at baseline as discrete fixed effects and baseline QOL-B respiratory symptoms domain score as continuous fixed effect.
TS. Patients with baseline and at least one on−treatment post−baseline value were included.

End point type	Secondary

End point timeframe:

Before the first drug administration (baseline, week 0) and 24 weeks after first drug administration.

End point values	Placebo	BI 1291583 1 mg	BI 1291583 2.5 mg	BI 1291583 5 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	103	52	51	99
Units: Score on a scale				
least squares mean (confidence interval 95%)	5.87 (3.03 to 8.71)	8.03 (4.03 to 12.03)	7.59 (3.55 to 11.63)	6.82 (3.92 to 9.72)

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Adjusted means were obtained using a restricted maximum likelihood (REML) estimation for the QOL-B respiratory symptoms domain based on an analysis of covariance (ANCOVA) model. This model included treatment, P. aeruginosa status (positive vs negative) and the maintenance use of macrolides (yes vs no) at baseline as discrete fixed effects and baseline QOL-B respiratory symptoms domain score as continuous fixed effect.

Comparison groups	Placebo v BI 1291583 1 mg
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	other[15]
Parameter estimate	Difference of adjusted means
Point estimate	2.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.75
upper limit	7.06
Variability estimate	Standard error of the mean
Dispersion value	2.49

Notes:

[15] - BI 1291583 1 mg - Placebo

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Adjusted means were obtained using a restricted maximum likelihood (REML) estimation for the QOL-B respiratory symptoms domain based on an analysis of covariance (ANCOVA) model. This model included treatment, P. aeruginosa status (positive vs negative) and the maintenance use of macrolides (yes vs no) at baseline as discrete fixed effects and baseline QOL-B respiratory symptoms domain score as continuous fixed effect.

Comparison groups	Placebo v BI 1291583 5 mg
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	other[16]
Parameter estimate	Difference of adjusted means
Point estimate	0.95

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.11
upper limit	5.01
Variability estimate	Standard error of the mean
Dispersion value	2.06

Notes:

[16] - BI 1291583 5 mg - Placebo

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Adjusted means were obtained using a restricted maximum likelihood (REML) estimation for the QOL-B respiratory symptoms domain based on an analysis of covariance (ANCOVA) model. This model included treatment, P. aeruginosa status (positive vs negative) and the maintenance use of macrolides (yes vs no) at baseline as discrete fixed effects and baseline QOL-B respiratory symptoms domain score as continuous fixed effect.

Comparison groups	Placebo v BI 1291583 2.5 mg
Number of subjects included in analysis	154
Analysis specification	Pre-specified
Analysis type	other[17]
Parameter estimate	Difference of adjusted means
Point estimate	1.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.22
upper limit	6.65
Variability estimate	Standard error of the mean
Dispersion value	2.51

Notes:

[17] - BI 1291583 2.5 mg - Placebo

Secondary: Relative change from baseline in neutrophil elastase (NE) activity in sputum at week 12 after first drug administration

End point title	Relative change from baseline in neutrophil elastase (NE) activity in sputum at week 12 after first drug administration

End point description:

The relative change from baseline in absolute neutrophil elastase (NE) activity in sputum at week 12 after first drug administration is reported.
Treated set (TS): includes all subjects who were randomized and were documented to have taken at least one dose of investigational treatment. Patients with baseline and a measurement at week 12 were included.

End point type	Secondary

End point timeframe:

Before the first drug administration (baseline: mean value of Screening and week 0 prior to the first treatment intake) and 12 weeks after first drug administration.

End point values	Placebo	BI 1291583 1 mg	BI 1291583 2.5 mg	BI 1291583 5 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	88	41	44	74
Units: RFU (Relative Fluorescent Unit)				
arithmetic mean (standard deviation)	2413.87 (± 19801.27)	760.71 (± 2837.37)	79.74 (± 549.53)	705.40 (± 4960.86)

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline in St. George’s Respiratory Questionnaire (SGRQ) Symptoms score at week 24 after first drug administration

End point title	Absolute change from baseline in St. George’s Respiratory Questionnaire (SGRQ) Symptoms score at week 24 after first drug administration

End point description:

Absolute change from baseline in SGRQ Symptoms score at week 24 after first drug administration is reported. The SGRQ, designed to measure health impairment in patients with Chronic Obstructive Pulmonary Disease, is divided into 2 parts measuring 3 domains: symptoms (part 1); activity limitation and social and emotional impact of disease (part 2). Total score is calculated by dividing the summed weights from the positive items in the questionnaire by the adjusted maximum possible weight. The result is expressed as a percentage: 100 represents the worst possible, and 0 the best possible health status.
Adjusted means were obtained using a REML estimation based on an ANCOVA model. The model included treatment, P. aeruginosa status (positive vs negative) and maintenance use of macrolides (yes vs no) at baseline as discrete fixed effects, baseline SGRQ Symptoms score as a continuous fixed effect. TS. Patients with baseline and at least one on−treatment post−baseline value were included.

End point type	Secondary

End point timeframe:

Before the first drug administration (baseline, week 0) and 24 weeks after first drug administration.

End point values	Placebo	BI 1291583 1 mg	BI 1291583 2.5 mg	BI 1291583 5 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	103	52	51	99
Units: Score on a scale				
least squares mean (confidence interval 95%)	-5.64 (-9.11 to -2.16)	-7.22 (-12.12 to -2.31)	-8.97 (-13.92 to -4.02)	-7.92 (-11.47 to -4.37)

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Adjusted means were obtained using a REML estimation based on an ANCOVA model. This model included treatment, P. aeruginosa status (positive vs negative) and the maintenance use of macrolides (yes vs no) at baseline as discrete fixed effects and baseline SGRQ Symptoms score as a continuous fixed effect.

Comparison groups	Placebo v BI 1291583 1 mg

Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	other[18]
Parameter estimate	Difference of adjusted means
Point estimate	-1.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.59
upper limit	4.43
Variability estimate	Standard error of the mean
Dispersion value	3.05

Notes:

[18] - BI 1291583 1 mg - Placebo

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Adjusted means were obtained using a REML estimation based on an ANCOVA model. This model included treatment, P. aeruginosa status (positive vs negative) and the maintenance use of macrolides (yes vs no) at baseline as discrete fixed effects and baseline SGRQ Symptoms score as a continuous fixed effect.

Comparison groups	Placebo v BI 1291583 5 mg
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	other[19]
Parameter estimate	Difference of adjusted means
Point estimate	-2.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.26
upper limit	2.68
Variability estimate	Standard error of the mean
Dispersion value	2.53

Notes:

[19] - BI 1291583 5 mg - Placebo

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Adjusted means were obtained using a REML estimation based on an ANCOVA model. This model included treatment, P. aeruginosa status (positive vs negative) and the maintenance use of macrolides (yes vs no) at baseline as discrete fixed effects and baseline SGRQ Symptoms score as a continuous fixed effect.

Comparison groups	Placebo v BI 1291583 2.5 mg
Number of subjects included in analysis	154
Analysis specification	Pre-specified
Analysis type	other[20]
Parameter estimate	Difference of adjusted means
Point estimate	-3.33

Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.38
upper limit	2.72
Variability estimate	Standard error of the mean
Dispersion value	3.07

Notes:

[20] - BI 1291583 2.5 mg - Placebo

Secondary: Absolute change from baseline in percent predicted post-bronchodilator forced expiratory volume in one second (FEV1%pred) at week 24 after first drug administration

End point title	Absolute change from baseline in percent predicted post-bronchodilator forced expiratory volume in one second (FEV1%pred) at week 24 after first drug administration

End point description:

The absolute change from baseline in percent predicted post-bronchodilator forced expiratory volume in one second (FEV1%pred) at week 24 after first drug administration is reported. A REML based approach using a MMRM was used. The model included fixed, categorical effects of treatment at each visit, P. aeruginosa status (positive vs negative) and the maintenance use of macrolides (yes vs no) at baseline and the fixed continuous effects of baseline FEV1 % pred at each visit. Visit were treated as the repeated measure with an unstructured covariance structure used to model the within patient measurements.
Treated set (TS): includes all subjects who were randomized and were documented to have taken at least one dose of investigational treatment. Patients with baseline and at least one on−treatment post−baseline value were included.

End point type	Secondary

End point timeframe:

Before the first drug administration (baseline, week 0) and 24 weeks after first drug administration.

End point values	Placebo	BI 1291583 1 mg	BI 1291583 2.5 mg	BI 1291583 5 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	105	53	53	99
Units: % of predicted post-bronchodilator FEV1				
least squares mean (confidence interval 95%)	-1.05 (-2.38 to 0.28)	-0.14 (-2.00 to 1.71)	1.16 (-0.71 to 3.03)	-0.90 (-2.30 to 0.50)

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

A REML based approach using a MMRM was used. The model included fixed, categorical effects of treatment at each visit, P. aeruginosa status (positive vs negative) and the maintenance use of macrolides (yes vs no) at baseline and the fixed continuous effects of baseline FEV1 % pred at each visit. Visit were treated as the repeated measure with an unstructured covariance structure used to model the within patient measurements.

Comparison groups	Placebo v BI 1291583 1 mg

Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	other[21]
Parameter estimate	Difference of adjusted means
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.38
upper limit	3.19
Variability estimate	Standard error of the mean
Dispersion value	1.16

Notes:

[21] - BI 1291583 1 mg - Placebo

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

A REML based approach using a MMRM was used. The model included fixed, categorical effects of treatment at each visit, P. aeruginosa status (positive vs negative) and the maintenance use of macrolides (yes vs no) at baseline and the fixed continuous effects of baseline FEV1 % pred at each visit. Visit were treated as the repeated measure with an unstructured covariance structure used to model the within patient measurements.

Comparison groups	Placebo v BI 1291583 5 mg
Number of subjects included in analysis	204
Analysis specification	Pre-specified
Analysis type	other[22]
Parameter estimate	Difference of adjusted means
Point estimate	0.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.79
upper limit	2.08
Variability estimate	Standard error of the mean
Dispersion value	0.98

Notes:

[22] - BI 1291583 5 mg - Placebo

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

A REML based approach using a MMRM was used. The model included fixed, categorical effects of treatment at each visit, P. aeruginosa status (positive vs negative) and the maintenance use of macrolides (yes vs no) at baseline and the fixed continuous effects of baseline FEV1 % pred at each visit. Visit were treated as the repeated measure with an unstructured covariance structure used to model the within patient measurements.

Comparison groups	Placebo v BI 1291583 2.5 mg
Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	other[23]
Parameter estimate	Difference of adjusted means
Point estimate	2.21

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.09
upper limit	4.51
Variability estimate	Standard error of the mean
Dispersion value	1.17

Notes:

[23] - BI 1291583 2.5 mg - Placebo

Secondary: Occurrence of an exacerbation by week 24 after first drug administration

End point title	Occurrence of an exacerbation by week 24 after first drug administration

End point description:

The occurrence of an exacerbation by week 24 after first drug administration is reported. The proportion of patients with an exacerbation within 24 weeks after first drug administration was based on a Kaplan Meier analysis.
Treated set (TS): includes all subjects who were randomized and were documented to have taken at least one dose of investigational treatment.

End point type	Secondary

End point timeframe:

From first drug administration, up to 24 weeks.

End point values	Placebo	BI 1291583 1 mg	BI 1291583 2.5 mg	BI 1291583 5 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	109	53	53	107
Units: Proportion of patients				
number (not applicable)	0.415	0.442	0.358	0.334

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Kaplan Meier survival probability at week 24 were compared between each BI 1291583 dose and placebo and the variance of each Kaplan Meier estimate was calculated by the Greenwood’s formula.

Comparison groups	Placebo v BI 1291583 1 mg
Number of subjects included in analysis	162
Analysis specification	Pre-specified
Analysis type	other[24]
Parameter estimate	Risk difference (RD)
Point estimate	0.027
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.137
upper limit	0.19

Notes:

[24] - BI 1291583 1 mg - Placebo

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Kaplan Meier survival probability at week 24 were compared between each BI 1291583 dose and placebo and the variance of each Kaplan Meier estimate was calculated by the Greenwood’s formula.

Comparison groups	Placebo v BI 1291583 5 mg
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	other[25]
Parameter estimate	Risk difference (RD)
Point estimate	-0.081
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.211
upper limit	0.048

Notes:

[25] - BI 1291583 5 mg - Placebo

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Kaplan Meier survival probability at week 24 were compared between each BI 1291583 dose and placebo and the variance of each Kaplan Meier estimate was calculated by the Greenwood’s formula.

Comparison groups	Placebo v BI 1291583 2.5 mg
Number of subjects included in analysis	162
Analysis specification	Pre-specified
Analysis type	other[26]
Parameter estimate	Risk difference (RD)
Point estimate	-0.057
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.216
upper limit	0.103

Notes:

[26] - BI 1291583 2.5 mg - Placebo

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first administration of study drug until 28 days (residual effect period) after last administration of study drug, up to 52 weeks.

Adverse event reporting additional description:

Treated set (TS): includes all subjects who were randomized and were documented to have taken at least one dose of investigational treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Patients with bronchiectasis administered placebo matching BI 1291583 as tablets orally once a day in the morning for at least 24 weeks, and up to 48 weeks or until the end of trial, whichever happens first.

Reporting group title	BI 1291583 5 mg

Reporting group description:

Patients with bronchiectasis administered one 5 mg dose of BI 1291583 as a tablet orally once a day in the morning for at least 24 weeks, and up to 48 weeks or until the end of trial, whichever happens first.

Reporting group title	BI 1291583 2.5 mg

Reporting group description:

Patients with bronchiectasis administered one 2.5 mg dose of BI 1291583 as a tablet orally once a day in the morning for at least 24 weeks, and up to 48 weeks or until the end of trial, whichever happens first.

Reporting group title	BI 1291583 1 mg

Reporting group description:

Patients with bronchiectasis administered one 1 milligram (mg) dose of BI 1291583 as a tablet orally once a day in the morning for at least 24 weeks, and up to 48 weeks or until the end of trial, whichever happens first.

Serious adverse events	Placebo	BI 1291583 5 mg	BI 1291583 2.5 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	30 / 109 (27.52%)	22 / 107 (20.56%)	6 / 53 (11.32%)
number of deaths (all causes)	1	1	0
number of deaths resulting from adverse events	0	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Soft tissue sarcoma			
subjects affected / exposed	0 / 109 (0.00%)	0 / 107 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			

subjects affected / exposed	1 / 109 (0.92%)	0 / 107 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestine adenocarcinoma			
subjects affected / exposed	0 / 109 (0.00%)	1 / 107 (0.93%)	0 / 53 (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
Bowen's disease			
subjects affected / exposed	0 / 109 (0.00%)	1 / 107 (0.93%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Hernia			
subjects affected / exposed	0 / 109 (0.00%)	0 / 107 (0.00%)	0 / 53 (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
Disease progression			
subjects affected / exposed	1 / 109 (0.92%)	0 / 107 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 109 (0.00%)	1 / 107 (0.93%)	0 / 53 (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
Immunodeficiency			
subjects affected / exposed	1 / 109 (0.92%)	0 / 107 (0.00%)	0 / 53 (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
Reproductive system and breast disorders			
Ovarian cyst			

subjects affected / exposed	0 / 109 (0.00%)	0 / 107 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 109 (0.00%)	1 / 107 (0.93%)	0 / 53 (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
Acute respiratory failure			
subjects affected / exposed	1 / 109 (0.92%)	0 / 107 (0.00%)	0 / 53 (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
Nasal septum deviation			
subjects affected / exposed	1 / 109 (0.92%)	0 / 107 (0.00%)	0 / 53 (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
Haemoptysis			
subjects affected / exposed	1 / 109 (0.92%)	0 / 107 (0.00%)	0 / 53 (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
Dysaesthesia pharynx			
subjects affected / exposed	0 / 109 (0.00%)	0 / 107 (0.00%)	0 / 53 (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
Chronic respiratory failure			
subjects affected / exposed	0 / 109 (0.00%)	1 / 107 (0.93%)	0 / 53 (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
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 109 (0.92%)	0 / 107 (0.00%)	0 / 53 (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
Bronchiectasis			

subjects affected / exposed	9 / 109 (8.26%)	5 / 107 (4.67%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 9	0 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasal turbinate hypertrophy			
subjects affected / exposed	1 / 109 (0.92%)	0 / 107 (0.00%)	0 / 53 (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
Obstructive sleep apnoea syndrome			
subjects affected / exposed	1 / 109 (0.92%)	0 / 107 (0.00%)	0 / 53 (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
Organising pneumonia			
subjects affected / exposed	1 / 109 (0.92%)	0 / 107 (0.00%)	0 / 53 (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
Pneumomediastinum			
subjects affected / exposed	1 / 109 (0.92%)	0 / 107 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	1 / 109 (0.92%)	0 / 107 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	1 / 109 (0.92%)	0 / 107 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Limb injury			
subjects affected / exposed	1 / 109 (0.92%)	0 / 107 (0.00%)	0 / 53 (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

Rib fracture			
subjects affected / exposed	0 / 109 (0.00%)	0 / 107 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper limb fracture			
subjects affected / exposed	0 / 109 (0.00%)	1 / 107 (0.93%)	0 / 53 (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
Contusion			
subjects affected / exposed	0 / 109 (0.00%)	0 / 107 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 109 (0.00%)	0 / 107 (0.00%)	0 / 53 (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
Congenital, familial and genetic disorders			
Urachal abnormality			
subjects affected / exposed	1 / 109 (0.92%)	0 / 107 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 109 (0.00%)	0 / 107 (0.00%)	1 / 53 (1.89%)
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	1 / 109 (0.92%)	0 / 107 (0.00%)	0 / 53 (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 / 109 (0.00%)	0 / 107 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Arrhythmia			
subjects affected / exposed	1 / 109 (0.92%)	0 / 107 (0.00%)	0 / 53 (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			
Bell's palsy			
subjects affected / exposed	0 / 109 (0.00%)	0 / 107 (0.00%)	0 / 53 (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
Dizziness			
subjects affected / exposed	0 / 109 (0.00%)	0 / 107 (0.00%)	0 / 53 (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
Transient ischaemic attack			
subjects affected / exposed	0 / 109 (0.00%)	1 / 107 (0.93%)	0 / 53 (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
Ear and labyrinth disorders			
Sudden hearing loss			
subjects affected / exposed	1 / 109 (0.92%)	0 / 107 (0.00%)	0 / 53 (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
Eye disorders			
Macular hole			
subjects affected / exposed	0 / 109 (0.00%)	0 / 107 (0.00%)	0 / 53 (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
Macular degeneration			
subjects affected / exposed	1 / 109 (0.92%)	0 / 107 (0.00%)	0 / 53 (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
Retinal tear			

subjects affected / exposed	0 / 109 (0.00%)	0 / 107 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	0 / 109 (0.00%)	1 / 107 (0.93%)	0 / 53 (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
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 109 (0.00%)	2 / 107 (1.87%)	0 / 53 (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
Cholecystitis			
subjects affected / exposed	0 / 109 (0.00%)	1 / 107 (0.93%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Cervical spinal stenosis			
subjects affected / exposed	1 / 109 (0.92%)	0 / 107 (0.00%)	0 / 53 (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
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 109 (0.92%)	0 / 107 (0.00%)	0 / 53 (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
Chronic sinusitis			
subjects affected / exposed	1 / 109 (0.92%)	0 / 107 (0.00%)	0 / 53 (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
Cellulitis			

subjects affected / exposed	1 / 109 (0.92%)	0 / 107 (0.00%)	0 / 53 (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
COVID-19			
subjects affected / exposed	2 / 109 (1.83%)	1 / 107 (0.93%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 109 (0.00%)	0 / 107 (0.00%)	0 / 53 (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 abscess			
subjects affected / exposed	1 / 109 (0.92%)	0 / 107 (0.00%)	0 / 53 (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
Lower respiratory tract infection viral			
subjects affected / exposed	1 / 109 (0.92%)	0 / 107 (0.00%)	0 / 53 (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
Influenza			
subjects affected / exposed	0 / 109 (0.00%)	2 / 107 (1.87%)	0 / 53 (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
Infective exacerbation of bronchiectasis			
subjects affected / exposed	5 / 109 (4.59%)	3 / 107 (2.80%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 7	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	2 / 109 (1.83%)	5 / 107 (4.67%)	3 / 53 (5.66%)
occurrences causally related to treatment / all	0 / 2	0 / 5	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			

subjects affected / exposed	3 / 109 (2.75%)	1 / 107 (0.93%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 6	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia respiratory syncytial viral			
subjects affected / exposed	1 / 109 (0.92%)	0 / 107 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	1 / 109 (0.92%)	0 / 107 (0.00%)	0 / 53 (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
Lyme disease			
subjects affected / exposed	1 / 109 (0.92%)	0 / 107 (0.00%)	0 / 53 (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
Parainfluenzae virus infection			
subjects affected / exposed	0 / 109 (0.00%)	2 / 107 (1.87%)	0 / 53 (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

Serious adverse events	BI 1291583 1 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 53 (15.09%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Soft tissue sarcoma			
subjects affected / exposed	0 / 53 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 53 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Small intestine adenocarcinoma			
subjects affected / exposed	0 / 53 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bowen's disease			
subjects affected / exposed	0 / 53 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Hernia			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Disease progression			
subjects affected / exposed	0 / 53 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 53 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immunodeficiency			
subjects affected / exposed	0 / 53 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma			

subjects affected / exposed	0 / 53 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute respiratory failure				
subjects affected / exposed	0 / 53 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nasal septum deviation				
subjects affected / exposed	0 / 53 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemoptysis				
subjects affected / exposed	0 / 53 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dysaesthesia pharynx				
subjects affected / exposed	1 / 53 (1.89%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chronic respiratory failure				
subjects affected / exposed	0 / 53 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chronic obstructive pulmonary disease				
subjects affected / exposed	0 / 53 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchiectasis				
subjects affected / exposed	0 / 53 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nasal turbinate hypertrophy				

subjects affected / exposed	0 / 53 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Obstructive sleep apnoea syndrome				
subjects affected / exposed	0 / 53 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Organising pneumonia				
subjects affected / exposed	0 / 53 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumomediastinum				
subjects affected / exposed	0 / 53 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	0 / 53 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Suicidal ideation				
subjects affected / exposed	0 / 53 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Limb injury				
subjects affected / exposed	0 / 53 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rib fracture				
subjects affected / exposed	1 / 53 (1.89%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Upper limb fracture				
subjects affected / exposed	0 / 53 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Contusion				
subjects affected / exposed	1 / 53 (1.89%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Fall				
subjects affected / exposed	1 / 53 (1.89%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Congenital, familial and genetic disorders				
Urachal abnormality				
subjects affected / exposed	0 / 53 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Tachycardia				
subjects affected / exposed	0 / 53 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure				
subjects affected / exposed	0 / 53 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				
subjects affected / exposed	0 / 53 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Arrhythmia				
subjects affected / exposed	0 / 53 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Nervous system disorders			
Bell's palsy			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dizziness			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Transient ischaemic attack			
subjects affected / exposed	0 / 53 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Sudden hearing loss			
subjects affected / exposed	0 / 53 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Macular hole			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Macular degeneration			
subjects affected / exposed	0 / 53 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Retinal tear			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastritis			

subjects affected / exposed	0 / 53 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 53 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cholecystitis			
subjects affected / exposed	0 / 53 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Cervical spinal stenosis			
subjects affected / exposed	0 / 53 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 53 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chronic sinusitis			
subjects affected / exposed	0 / 53 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	0 / 53 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
COVID-19			
subjects affected / exposed	0 / 53 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Infection				
subjects affected / exposed	1 / 53 (1.89%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lung abscess				
subjects affected / exposed	0 / 53 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection viral				
subjects affected / exposed	0 / 53 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	0 / 53 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infective exacerbation of bronchiectasis				
subjects affected / exposed	2 / 53 (3.77%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	0 / 53 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia bacterial				
subjects affected / exposed	0 / 53 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia respiratory syncytial viral				
subjects affected / exposed	0 / 53 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection				

subjects affected / exposed	0 / 53 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lyme disease			
subjects affected / exposed	0 / 53 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Parainfluenzae virus infection			
subjects affected / exposed	0 / 53 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo	BI 1291583 5 mg	BI 1291583 2.5 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	81 / 109 (74.31%)	69 / 107 (64.49%)	38 / 53 (71.70%)
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 109 (2.75%)	1 / 107 (0.93%)	4 / 53 (7.55%)
occurrences (all)	3	1	4
Nervous system disorders			
Headache			
subjects affected / exposed	11 / 109 (10.09%)	6 / 107 (5.61%)	2 / 53 (3.77%)
occurrences (all)	12	6	2
Dizziness			
subjects affected / exposed	3 / 109 (2.75%)	2 / 107 (1.87%)	3 / 53 (5.66%)
occurrences (all)	3	2	3
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	8 / 109 (7.34%)	5 / 107 (4.67%)	0 / 53 (0.00%)
occurrences (all)	8	5	0
Pyrexia			
subjects affected / exposed	6 / 109 (5.50%)	3 / 107 (2.80%)	0 / 53 (0.00%)
occurrences (all)	10	3	0

Gastrointestinal disorders			
Nausea			
subjects affected / exposed	2 / 109 (1.83%)	1 / 107 (0.93%)	3 / 53 (5.66%)
occurrences (all)	2	1	3
Diarrhoea			
subjects affected / exposed	10 / 109 (9.17%)	5 / 107 (4.67%)	1 / 53 (1.89%)
occurrences (all)	12	5	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	10 / 109 (9.17%)	10 / 107 (9.35%)	9 / 53 (16.98%)
occurrences (all)	11	17	10
Bronchiectasis			
subjects affected / exposed	30 / 109 (27.52%)	33 / 107 (30.84%)	15 / 53 (28.30%)
occurrences (all)	40	61	22
Dyspnoea			
subjects affected / exposed	6 / 109 (5.50%)	10 / 107 (9.35%)	2 / 53 (3.77%)
occurrences (all)	6	14	2
Haemoptysis			
subjects affected / exposed	9 / 109 (8.26%)	2 / 107 (1.87%)	1 / 53 (1.89%)
occurrences (all)	14	2	2
Sputum increased			
subjects affected / exposed	7 / 109 (6.42%)	9 / 107 (8.41%)	3 / 53 (5.66%)
occurrences (all)	8	13	3
Oropharyngeal pain			
subjects affected / exposed	1 / 109 (0.92%)	3 / 107 (2.80%)	2 / 53 (3.77%)
occurrences (all)	1	3	3
Skin and subcutaneous tissue disorders			
Skin exfoliation			
subjects affected / exposed	1 / 109 (0.92%)	7 / 107 (6.54%)	1 / 53 (1.89%)
occurrences (all)	2	9	1
Dry skin			
subjects affected / exposed	3 / 109 (2.75%)	2 / 107 (1.87%)	4 / 53 (7.55%)
occurrences (all)	3	2	4
Musculoskeletal and connective tissue disorders			
Back pain			

subjects affected / exposed	9 / 109 (8.26%)	3 / 107 (2.80%)	4 / 53 (7.55%)
occurrences (all)	12	3	4
Infections and infestations			
Bronchitis			
subjects affected / exposed	3 / 109 (2.75%)	0 / 107 (0.00%)	3 / 53 (5.66%)
occurrences (all)	4	0	4
COVID-19			
subjects affected / exposed	10 / 109 (9.17%)	5 / 107 (4.67%)	6 / 53 (11.32%)
occurrences (all)	10	5	6
Infective exacerbation of bronchiectasis			
subjects affected / exposed	24 / 109 (22.02%)	16 / 107 (14.95%)	7 / 53 (13.21%)
occurrences (all)	46	29	9
Influenza			
subjects affected / exposed	5 / 109 (4.59%)	2 / 107 (1.87%)	1 / 53 (1.89%)
occurrences (all)	5	2	1
Urinary tract infection			
subjects affected / exposed	2 / 109 (1.83%)	3 / 107 (2.80%)	1 / 53 (1.89%)
occurrences (all)	2	4	1
Nasopharyngitis			
subjects affected / exposed	12 / 109 (11.01%)	11 / 107 (10.28%)	8 / 53 (15.09%)
occurrences (all)	14	17	10

Non-serious adverse events	BI 1291583 1 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	39 / 53 (73.58%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 53 (13.21%)		
occurrences (all)	7		
Dizziness			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	2		
General disorders and administration			

site conditions Fatigue subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all)	 3 / 53 (5.66%) 3 4 / 53 (7.55%) 5		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all)	 2 / 53 (3.77%) 2 4 / 53 (7.55%) 4		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Bronchiectasis subjects affected / exposed occurrences (all) Dyspnoea subjects affected / exposed occurrences (all) Haemoptysis subjects affected / exposed occurrences (all) Sputum increased subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all)	 2 / 53 (3.77%) 3 18 / 53 (33.96%) 35 2 / 53 (3.77%) 2 2 / 53 (3.77%) 2 1 / 53 (1.89%) 1 5 / 53 (9.43%) 6		
Skin and subcutaneous tissue disorders Skin exfoliation			

subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
Dry skin			
subjects affected / exposed	0 / 53 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 53 (3.77%)		
occurrences (all)	2		
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
COVID-19			
subjects affected / exposed	5 / 53 (9.43%)		
occurrences (all)	5		
Infective exacerbation of bronchiectasis			
subjects affected / exposed	11 / 53 (20.75%)		
occurrences (all)	15		
Influenza			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	3		
Urinary tract infection			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	3		
Nasopharyngitis			
subjects affected / exposed	5 / 53 (9.43%)		
occurrences (all)	5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 May 2022	Global amendment 1 part 1 - The following main changes were introduced: 1) the "rate of pulmonary exacerbations up to 48 weeks", which had been a secondary endpoint in the initial protocol, was defined as key secondary endpoint. Section 7 was partially re-structured to reflect this change. 2) In the initial protocol, Quality of Life Questionnaire – Bronchiectasis (QOL-B) was a further endpoint. It was changed to 'QOL-B respiratory symptoms domain score' as a secondary endpoint, and 'QOL-B scores except respiratory symptoms domain score' as further endpoint. 3) Second sampling time point was added for P. aeruginosa at End of treatment (EOT). 4) Updates to the flow chart were made for clarification. 5) Bone metabolism markers were removed from safety parameters and added as biomarkers. It was clarified that sampling was to take place fasting and at the same time of the day, if possible. Sampling frequency was increased and a new additional bone metabolism marker (Tartrate resistant acid phosphatase 5b - TRAP5B) was added. 6) Clarification that chronic treatment with concomitant strong Cytochrome P450 3A4 (CYP3A4) and P-glycoprotein (P-gp) inhibitors and inducers was restricted. Examples for such medications were provided. 7) Safety monitoring committee was replaced by Data Monitoring Committee (DMC). No Sponsor-internal personnel was involved in interim analyses. 8) Changes were made in contraception requirements: a) footnote on definition of postmenopausal status: statement added that Follicle stimulating hormone (FSH) level could be used for confirmation in questionable cases; b) Contraception was extended from 30 days to 75 days after last drug intake for both Women of childbearing potential (WOCBP) and male participants with WOCBP partners. 9) For Korea, legal age of 19 was added and Korea was namely mentioned as a country where WOCBP were not allowed to participate.
03 May 2022	Global amendment 1 part 2 - 10) Exclusion criterion #1 was changed to: Aspartate aminotransferase (AST) and / or Alanine aminotransferase (ALT) >3.0 x Upper limit of normal (ULN) at Visit 1, or moderate or severe liver disease (defined by Child-Pugh score B or C hepatic impairment). 11) Exclusion criterion #4: it was clarified that patients who may be at risk by participating in the trial were not to be included, and it was added that this judgement was to be made by the investigator based on laboratory and medical examinations. 12) Exclusion criterion #6: it was added that patients with allergic bronchopulmonary aspergillosis being treated or requiring treatment were to be excluded, and clarified that patients with fungal infection and not responsive to treatment should be excluded. 13) Exclusion criterion #7: it was clarified that patients with acute infections in the need of treatment were not to be randomised. 14) Exclusion criterion #17 was changed to: currently enrolled in another investigational device or drug trial, or less than 30 days or 5 half-lives, whichever was longer, prior to Visit 2 since ending another investigational device or drug trial(s). 15) New exclusion criterion #20: Contraindications to the class of drugs under study including known hypersensitivity to the drug or its excipients. 16) Additional discontinuation criterion: The investigator considered that treatment continuation was negatively impacting the well-being of the patient, and that treatment discontinuation was in the best interest of the patient.

02 December 2022	Global amendment 3 - The following main changes were introduced: 1) addition of new data on embryofoetal developmental toxicology outcomes. 2) The Pharmacokinetic (PK) safety evaluation of brensocatib was referenced. 3) New data from the Phase I trial 1397-0003 were added. 4) The Leicester Cough Questionnaire (LCQ) and Cough and Sputum Assessment Questionnaire (CASA-Q) were removed, and the Chronic Obstructive Pulmonary Disease (COPD) Assessment Test (CAT) was included. 5) A new section was added on Salbutamol/Albuterol as an Auxiliary medicinal product (AxMP). 6) Medications were added that needed to be stable prior to randomisation to reduce variability of bone turnover biomarkers. 7) A new major metabolite was added. 8) Information on Adverse events (AEs) was updated. 9) The wording regarding male and female contraception was revised. 10) Exclusion criteria: 'acute Severe acute respiratory syndrome coronavirus (SARS CoV) 2 infection' was deleted as an individual criterion and added into exclusion criterion #7 instead. 11) The contraception requirement after last trial drug intake was prolonged from 75 days to 9 months for WOCBP, and to 6 months for male participants with WOCBP partners. 12) It was added that for Hepatitis C virus (HCV) a Ribonucleic acid (RNA) test was to be performed if Hepatitis C antibodies result was positive, to confirm if the infection was active. Global amendment 3 includes the changes made in the global amendement 2, which was an internal version and never submitted to any Competent Authority (CA)/Institutional Review Board (IRB)/Independent Ethics Committee (IEC).
14 April 2023	Global amendment 4 - The following main changes were introduced: 1) It was clarified that an interim pharmacodynamic analysis was not planned. 2) The implementation of an adjudication committee was introduced, and a further endpoint 'rate of adjudicated pulmonary exacerbation' was added. 3) Periodontal discontinuation criteria were corrected, and assessment procedures clarified. 4) The subgroups with history of pulmonary exacerbations at baseline were changed from '0-2, ≥ 3' to '0-1, ≥ 2'. 5) Pre-dose PK time window for trough samples at Visits 3, 5 and 7 was extended from -1 h to -2 h.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported