Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of BG00011 in Patients With Idiopathic Pulmonary Fibrosis

Summary

EudraCT number	2017-003158-18
Trial protocol	CZ GB DK NL GR BE ES DE PL IT
Global end of trial date	14 November 2019

Results information

Result version number	v1 (current)
This version publication date	14 November 2020
First version publication date	14 November 2020

Trial information

Trial identification

Sponsor protocol code	203PF203

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03573505
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Biogen
Sponsor organisation address	250 Binney Street, Cambridge, United States, 02142
Public contact	Biogen Study Medical Director, Biogen, clinicaltrials@biogen.com
Scientific contact	Biogen Study Medical Director, Biogen, clinicaltrials@biogen.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	14 November 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 November 2019
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the efficacy of BG00011 compared with placebo in subjects with Idiopathic Pulmonary Fibrosis (IPF).

Protection of trial subjects:

Written informed consent was obtained from each subject or subject's legally authorized representative (e.g., parent or legal guardian), as applicable, prior to evaluations performed for eligibility. Subjects or the subject's legally authorized representative were given adequate time to review the information in the informed consent/assent and were allowed to ask, and have answered, questions concerning all portions of the conduct of the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 September 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	2 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 29
Country: Number of subjects enrolled	Australia: 28
Country: Number of subjects enrolled	Netherlands: 8
Country: Number of subjects enrolled	Korea, Republic of: 7
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	Chile: 6
Country: Number of subjects enrolled	Czech Republic: 6
Country: Number of subjects enrolled	Greece: 3
Country: Number of subjects enrolled	Italy: 3
Country: Number of subjects enrolled	Argentina: 2
Country: Number of subjects enrolled	Denmark: 2
Country: Number of subjects enrolled	Poland: 2
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Israel: 1
Country: Number of subjects enrolled	Russian Federation: 1
Country: Number of subjects enrolled	Spain: 1

Worldwide total number of subjects	106
EEA total number of subjects	32

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)	30
From 65 to 84 years	76
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were enrolled at 47 investigational sites in 16 countries from September 24, 2018 to November 14, 2019. Out of 109 enrolled subjects, 106 were treated (mITT population) and 3 were not treated. Data for subject number per country and age-group breakdown is provided for 106 subjects as data for age for one of the subjects was not collected.

Pre-assignment

Screening details:

A total of 109 subjects with Idiopathic pulmonary fibrosis (IPF) were enrolled and randomized in this study. Of which, 106 subjects received at least one dose of study drug (mITT). The maximum length of the dosing period was up to Week 46. Subjects were then followed-up for safety for up to Week 60.

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, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Subjects received BG00011-matching placebo, once weekly by subcutaneous (SC) injection up to a maximum of 46 weeks. Median exposure to placebo was for 19.14 weeks.

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

Dosage and administration details:

Subcutaneous (SC) injection, once weekly.

Arm title	BG00011

Arm description:

Subjects received BG00011 56 milligram (mg), once weekly by SC injection up to a maximum of 46 weeks. Median exposure to BG00011 was for 17.14 weeks.

Arm type	Experimental
Investigational medicinal product name	BG00011
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

SC injection, once weekly.

Number of subjects in period 1	Placebo	BG00011
Started	52	54
Completed	0	0
Not completed	52	54
Disease progression	-	1
Adverse Event	1	1
Death	-	4
Study terminated by sponsor	50	45
Site Terminated by Sponsor	1	1
Reason not specified	-	1
Consent withdrawn	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects received BG00011-matching placebo, once weekly by subcutaneous (SC) injection up to a maximum of 46 weeks. Median exposure to placebo was for 19.14 weeks.	
Reporting group title	BG00011
Reporting group description:	
Subjects received BG00011 56 milligram (mg), once weekly by SC injection up to a maximum of 46 weeks. Median exposure to BG00011 was for 17.14 weeks.	

Reporting group values	Placebo	BG00011	Total
Number of subjects	52	54	106
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	68.50	69.46	
standard deviation	± 6.652	± 7.570	-
Sex: Female, Male Units: subjects			
Female	12	11	23
Male	40	43	83
Race/Ethnicity Customized Units: Subjects			
Hispanic or Latino	6	5	11
Not Hispanic or Latino	46	49	95
Race/Ethnicity Customized Units: Subjects			
Asian	2	5	7
Black or African American	0	1	1
White	49	47	96
Other	1	1	2

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Subjects received BG00011-matching placebo, once weekly by subcutaneous (SC) injection up to a maximum of 46 weeks. Median exposure to placebo was for 19.14 weeks.	
Reporting group title	BG00011
Reporting group description:	
Subjects received BG00011 56 milligram (mg), once weekly by SC injection up to a maximum of 46 weeks. Median exposure to BG00011 was for 17.14 weeks.	

Primary: Change from Baseline in Forced (Expiratory) Vital Capacity (FVC) at Week 52

End point title	Change from Baseline in Forced (Expiratory) Vital Capacity (FVC) at Week 52[1]
End point description:	
FVC is the total amount of air exhaled during the forced expiratory volume test that is measured during spirometry and is the most important measurement of lung function. This test requires subject to breath into a tube connected to a machine that measures the amount of air that can be moved in and out of the lungs. Change from baseline is defined as post-baseline value minus baseline value. A negative change from baseline indicates decline. MITT population included all subjects who were randomised and received at least 1 dose of study treatment (BG00011 or placebo). 'n' are the subjects who were assessed at the specified timepoint in this endpoint. 'n' at Week 52, are a few subjects whose early termination visit fell into the analysis visit window of the Week 52 visit. No subject received Week 52 dosing.	
End point type	Primary
End point timeframe:	
Baseline, Week 52	
Notes:	
[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: Statistical analysis was not performed for this endpoint.	

End point values	Placebo	BG00011		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	54		
Units: litres (L)				
arithmetic mean (standard deviation)				
Baseline (n=52,54)	2.883 (± 0.7037)	2.867 (± 0.8607)		
Change at Week 52 (n=5,4)	-0.308 (± 0.1768)	-0.455 (± 0.2849)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in FVC, Expressed in Percent Predicted at Week 52

End point title	Change from Baseline in FVC, Expressed in Percent Predicted at

	Week 52

End point description:

FVC is the total amount of air exhaled during the forced expiratory volume test measured during spirometry and is the most important measurement of lung function. It requires subject to breath into a tube connected to a machine that measures the amount of air that can be moved in and out of the lungs after taking an inhaled bronchodilator medicine which is used to dilate subject's bronchial (breathing) tubes. Percent predicted FVC (in %, here FVC was measured in litres) = [(observed FVC)/(predicted FVC)]*100. Change from baseline is defined as post-baseline value minus baseline value. A negative change from baseline indicates decline. MITT population included all subjects who were randomised and received at least 1 dose of study treatment (BG00011 or placebo). 'n' are the subjects who were assessed at the specified timepoint. 'n' at Week 52, are a few subjects whose early termination visit fell into the analysis visit window of the Week 52 visit. No subject received Week 52 dosing.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Placebo	BG00011		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	54		
Units: percentage of of predicted FVC				
arithmetic mean (standard deviation)				
Baseline (n=52,54)	76.1 (± 15.46)	77.4 (± 17.07)		
Change at Week 52 (n=5,4)	-7.6 (± 5.22)	-11.5 (± 6.95)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Progression

End point title	Time to Progression

End point description:

Time to progression is defined by a composite endpoint, including any of the following events: Absolute decline of 10% predicted in FVC (FVC percent predicted (baseline) - FVC percent predicted (progression) ≥10%); Non-elective hospitalization for respiratory events; Lung transplantation or death. The earliest time to meet at least 1 composite criterion was calculated. MITT population included all subjects who were randomised and received at least 1 dose of study treatment (BG00011 or placebo). 'Number of subjects analysed' are the subjects who were assessed in this outcome measure.

End point type	Secondary

End point timeframe:

Up to Week 60 (End of Study)

End point values	Placebo	BG00011		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	15		
Units: days				
median (full range (min-max))	127.5 (29 to 235)	119.0 (28 to 302)		

Statistical analyses

Statistical analysis title	Placebo vs BG00011

Statistical analysis description:

A cox proportional hazards model with terms for treatment (BG00011 vs. placebo) and randomization stratification factor is used. A stratified log-rank test is used to compare the 2 treatment groups using randomization stratus as the stratification factor. An HR (Hazard Ratio) < 1 indicates lower risk of event for the BG00011 group where HR is based on Cox proportional hazard model with treatment (Placebo, BG00011) as the categorical covariate.

Comparison groups	Placebo v BG00011
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.112
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	2.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	4.73

Secondary: Time to First Acute Idiopathic Pulmonary Fibrosis (IPF) Exacerbation

End point title	Time to First Acute Idiopathic Pulmonary Fibrosis (IPF) Exacerbation

End point description:

Time to first acute IPF exacerbation is defined as time from randomization to the first occurrence of acute IPF exacerbation. Acute IPF exacerbation is defined as a clinically significant deterioration of unidentifiable cause in a subject with underlying IPF. The diagnostic criteria for IPF used in this study were derived from evidence-based guidelines developed by the American Thoracic Society/European Respiratory Society/Japanese Respiratory Society/Latin American Thoracic Association (ATS/ERS/JRS/ALAT) joint task force for the diagnosis and management of IPF. Participants were assessed according to the modified 2007 diagnostic criteria for acute IPF exacerbation. MITT population included all subjects who were randomised and received at least 1 dose of study treatment (BG00011 or placebo). 'Number of subjects analysed' are the subjects who had at least one acute IPF exacerbation.

End point type	Secondary

End point timeframe:

Up to Early Termination Visit (Up to Week 52)

End point values	Placebo	BG00011		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	7		
Units: days				
median (full range (min-max))	(to)	114.0 (42 to 223)		

Notes:

[2] - No subjects had at least one acute IPF exacerbation in Placebo arm.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with at Least One Acute IPF Exacerbation

End point title	Number of Subjects with at Least One Acute IPF Exacerbation

End point description:

Acute IPF exacerbation is defined as a clinically significant deterioration of unidentifiable cause in a subject with underlying IPF. The diagnostic criteria for IPF used in this study were derived from evidence-based guidelines developed by the American Thoracic Society/European Respiratory Society/Japanese Respiratory Society/Latin American Thoracic Association (ATS/ERS/JRS/ALAT) joint task force for the diagnosis and management of IPF. Participants were assessed according to the modified 2007 diagnostic criteria for acute IPF exacerbation. MITT population included all subjects who were randomised and received at least 1 dose of study treatment (BG00011 or placebo).

End point type	Secondary

End point timeframe:

Up to Early Termination Visit (Up to Week 52)

End point values	Placebo	BG00011		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	54		
Units: subjects	0	7		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of IPF Exacerbations

End point title	Number of IPF Exacerbations

End point description:

The IPF exacerbation is defined as a clinically significant deterioration of unidentifiable cause in a subject with underlying IPF. The diagnostic criteria for IPF used in this study were derived from evidence-based guidelines developed by the American Thoracic Society/European Respiratory Society/Japanese Respiratory Society/Latin American Thoracic Association (ATS/ERS/JRS/ALAT) joint task force for the diagnosis and management of IPF. Participants were assessed according to the modified 2007 diagnostic criteria for acute IPF exacerbation. MITT population included all subjects who were randomised and received at least 1 dose of study treatment (BG00011 or placebo).

End point type	Secondary

End point timeframe:

Up to Early Termination Visit (Up to Week 52)

End point values	Placebo	BG00011		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	54		
Units: exacerbations	0	8		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Absolute Decline of 10% Predicted in FVC

End point title	Number of Subjects with Absolute Decline of 10% Predicted in FVC

End point description:

FVC is the is the total amount of air exhaled during the forced expiratory volume test that is measured during spirometry and is the most important measurement of lung function. This test requires subject to breath into a tube connected to a machine that measures the amount of air that can be moved in and out of the lungs after taking an inhaled bronchodilator medicine which is used to dilate subject's bronchial (breathing) tubes. Absolute Decline of 10% = FVC percent predicted (baseline) - FVC percent predicted (progression) ≥10%. MITT population included all subjects who were randomised and received at least 1 dose of study treatment (BG00011 or placebo).

End point type	Secondary

End point timeframe:

Up to Early Termination Visit (Up to Week 52)

End point values	Placebo	BG00011		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	54		
Units: subjects	6	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Death or Lung Transplantation

End point title	Time to Death or Lung Transplantation

End point description:

Time to Death or Lung Transplantation is defined as the time from randomization to the first occurrence of any one of the event (death or lung transplantation). MITT population included all subjects who were randomised and received at least 1 dose of study treatment (BG00011 or Placebo).

End point type	Secondary

End point timeframe:

Up to Week 60 (End of Study)

End point values	Placebo	BG00011		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[3]	54		
Units: days				
median (full range (min-max))				
Time to Death	(to)	83.0 (60 to 137)		
Time to Lung Transplantation	(to)	155.0 (155 to 155)		

Notes:

[3] - No subjects were analysed for this endpoint in the Placebo arm.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to All Non-elective Hospitalizations

End point title	Time to All Non-elective Hospitalizations

End point description:

Time to all non-elective hospitalizations is defined as the time from randomization to the first occurrence of hospitalization which was not elected by the participant. The MITT population included all subjects who were randomised and received at least 1 dose of study treatment (BG00011 or Placebo). 'Number of subjects analysed' are the subjects who had at least one episode of non-elective hospitalization.

End point type	Secondary

End point timeframe:

Up to Week 60 (End of Study)

End point values	Placebo	BG00011		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	11		
Units: days				
median (full range (min-max))	133.0 (61 to 235)	119.0 (42 to 302)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to All Non-Elective Respiratory Hospitalizations

End point title	Time to All Non-Elective Respiratory Hospitalizations

End point description:

Time to all non-elective respiratory hospitalizations is defined as the time from randomization to the first occurrence of hospitalization due to respiratory problems, which was not elected by the participant. The MITT population included all subjects who were randomised and received at least 1 dose of study

treatment (BG00011 or Placebo). 'Number of subjects analysed' are the subjects who had at least one episode of non-elective respiratory hospitalization.

End point type	Secondary

End point timeframe:

Up to Week 60 (End of Study)

End point values	Placebo	BG00011		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	9		
Units: days				
median (full range (min-max))	205.0 (175 to 235)	119.0 (42 to 223)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Absolute FVC

End point title	Change from Baseline in Absolute FVC

End point description:

FVC is the total amount of air exhaled during the forced expiratory volume test that is measured during spirometry and is the most important measurement of lung function. This test requires subject to breath into a tube connected to a machine that measures the amount of air that can be moved in and out of the lungs after taking an inhaled bronchodilator medicine which is used to dilate subject's bronchial (breathing) tubes. Change from baseline is defined as post-baseline value minus baseline value. A negative change from baseline indicates decline. MITT population included all subjects who were randomised and received at least 1 dose of study treatment (BG00011 or placebo). 'n' are the subjects who were assessed at the specified timepoint in this endpoint.

End point type	Secondary

End point timeframe:

Up to Week 44

End point values	Placebo	BG00011		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	54		
Units: litres				
arithmetic mean (standard deviation)				
Baseline (n=52,54)	2.883 (± 0.7037)	2.867 (± 0.8607)		
Change at Week 4 (n=51,52)	0.006 (± 0.1544)	0.032 (± 0.1526)		
Change at Week 8 (n=45,45)	-0.030 (± 0.1575)	0.007 (± 0.1513)		
Change at Week 12 (n=41,39)	-0.020 (± 0.1846)	0.000 (± 0.2247)		
Change at Week 16 (n=37,39)	-0.046 (± 0.1819)	-0.042 (± 0.2400)		

Change at Week 20 (n=30,31)	-0.086 (± 0.1921)	-0.121 (± 0.3318)		
Change at Week 26 (n=23,20)	-0.079 (± 0.1949)	-0.069 (± 0.3045)		
Change at Week 32 (n=17,13)	-0.078 (± 0.1979)	-0.152 (± 0.3142)		
Change at Week 38 (n=12,11)	-0.131 (± 0.1847)	-0.275 (± 0.3436)		
Change at Week 44 (n=8,4)	-0.200 (± 0.2153)	-0.485 (± 0.3816)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Percent Predicted FVC

End point title	Change from Baseline in Percent Predicted FVC

End point description:

FVC is the total amount of air exhaled during the forced expiratory volume test that is measured during spirometry and is the most important measurement of lung function. This test requires subject to breath into a tube connected to a machine that measures the amount of air that can be moved in and out of the lungs after taking an inhaled bronchodilator medicine which is used to dilate subject's bronchial (breathing) tubes. Percent predicted FVC (in %) = [(observed FVC)/(predicted FVC)]*100. Change from baseline is defined as post-baseline value minus baseline value. A negative change from baseline indicates decline. MITT population included all subjects who were randomised and received at least 1 dose of study treatment (BG00011 or placebo). 'n' are the subjects who were assessed at the specified timepoint in this endpoint.

End point type	Secondary

End point timeframe:

Up to Week 44

End point values	Placebo	BG00011		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	54		
Units: percentage of predicted FVC				
arithmetic mean (standard deviation)				
Baseline (n=52,54)	76.1 (± 15.46)	77.4 (± 17.07)		
Change at Week 4 (n=51,52)	0.1 (± 4.13)	1.1 (± 4.52)		
Change at Week 8 (n=45,45)	-0.7 (± 4.22)	0.4 (± 4.12)		
Change at Week 12 (n=41,39)	-0.4 (± 5.31)	0.1 (± 5.79)		
Change at Week 16 (n=37,39)	-1.1 (± 4.97)	-0.8 (± 6.24)		
Change at Week 20 (n=30,31)	-2.3 (± 5.04)	-3.0 (± 8.08)		
Change at Week 26 (n=23,20)	-2.0 (± 5.60)	-1.6 (± 8.19)		
Change at Week 32 (n=17,13)	-1.9 (± 5.44)	-3.7 (± 8.66)		
Change at Week 38 (n=12,11)	-3.4 (± 5.43)	-7.4 (± 8.44)		
Change at Week 44 (n=8,4)	-5.1 (± 6.08)	-12.5 (± 9.26)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Absolute Carbon Monoxide Diffusion Capacity (DLco)

End point title	Change from Baseline in Absolute Carbon Monoxide Diffusion Capacity (DLco)

End point description:

DLCO is a measurement of the ability of the lungs to transfer gases from the air to the blood. Evaluation of DLco was be performed by single-breath carbon monoxide diffusing capacity. DLCO was assessed in milliliters per minute per millimeter of mercury (mL/min/mmHg). Change from baseline is defined as post-baseline value minus baseline value. A negative change from baseline indicates decline. MITT population included all subjects who were randomised and received at least 1 dose of study treatment (BG00011 or placebo). 'n' are the subjects who were assessed at the specified timepoint in this endpoint.

End point type	Secondary

End point timeframe:

Up to Early Termination Visit (Up to Week 52)

End point values	Placebo	BG00011		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	54		
Units: mL/min/mmHg				
arithmetic mean (standard deviation)				
Baseline (n=52,54)	4.397 (± 1.1853)	4.036 (± 1.1043)		
Change at Week 4 (n=50,52)	-0.094 (± 0.4783)	0.019 (± 0.4431)		
Change at Week 8 (n=46,43)	-0.108 (± 0.5583)	0.028 (± 0.6078)		
Change at Week 16 (n=34,38)	-0.205 (± 0.6579)	-0.263 (± 0.5472)		
Change at Week 26 (n=23,20)	-0.074 (± 0.7756)	-0.383 (± 0.7427)		
Change at Week 38 (n=11,11)	-0.025 (± 0.5611)	-0.445 (± 0.6153)		
Change at Week 52 (n=5,4)	-0.228 (± 0.1839)	-0.400 (± 0.7921)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Percent Predicted Carbon Monoxide Diffusion Capacity (DLco)

End point title	Change from Baseline in Percent Predicted Carbon Monoxide Diffusion Capacity (DLco)

End point description:

DLCO is a measurement of the ability of the lungs to transfer gases from the air to the blood. Evaluation of DLco was be performed by single-breath carbon monoxide diffusing capacity. Percent of predicted DLco (in %) = [(observed DLco)/(predicted DLco)]*100. Change from baseline is defined as post-

baseline value minus baseline value. A negative change from baseline indicates decline. MITT population included all subjects who were randomised and received at least 1 dose of study treatment (BG00011 or placebo). 'n' are the subjects who were assessed at the specified timepoint in this endpoint.

End point type	Secondary

End point timeframe:

Up to Early Termination Visit (Up to Week 52)

End point values	Placebo	BG00011		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	54		
Units: percentage of predicted DLco				
arithmetic mean (standard deviation)				
Baseline (n=52,54)	52.6 (± 13.56)	49.1 (± 11.15)		
Change at Week 4 (n=50,52)	-1.1 (± 5.62)	0.4 (± 5.08)		
Change at Week 8 (n=46,43)	-1.5 (± 6.75)	0.5 (± 7.78)		
Change at Week 16 (n=34,38)	-2.4 (± 7.48)	-3.1 (± 6.49)		
Change at Week 26 (n=23,20)	-1.3 (± 9.10)	-4.8 (± 8.78)		
Change at Week 38 (n=11,11)	-0.5 (± 6.42)	-5.5 (± 6.82)		
Change at Week 52 (n=5,4)	-2.4 (± 1.82)	-4.0 (± 9.56)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Absolute Total Lung Capacity (TLC)

End point title	Change from Baseline in Absolute Total Lung Capacity (TLC)

End point description:

Total lung capacity is the measure of lung volume was measured by full-body plethysmography. Change from baseline is defined as post-baseline value minus baseline value. A negative change from baseline indicates decline. MITT population included all subjects who were randomised and received at least 1 dose of study treatment (BG00011 or placebo). 'n' are the subjects who were assessed at the specified timepoint in this endpoint. 9999 indicates that the data was not reported as no subjects were evaluated at the given time point.

End point type	Secondary

End point timeframe:

Up to Early Termination Visit (Up to Week 52)

End point values	Placebo	BG00011		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	54		
Units: litres				
arithmetic mean (standard deviation)				
Baseline (n=52,54)	4.472 (± 1.0497)	4.413 (± 1.0560)		

Change at Week 4 (n=1,4)	0.090 (± 99999)	-0.080 (± 0.2276)		
Change at Week 8 (n=1,0)	-0.010 (± 99999)	9999 (± 9999)		
Change at Week 12 (n=3,1)	-0.113 (± 0.3272)	0.380 (± 99999)		
Change at Week 16 (n=1,4)	0.060 (± 99999)	-0.350 (± 0.2131)		
Change at Week 20 (n=5,5)	-0.002 (± 0.2344)	-0.310 (± 0.3476)		
Change at Week 26 (n=9,9)	-0.103 (± 0.2293)	-0.214 (± 0.4403)		
Change at Week 32 (n=1,1)	-0.370 (± 99999)	0.140 (± 99999)		
Change at Week 38 (n=2,3)	-0.090 (± 0.2263)	-0.023 (± 0.4754)		
Change at Week 44 (n=2,0)	-0.160 (± 0.0283)	9999 (± 9999)		
Change at Week 52 (n=3,2)	-0.197 (± 0.3075)	-0.695 (± 0.3465)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Percent Predicted TLC

End point title	Change from Baseline in Percent Predicted TLC

End point description:

Total lung capacity is the measure of lung volume was measured by full-body plethysmography. Percent of predicted TLC (in %) = [(observed TLC)/(predicted TLC)]*100. Change from baseline is defined as post-baseline value minus baseline value. A negative change from baseline indicates decline. MITT population included all participants who were randomized and received at least 1 dose of study treatment (BG00011 or placebo). 'n' are the subjects who were assessed at the specified time point in this endpoint. 99999 indicates that SD was not calculable as there was only 1 subject. 9999 indicates that the data was not reported as no subjects were evaluated at the given time point.

End point type	Secondary

End point timeframe:

Up to Early Termination Visit (Up to Week 52)

End point values	Placebo	BG00011		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	54		
Units: percentage of predicted TLC				
arithmetic mean (standard deviation)				
Baseline (n=52,54)	69.6 (± 14.67)	67.7 (± 12.74)		
Change at Week 4 (n=1,4)	2.0 (± 99999)	-1.3 (± 3.50)		
Change at Week 8 (n=1,0)	0.0 (± 99999)	9999 (± 9999)		
Change at Week 12 (n=3,1)	-1.3 (± 4.93)	5.0 (± 99999)		
Change at Week 16 (n=1,4)	1.0 (± 99999)	-4.8 (± 2.75)		
Change at Week 20 (n=5,5)	0.0 (± 3.81)	-5.8 (± 5.76)		
Change at Week 26 (n=9,9)	-1.6 (± 3.78)	-3.0 (± 6.12)		

Change at Week 32 (n=1,1)	-5.0 (± 99999)	3.0 (± 99999)		
Change at Week 38 (n=2,3)	-2.0 (± 4.24)	-0.3 (± 6.51)		
Change at Week 44 (n=2,0)	-2.0 (± 0.00)	9999 (± 9999)		
Change at Week 52 (n=3,2)	-2.7 (± 3.79)	-10.5 (± 3.54)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in 6 Minute Walk Test (6MWT) Parameters

End point title	Change from Baseline in 6 Minute Walk Test (6MWT) Parameters

End point description:

The 6MWT measures the distance (in meters), a subject is able to walk in 6 minutes. This test measures the distance a person can walk quickly on a flat, hard surface in 6 minutes and reflects an individual's ability to perform daily physical activities. MITT population included all subjects who were randomised and received at least 1 dose of study treatment (BG00011 or placebo). 'n' are subjects with data available for analyses at given timepoint. Subjects at Week 52, are a few subjects whose early termination visit fell into the analysis visit window of the Week 52 visit. No subjects received Week 52 dosing.

End point type	Secondary

End point timeframe:

Baseline, Week 26 and Week 52

End point values	Placebo	BG00011		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	54		
Units: meters				
arithmetic mean (standard deviation)				
Baseline (n=52,54)	458.4 (± 115.33)	404.0 (± 122.61)		
Change at Week 26 (n=24,20)	-5.9 (± 38.79)	-28.6 (± 67.21)		
Change at Week 52 (n=4,4)	44.8 (± 87.16)	-40.0 (± 94.60)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	Number of Subjects with Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point description:

An AE is any untoward medical occurrence in a subject administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment. An AE can therefore be any

unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product. An SAE is any untoward medical occurrence that at any dose results in death, requires inpatient hospitalization, results in persistent or significant disability and/or results in a congenital anomaly. The safety population included all subjects who were randomised and receive at least 1 dose of study treatment (BG00011 or placebo).

End point type	Secondary

End point timeframe:

Up to Week 60 (End of Study)

End point values	Placebo	BG00011		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	54		
Units: subjects				
AEs	39	47		
SAEs	7	15		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Anti-BG00011 Antibodies in the Serum

End point title	Number of Subjects With Anti-BG00011 Antibodies in the Serum

End point description:

The immunogenicity population defined as subjects from mITT population who have at least 1 postdose immunogenicity sample evaluated for anti-BG00011 antibodies. 'n' are the subjects who were assessed in this endpoint.

End point type	Secondary

End point timeframe:

Up to Week 60 (End of Study)

End point values	Placebo	BG00011		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	42		
Units: subjects	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of BG00011 in the Serum

End point title	Concentration of BG00011 in the Serum[4]

End point description:

Pharmacokinetics (PK) population included all subjects who received at least 1 dose of study treatment and had at least one PK concentration measurement. "n" indicates number of subjects analysed at the give time point. Subjects at Week 52 are a few subjects whose early termination visit fell into the analysis visit window of the Week 52 visit. No participant received Week 52 dosing.

End point type	Secondary

End point timeframe:

Predose on Day 0, Day 5, Week 4, Week 8, Week 12, Week 26, Week 38, Week 52, and Safety Follow-up Visit (Up to Week 60).

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The serum concentration of BG00011 is measured in subjects in BG00011 arm.

End point values	BG00011			
Subject group type	Reporting group			
Number of subjects analysed	54			
Units: nanograms (ng)/mL				
arithmetic mean (standard deviation)				
Baseline (n=54)	0 (± 0)			
Day 5 (n=53)	2292.83 (± 1778.376)			
Week 4 (n=53)	5323.08 (± 3058.436)			
Week 8 (n=44)	7971.05 (± 4912.091)			
Week 12 (n=39)	7768.33 (± 5139.179)			
Week 16 (n=37)	6934.86 (± 4288.642)			
Week 20 (n=29)	6614.24 (± 4203.020)			
Week 26 (n=19)	8579.42 (± 9754.642)			
Week 38 (n=10)	3560.00 (± 2771.630)			
Week 52 (n=3)	1085.33 (± 455.978)			
Safety follow-up (n=9)	344.64 (± 701.639)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 60 Weeks (End of Study)

Adverse event reporting additional description:

The safety population included all the subjects who were randomised and receive at least 1 dose of study treatment (BG00011 or placebo).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	Placebo

Reporting group description: -

Reporting group title	BG00011

Reporting group description: -

Serious adverse events	Placebo	BG00011	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 52 (13.46%)	15 / 54 (27.78%)	
number of deaths (all causes)	0	4	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	1 / 52 (1.92%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian adenoma			
subjects affected / exposed	1 / 52 (1.92%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	0 / 52 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			

Joint dislocation			
subjects affected / exposed	1 / 52 (1.92%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Steal syndrome			
subjects affected / exposed	1 / 52 (1.92%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Carotid artery stenosis			
subjects affected / exposed	0 / 52 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	1 / 52 (1.92%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diverticulum			
subjects affected / exposed	0 / 52 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Fallopian tube cyst			
subjects affected / exposed	1 / 52 (1.92%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst			
subjects affected / exposed	1 / 52 (1.92%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			

subjects affected / exposed	0 / 52 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Dyspnoea			
subjects affected / exposed	0 / 52 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Idiopathic pulmonary fibrosis			
subjects affected / exposed	0 / 52 (0.00%)	8 / 54 (14.81%)	
occurrences causally related to treatment / all	0 / 0	2 / 9	
deaths causally related to treatment / all	0 / 0	0 / 2	
Pneumothorax spontaneous			
subjects affected / exposed	1 / 52 (1.92%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 52 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 52 (1.92%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip deformity			
subjects affected / exposed	1 / 52 (1.92%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 52 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Influenza			
subjects affected / exposed	1 / 52 (1.92%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 52 (0.00%)	2 / 54 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Urinary tract infection			
subjects affected / exposed	0 / 52 (0.00%)	2 / 54 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	BG00011	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 52 (59.62%)	40 / 54 (74.07%)	
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 52 (0.00%)	3 / 54 (5.56%)	
occurrences (all)	0	3	
Fall			
subjects affected / exposed	1 / 52 (1.92%)	4 / 54 (7.41%)	
occurrences (all)	1	4	
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 52 (9.62%)	1 / 54 (1.85%)	
occurrences (all)	6	1	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	8 / 52 (15.38%)	4 / 54 (7.41%)	
occurrences (all)	8	4	
Injection site bruising			

subjects affected / exposed	4 / 52 (7.69%)	2 / 54 (3.70%)	
occurrences (all)	4	2	
Injection site pain			
subjects affected / exposed	0 / 52 (0.00%)	4 / 54 (7.41%)	
occurrences (all)	0	4	
Eye disorders			
Cataract			
subjects affected / exposed	0 / 52 (0.00%)	3 / 54 (5.56%)	
occurrences (all)	0	4	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	5 / 52 (9.62%)	13 / 54 (24.07%)	
occurrences (all)	7	14	
Nausea			
subjects affected / exposed	5 / 52 (9.62%)	5 / 54 (9.26%)	
occurrences (all)	8	6	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	15 / 52 (28.85%)	11 / 54 (20.37%)	
occurrences (all)	17	14	
Dyspnoea			
subjects affected / exposed	10 / 52 (19.23%)	9 / 54 (16.67%)	
occurrences (all)	11	10	
Epistaxis			
subjects affected / exposed	1 / 52 (1.92%)	3 / 54 (5.56%)	
occurrences (all)	1	8	
Idiopathic pulmonary fibrosis			
subjects affected / exposed	0 / 52 (0.00%)	6 / 54 (11.11%)	
occurrences (all)	0	7	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	3 / 52 (5.77%)	0 / 54 (0.00%)	
occurrences (all)	4	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			

subjects affected / exposed	3 / 52 (5.77%)	3 / 54 (5.56%)	
occurrences (all)	3	3	
Back pain			
subjects affected / exposed	2 / 52 (3.85%)	3 / 54 (5.56%)	
occurrences (all)	2	4	
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 52 (0.00%)	3 / 54 (5.56%)	
occurrences (all)	0	3	
Lower respiratory tract infection			
subjects affected / exposed	1 / 52 (1.92%)	3 / 54 (5.56%)	
occurrences (all)	1	3	
Nasopharyngitis			
subjects affected / exposed	3 / 52 (5.77%)	7 / 54 (12.96%)	
occurrences (all)	4	8	
Upper respiratory tract infection			
subjects affected / exposed	6 / 52 (11.54%)	5 / 54 (9.26%)	
occurrences (all)	7	7	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 July 2019	The primary reason for this amendment to Protocol 203PF203 is to reflect current modified (2018) American Thoracic Society (ATS) guidelines for idiopathic pulmonary fibrosis (IPF) diagnosis. • The stratification of subjects on background therapy was clarified. • Text was added to clarify that the Investigator should attempt to complete the Investigator's determination of IPF exacerbation as soon as possible. • The exclusion criteria due to current hepatitis C or hepatitis B infection was clarified. • Liver chemistry threshold discontinuation criteria were added. • Dosing can be performed 2 days from the dose schedule. • A subject may continue in the study on their assigned study treatment if background therapy is initiated or adjusted. • The interim analysis when approximately 50% of subjects completed the week 52 visit was removed. A potential interim database lock and its associated interim analysis for efficacy and safety data is added.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

The study was terminated early due to safety findings

Notes: