Clinical trial results:
A randomised, double-blind, placebo-controlled parallel group study in IPF patients over 12 weeks evaluating efficacy, safety and tolerability of BI 1015550 taken orally

Summary

EudraCT number	2019-004167-45
Trial protocol	FI NL DK CZ DE HU GB AT PL SK GR IT
Global end of trial date	15 October 2021

Results information

Result version number	v1 (current)
This version publication date	21 October 2022
First version publication date	21 October 2022

Trial information

Trial identification

Sponsor protocol code	1305-0013

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04419506
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Boehringer Ingelheim
Sponsor organisation address	Binger Strasse 173, Ingelheim am Rhein, Germany, 001
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	19 November 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 October 2021
Global end of trial reached?	Yes
Global end of trial date	15 October 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the efficacy of BI 1015550 compared to placebo based on the change from baseline in forced vital capacity (FVC) in patients with Idiopathic Pulmonary Fibrosis (IPF).
To investigate the safety and tolerability of BI 1015550 in patients with IPF.

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	17 September 2020
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	Argentina: 1
Country: Number of subjects enrolled	Canada: 23
Country: Number of subjects enrolled	Chile: 7
Country: Number of subjects enrolled	China: 10
Country: Number of subjects enrolled	Czechia: 7
Country: Number of subjects enrolled	Denmark: 11
Country: Number of subjects enrolled	Finland: 15
Country: Number of subjects enrolled	Germany: 31
Country: Number of subjects enrolled	Greece: 6
Country: Number of subjects enrolled	Hungary: 5
Country: Number of subjects enrolled	Italy: 8
Country: Number of subjects enrolled	Japan: 24
Country: Number of subjects enrolled	Netherlands: 7
Country: Number of subjects enrolled	Poland: 1
Country: Number of subjects enrolled	Russian Federation: 9
Country: Number of subjects enrolled	Korea, Republic of: 8
Country: Number of subjects enrolled	Ukraine: 11
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	United States: 27

Country: Number of subjects enrolled	Spain: 11
Country: Number of subjects enrolled	Austria: 3
Country: Number of subjects enrolled	Australia: 2
Worldwide total number of subjects	233
EEA total number of subjects	105

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)	48
From 65 to 84 years	179
85 years and over	6

Subject disposition

Recruitment

Recruitment details:

This was a trial with a randomised, placebo-controlled, double-blind, parallel-group design over 12 weeks, including a screening period of up to 44 days, a 12-week treatment period, and a 1-week follow-up period in patients with idiopathic pulmonary fibrosis (IPF) stratified by baseline antifibrotic treatment.

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 (except bioanalytics and possibly Data Monitoring Committee members) or with any other interest in this double-blind trial, remained blinded with regard to the randomised treatment assignments until after database lock.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo - Antifibrotics at baseline

Arm description:

Idiopathic pulmonary fibrosis (IPF) patients on antifibrotic treatment with nintedanib or pirfenidone at baseline were administered placebo matching BI 1015550 taken orally as film-coated tablets (matching the respective BI 1015550 tablets) twice daily, in the morning and in the evening for 12 weeks. During the 12-weeks of administration of BI 1015550 patients stayed on their background therapy of nintedanib or prifenidone.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo matching BI 1015550 taken orally as film-coated tablets (matching the respective BI 1015550 tablets) twice daily, in the morning and in the evening for 12 weeks.

Arm title	BI 1015550 - Antifibrotics at baseline

Arm description:

Idiopathic pulmonary fibrosis (IPF) patients on antifibrotic treatment with nintedanib or pirfenidone at baseline were administered 18 milligram (mg) BI 1015550 taken orally as film-coated tablets (1x 6mg tablet, 1x 12 mg tablet) twice daily (36 mg daily), in the morning and in the evening for 12 weeks. During the 12-weeks of administration of BI 1015550 patients stayed on their background therapy of nintedanib or prifenidone.

Arm type	Experimental

Investigational medicinal product name	BI 1015550
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

18 milligram (mg) BI 1015550 taken orally as film-coated tablets (1x 6mg tablet, 1x 12 mg tablet) twice daily (36 mg daily), in the morning and in the evening for 12 weeks.

Arm title	Placebo - Non-antifibrotics at baseline

Arm description:

Idiopathic pulmonary fibrosis (IPF) patients not on antifibrotic treatment at baseline were administered placebo matching BI 1015550 taken orally as film-coated tablets (matching the respective BI 1015550 tablets) twice daily, in the morning and in the evening for 12 weeks. Patients were not expected to start antifibrotic treatment during the 12 weeks of placebo treatment.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo matching BI 1015550 taken orally as film-coated tablets (matching the respective BI 1015550 tablets) twice daily, in the morning and in the evening for 12 weeks.

Arm title	BI 1015550 - Non-antifibrotics at baseline

Arm description:

Idiopathic pulmonary fibrosis (IPF) patients not on antifibrotic treatment at baseline were administered 18 milligram (mg) BI 1015550 taken orally as film-coated tablets (1x 6mg tablet, 1x 12 mg tablet) twice daily (36 mg daily), in the morning and in the evening for 12 weeks. Patients were not expected to start antifibrotic treatment during the 12 weeks of BI 1015550 treatment.

Arm type	Experimental
Investigational medicinal product name	BI 1015550
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

18 milligram (mg) BI 1015550 taken orally as film-coated tablets (1x 6mg tablet, 1x 12 mg tablet) twice daily (36 mg daily), in the morning and in the evening for 12 weeks.

Number of subjects in period 1[1]	Placebo - Antifibrotics at baseline	BI 1015550 - Antifibrotics at baseline	Placebo - Non-antifibrotics at baseline
Started	25	49	25
Completed	25	39	25
Not completed	0	10	0
Consent withdrawn by subject	-	-	-
Adverse event, non-fatal	-	10	-
Poor compliance	-	-	-

Number of subjects in period 1	BI 1015550 - Non-antifibrotics at

[1]	baseline
Started	48
Completed	43
Not completed	5
Consent withdrawn by subject	1
Adverse event, non-fatal	3
Poor compliance	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 233 enrolled subjects, 147 subjects were randomized.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo - Antifibrotics at baseline
Reporting group description:	
Idiopathic pulmonary fibrosis (IPF) patients on antifibrotic treatment with nintedanib or pirfenidone at baseline were administered placebo matching BI 1015550 taken orally as film-coated tablets (matching the respective BI 1015550 tablets) twice daily, in the morning and in the evening for 12 weeks. During the 12-weeks of administration of BI 1015550 patients stayed on their background therapy of nintedanib or prifenidone.	
Reporting group title	BI 1015550 - Antifibrotics at baseline
Reporting group description:	
Idiopathic pulmonary fibrosis (IPF) patients on antifibrotic treatment with nintedanib or pirfenidone at baseline were administered 18 milligram (mg) BI 1015550 taken orally as film-coated tablets (1x 6mg tablet, 1x 12 mg tablet) twice daily (36 mg daily), in the morning and in the evening for 12 weeks. During the 12-weeks of administration of BI 1015550 patients stayed on their background therapy of nintedanib or prifenidone.	
Reporting group title	Placebo - Non-antifibrotics at baseline
Reporting group description:	
Idiopathic pulmonary fibrosis (IPF) patients not on antifibrotic treatment at baseline were administered placebo matching BI 1015550 taken orally as film-coated tablets (matching the respective BI 1015550 tablets) twice daily, in the morning and in the evening for 12 weeks. Patients were not expected to start antifibrotic treatment during the 12 weeks of placebo treatment.	
Reporting group title	BI 1015550 - Non-antifibrotics at baseline
Reporting group description:	
Idiopathic pulmonary fibrosis (IPF) patients not on antifibrotic treatment at baseline were administered 18 milligram (mg) BI 1015550 taken orally as film-coated tablets (1x 6mg tablet, 1x 12 mg tablet) twice daily (36 mg daily), in the morning and in the evening for 12 weeks. Patients were not expected to start antifibrotic treatment during the 12 weeks of BI 1015550 treatment.	

Reporting group values	Placebo - Antifibrotics at baseline	BI 1015550 - Antifibrotics at baseline	Placebo - Non-antifibrotics at baseline
Number of subjects	25	49	25
Age categorical			
Treated Set (TS): all patients who received at least one dose of trial drug.			
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)	10	7	3
From 65-84 years	14	42	22
85 years and over	1	0	0
Age Continuous			
Treated Set (TS): all patients who received at least one dose of trial drug.			
Units: years			
arithmetic mean	67.5	69.3	71.8
standard deviation	± 10.7	± 6.6	± 9.3

Sex: Female, Male			
Treated Set (TS): all patients who received at least one dose of trial drug.			
Units: Participants			
Female	7	5	8
Male	18	44	17
Race (NIH/OMB)			
Treated Set (TS): all patients who received at least one dose of trial drug.			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	4	12	4
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	21	37	21
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB)			
Treated Set (TS): all patients who received at least one dose of trial drug.			
Units: Subjects			
Hispanic or Latino	1	3	4
Not Hispanic or Latino	24	46	21
Unknown or Not Reported	0	0	0
Forced vital capacity (FVC)			
Forced vital capacity (FVC) at baseline. FVC is the total amount of air exhaled during a Forced expiratory volume (FEV) test. Treated Set (TS): all patients who received at least one dose of trial drug.			
Units: Milliliter			
arithmetic mean	2690.000	2875.551	2864.920
standard deviation	± 889.985	± 752.818	± 1015.104

Reporting group values	BI 1015550 - Non-antifibrotics at baseline	Total	
Number of subjects	48	147	
Age categorical			
Treated Set (TS): all patients who received at least one dose of trial drug.			
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)	11	31	
From 65-84 years	35	113	
85 years and over	2	3	
Age Continuous			
Treated Set (TS): all patients who received at least one dose of trial drug.			
Units: years			
arithmetic mean	69.9		
standard deviation	± 8.3	-	

Sex: Female, Male			
Treated Set (TS): all patients who received at least one dose of trial drug.			
Units: Participants			
Female	14	34	
Male	34	113	
Race (NIH/OMB)			
Treated Set (TS): all patients who received at least one dose of trial drug.			
Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	12	32	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	36	115	
More than one race	0	0	
Unknown or Not Reported	0	0	
Ethnicity (NIH/OMB)			
Treated Set (TS): all patients who received at least one dose of trial drug.			
Units: Subjects			
Hispanic or Latino	5	13	
Not Hispanic or Latino	43	134	
Unknown or Not Reported	0	0	
Forced vital capacity (FVC)			
Forced vital capacity (FVC) at baseline. FVC is the total amount of air exhaled during a Forced expiratory volume (FEV) test. Treated Set (TS): all patients who received at least one dose of trial drug.			
Units: Milliliter			
arithmetic mean	2782.938		
standard deviation	± 835.104	-	

End points

End points reporting groups

Reporting group title	Placebo - Antifibrotics at baseline

Reporting group description:

Idiopathic pulmonary fibrosis (IPF) patients on antifibrotic treatment with nintedanib or pirfenidone at baseline were administered placebo matching BI 1015550 taken orally as film-coated tablets (matching the respective BI 1015550 tablets) twice daily, in the morning and in the evening for 12 weeks. During the 12-weeks of administration of BI 1015550 patients stayed on their background therapy of nintedanib or prifenidone.

Reporting group title	BI 1015550 - Antifibrotics at baseline

Reporting group description:

Idiopathic pulmonary fibrosis (IPF) patients on antifibrotic treatment with nintedanib or pirfenidone at baseline were administered 18 milligram (mg) BI 1015550 taken orally as film-coated tablets (1x 6mg tablet, 1x 12 mg tablet) twice daily (36 mg daily), in the morning and in the evening for 12 weeks. During the 12-weeks of administration of BI 1015550 patients stayed on their background therapy of nintedanib or prifenidone.

Reporting group title	Placebo - Non-antifibrotics at baseline

Reporting group description:

Idiopathic pulmonary fibrosis (IPF) patients not on antifibrotic treatment at baseline were administered placebo matching BI 1015550 taken orally as film-coated tablets (matching the respective BI 1015550 tablets) twice daily, in the morning and in the evening for 12 weeks. Patients were not expected to start antifibrotic treatment during the 12 weeks of placebo treatment.

Reporting group title	BI 1015550 - Non-antifibrotics at baseline

Reporting group description:

Idiopathic pulmonary fibrosis (IPF) patients not on antifibrotic treatment at baseline were administered 18 milligram (mg) BI 1015550 taken orally as film-coated tablets (1x 6mg tablet, 1x 12 mg tablet) twice daily (36 mg daily), in the morning and in the evening for 12 weeks. Patients were not expected to start antifibrotic treatment during the 12 weeks of BI 1015550 treatment.

Primary: The change from baseline in Forced vital capacity (FVC) at 12 weeks

End point title	The change from baseline in Forced vital capacity (FVC) at 12 weeks

End point description:

The change from baseline in Forced vital capacity (FVC) at 12 weeks. Data were analysed with a restricted maximum likelihood (REML)-based approach using a mixed model with repeated measures (MMRM). The analysis included the fixed, categorical effect of treatment at each visit, and the fixed, continuous effects of baseline FVC at each visit. Visit was treated as the repeated measure, with an unstructured covariance structure used to model the within-patient measurements.
Full Analysis Set (FAS): all patients who received at least one dose of trial drug and who had a baseline and at least one post-baseline measurement available for Forced Vital Capacity (FVC), Forced Expiratory Volume in one second (FEV1) or Diffusion Capacity of the Lung for Carbon Monoxide (DLCO).

End point type	Primary

End point timeframe:

Baseline (day 1) and week 12.

End point values	Placebo - Antifibrotics at baseline	BI 1015550 - Antifibrotics at baseline	Placebo - Non-antifibrotics at baseline	BI 1015550 - Non-antifibrotics at baseline
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	25[1]	48[2]	25[3]	47[4]
Units: Milliliter				
arithmetic mean (confidence interval 95%)	-77.70 (-124.87 to -30.53)	2.72 (-33.46 to 38.89)	-95.62 (-157.13 to -34.10)	6.10 (-39.67 to 51.88)

Notes:

[1] - Mean and confidence interval are adjusted

[2] - Mean and confidence interval are adjusted

[3] - Mean and confidence interval are adjusted

[4] - Mean and confidence interval are adjusted

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Adjusted means in the placebo group were combined with the meta-analytic predictive priors derived based on the clinical trials in the nintedanib clinical development program in IPF. In order to evaluate the treatment effects, the posterior distribution for the treatment difference of BI 1015550 versus placebo with respect to the primary endpoint was used. The median of the posterior distribution for the treatment difference (and 95% credible intervals) was calculated.

Comparison groups	Placebo - Non-antifibrotics at baseline v BI 1015550 - Non-antifibrotics at baseline
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Posterior difference
Point estimate	88.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	29.5
upper limit	154.2

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Adjusted means in the placebo group were combined with the meta-analytic predictive priors derived based on the clinical trials in the nintedanib clinical development program in IPF. In order to evaluate the treatment effects, the posterior distribution for the treatment difference of BI 1015550 versus placebo with respect to the primary endpoint was used. The median of the posterior distribution for the treatment difference (and 95% credible intervals) was calculated.

Comparison groups	Placebo - Antifibrotics at baseline v BI 1015550 - Antifibrotics at baseline
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted mean difference
Point estimate	62.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	6.3
upper limit	125.5

Secondary: The number of patients with treatment emergent adverse event

End point title	The number of patients with treatment emergent adverse event

End point description:

The number of patients with any adverse event during the on-treatment period.

Treated Set (TS): all patients who received at least one dose of trial drug.

End point type	Secondary

End point timeframe:

From the start of treatment till the end of treatment + 7 days residual effect period, an average of 87.4 days.

End point values	Placebo - Antifibrotics at baseline	BI 1015550 - Antifibrotics at baseline	Placebo - Non-antifibrotics at baseline	BI 1015550 - Non-antifibrotics at baseline
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	25	49	25	48
Units: Participants	5	18	5	9

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the start of treatment till the end of treatment + 7 days residual effect period, an average of 87.4 days.

Adverse event reporting additional description:

Treated Set (TS): all patients who received at least one dose of trial drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Placebo, Antifibrotics at baseline

Reporting group description:

Idiopathic pulmonary fibrosis (IPF) patients on stable antifibrotic treatment with nintedanib or pirfenidone at baseline were administered placebo matching BI 1015550 taken orally as film-coated tablets (matching the respective BI 1015550 tablets) twice daily, in the morning and in the evening for 12 weeks. During the 12-weeks of administration of BI 1015550 patients stayed on their stable background therapy of nintedanib or prifenidone.

Reporting group title	Placebo, Non-antifibrotics at baseline

Reporting group description:

Idiopathic pulmonary fibrosis (IPF) patients not on stable antifibrotic treatment at baseline were administered placebo matching BI 1015550 taken orally as film-coated tablets (matching the respective BI 1015550 tablets) twice daily, in the morning and in the evening for 12 weeks. Patients were not expected to start antifibrotic treatment during the 12 weeks of placebo treatment.

Reporting group title	BI 1015550, Non-antifibrotics at baseline

Reporting group description:

Idiopathic pulmonary fibrosis (IPF) patients not on stable antifibrotic treatment at baseline were administered 18 milligram (mg) BI 1015550 taken orally as film-coated tablets (1x 6mg tablet, 1x 12 mg tablet) twice daily (36 mg daily), in the morning and in the evening for 12 weeks. Patients not on background antifibrotic treatment at baseline. Patients were not expected to start antifibrotic treatment during the 12 weeks of BI 1015550 treatment.

Reporting group title	BI 1015550, Antifibrotics at baseline

Reporting group description:

Idiopathic pulmonary fibrosis (IPF) patients on stable antifibrotic treatment with nintedanib or pirfenidone at baseline were administered 18 milligram (mg) BI 1015550 taken orally as film-coated tablets (1x 6mg tablet, 1x 12 mg tablet) twice daily (36 mg daily), in the morning and in the evening for 12 weeks. During the 12-weeks of administration of BI 1015550 patients stayed on their stable background therapy of nintedanib or prifenidone.

Serious adverse events	Placebo, Antifibrotics at baseline	Placebo, Non-antifibrotics at baseline	BI 1015550, Non-antifibrotics at baseline
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 25 (0.00%)	5 / 25 (20.00%)	3 / 48 (6.25%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung neoplasm			

subjects affected / exposed	0 / 25 (0.00%)	0 / 25 (0.00%)	1 / 48 (2.08%)
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			
Vasculitis			
subjects affected / exposed	0 / 25 (0.00%)	0 / 25 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac failure congestive			
subjects affected / exposed	0 / 25 (0.00%)	0 / 25 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Peripheral nerve paresis			
subjects affected / exposed	0 / 25 (0.00%)	0 / 25 (0.00%)	0 / 48 (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 / 25 (0.00%)	1 / 25 (4.00%)	0 / 48 (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
General disorders and administration site conditions			
Condition aggravated			
subjects affected / exposed	0 / 25 (0.00%)	0 / 25 (0.00%)	0 / 48 (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			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 25 (0.00%)	0 / 25 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			

subjects affected / exposed	0 / 25 (0.00%)	0 / 25 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermatitis exfoliative			
subjects affected / exposed	0 / 25 (0.00%)	1 / 25 (4.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 25 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Urosepsis			
subjects affected / exposed	0 / 25 (0.00%)	1 / 25 (4.00%)	0 / 48 (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
Wound infection			
subjects affected / exposed	0 / 25 (0.00%)	1 / 25 (4.00%)	0 / 48 (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
Metabolism and nutrition disorders			
Diabetic metabolic decompensation			
subjects affected / exposed	0 / 25 (0.00%)	1 / 25 (4.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	BI 1015550, Antifibrotics at baseline		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 49 (6.12%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	1		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung neoplasm			

subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Vasculitis			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Cardiac disorders			
Cardiac failure congestive			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Peripheral nerve paresis			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Transient ischaemic attack			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Condition aggravated			
subjects affected / exposed	2 / 49 (4.08%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			

subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Dermatitis exfoliative			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urosepsis			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Wound infection			
subjects affected / exposed	0 / 49 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Diabetic metabolic decompensation			
subjects affected / exposed	0 / 49 (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, Antifibrotics at baseline	Placebo, Non-antifibrotics at baseline	BI 1015550, Non-antifibrotics at baseline
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 25 (40.00%)	5 / 25 (20.00%)	18 / 48 (37.50%)
Nervous system disorders			

Headache			
subjects affected / exposed	1 / 25 (4.00%)	0 / 25 (0.00%)	3 / 48 (6.25%)
occurrences (all)	1	0	5
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 25 (0.00%)	3 / 48 (6.25%)
occurrences (all)	0	0	3
Fatigue			
subjects affected / exposed	3 / 25 (12.00%)	1 / 25 (4.00%)	2 / 48 (4.17%)
occurrences (all)	3	1	3
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	2 / 25 (8.00%)	0 / 25 (0.00%)	1 / 48 (2.08%)
occurrences (all)	2	0	1
Diarrhoea			
subjects affected / exposed	4 / 25 (16.00%)	2 / 25 (8.00%)	8 / 48 (16.67%)
occurrences (all)	7	4	9
Dyspepsia			
subjects affected / exposed	1 / 25 (4.00%)	0 / 25 (0.00%)	3 / 48 (6.25%)
occurrences (all)	1	0	3
Flatulence			
subjects affected / exposed	1 / 25 (4.00%)	1 / 25 (4.00%)	3 / 48 (6.25%)
occurrences (all)	1	1	3
Nausea			
subjects affected / exposed	0 / 25 (0.00%)	2 / 25 (8.00%)	2 / 48 (4.17%)
occurrences (all)	0	2	2
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 25 (8.00%)	1 / 25 (4.00%)	3 / 48 (6.25%)
occurrences (all)	2	1	3
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	2 / 25 (8.00%)	0 / 25 (0.00%)	0 / 48 (0.00%)
occurrences (all)	2	0	0
Infections and infestations			

Nasopharyngitis			
subjects affected / exposed	0 / 25 (0.00%)	0 / 25 (0.00%)	0 / 48 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	BI 1015550, Antifibrotics at baseline		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 49 (48.98%)		
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 49 (6.12%)		
occurrences (all)	3		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences (all)	1		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	15 / 49 (30.61%)		
occurrences (all)	16		
Dyspepsia			
subjects affected / exposed	2 / 49 (4.08%)		
occurrences (all)	2		
Flatulence			
subjects affected / exposed	2 / 49 (4.08%)		
occurrences (all)	2		
Nausea			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			

Cough subjects affected / exposed occurrences (all)	4 / 49 (8.16%) 4		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	0 / 49 (0.00%) 0		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	4 / 49 (8.16%) 4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 May 2020	In this revision of the Clinical Trial Protocol (CTP), the dose and regimen of trial drug were deleted from the title to fulfil internal rules of disclosure.
02 June 2020	In this revision of the Clinical Trial Protocol (CTP), the table of risks was updated so that the risks associated with blood sampling, High-Resolution Computed Tomography (HRCT) and lung measurements (Pulmonary Function Test (PFT) and Diffusion Capacity of the Lung for Carbon Monoxide (DLCO)), as well as the risk and mitigation plan for placebo use, were legible. The procedures in case of acute Idiopathic Pulmonary Fibrosis (IPF) exacerbation were clarified. The description of Electrocardiogram (ECG) recording was corrected to remove the postdose ECG at Visit 2 and to clarify that triplicate ECGs were not expected (single ECG were to be performed). Regarding the optional substudy on digital lung auscultation test, fewer points of auscultations were to be used and the results were not meant to be reported in the Clinical Trial Report (CTR). Regarding the optional substudy on 24-hour cough measurements, an inclusion criterion to enter the substudy was added to ensure that participants coughed enough; the evaluations to be performed were clarified.
09 September 2020	In this revision of the Clinical Trial Protocol (CTP), the trial-related risks were updated to add the risk assessment due to the Coronavirus Disease 2019 (COVID-19) pandemic. An exclusion criterion was added to exclude patients with a Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) infection as this was a potential additional risk. The criteria to discontinue trial treatment were updated to include the patients who meet Adverse Event of Special Interest (AESI) definition of hepatic injury and the patients who experience infection with SARS-CoV-2 (for safety reasons).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported