Clinical trial results:
A Phase 3, randomized, double-blind, parallel-group, placebo-controlled, multi-center study to evaluate the efficacy and safety of two doses of GLPG1690 in addition to local standard of care for minimum 52 weeks in subjects with idiopathic pulmonary fibrosis

Summary

EudraCT number	2018-001405-87
Trial protocol	DK DE BE GB CZ ES GR
Global end of trial date	30 March 2021

Results information

Result version number	v1 (current)
This version publication date	08 March 2022
First version publication date	08 March 2022

Trial information

Trial identification

Sponsor protocol code	GLPG1690-CL-303

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03711162
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Galapagos NV
Sponsor organisation address	Generaal De Wittelaan L11 A3, Mechelen, Belgium, 2800
Public contact	Galapagos Medical Information, Galapagos NV, medicalinfo@glpg.com
Scientific contact	Galapagos Medical Information, Galapagos NV, medicalinfo@glpg.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	30 March 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 March 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of two doses of GLPG1690 in addition to local standard of care compared to placebo in subjects with idiopathic pulmonary fibrosis (IPF) as evaluated by the rate of decline of forced vital capacity (FVC) over a period of 52 weeks

Protection of trial subjects:

The study was performed in accordance with the ethical principles that have their origin in the "Declaration of Helsinki" and its amendments in force at the time of the study (2013 version). It was also carried out in conformity with the protocol, the International Council for Harmonization Guideline for Good Clinical Practice (ICH-GCP) E6 (R2), and local ethical and legal requirements. The investigator informed the subjects of the risks and benefits of the study. The subjects were informed that they could withdraw from the study at any time for any reason. Consent was obtained in writing prior to any study-related activities; the investigator retained a copy of the informed consent forms (ICFs), which are available to the sponsor for inspection. The subjects were covered by the sponsor's insurance according to local legal requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 November 2018
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: 51
Country: Number of subjects enrolled	Chile: 57
Country: Number of subjects enrolled	Peru: 21
Country: Number of subjects enrolled	Turkey: 24
Country: Number of subjects enrolled	Belgium: 27
Country: Number of subjects enrolled	Czechia: 16
Country: Number of subjects enrolled	Denmark: 28
Country: Number of subjects enrolled	Germany: 41
Country: Number of subjects enrolled	Greece: 15
Country: Number of subjects enrolled	Japan: 3
Country: Number of subjects enrolled	Spain: 39
Country: Number of subjects enrolled	United Kingdom: 30
Country: Number of subjects enrolled	United States: 150
Country: Number of subjects enrolled	Taiwan: 21

Worldwide total number of subjects	523
EEA total number of subjects	166

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)	116
From 65 to 84 years	398
85 years and over	9

Subject disposition

Recruitment

Recruitment details:

Participants with centrally confirmed diagnosis of IPF were enrolled at 106 sites.

Pre-assignment

Screening details:

A total of 1116 participants were screened for the study, and 525 were randomized and 523 were treated.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	GLPG1690 600 mg

Arm description:

Participants received GLPG1690 (ziritaxestat) 600 milligrams (mg), film-coated tablets orally once daily (mean GLPG1690 exposure was up to 325.3 days) in addition to local standard of care. Standard of care included either pirfenidone or nintedanib at a stable dose for at least 2 months before screening, and during screening; or neither pirfenidone or nintedanib (for any reason).

Arm type	Experimental
Investigational medicinal product name	Ziritaxestat
Investigational medicinal product code	GLPG1690
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

GLPG1690 (ziritaxestat) 600 mg, film-coated tablets orally once daily (mean GLPG1690 exposure was up to 325.3 days)

Arm title	GLPG1690 200 mg

Arm description:

Participants received GLPG1690 (ziritaxestat) 200 mg as film-coated tablet for oral use once daily (mean GLPG1690 exposure was up to 356.0 days) in addition to local standard of care. Standard of care included either pirfenidone or nintedanib at a stable dose for at least 2 months before screening, and during screening; or neither pirfenidone or nintedanib (for any reason).

Arm type	Experimental
Investigational medicinal product name	Ziritaxestat
Investigational medicinal product code	GLPG1690
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

GLPG1690 (ziritaxestat) 200 mg as film-coated tablet for oral use once daily (mean GLPG1690 exposure was up to 356.0 days)

Arm title	Placebo

Arm description:

Participants received GLPG1690 (ziritaxestat) matching placebo tablets for oral use once daily (mean GLPG1690 exposure was up to 353.4 days) in addition to local standard of care. Standard of care

included either pirfenidone or nintedanib at a stable dose for at least 2 months before screening, and during screening; or neither pirfenidone or nintedanib (for any reason).

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:

GLPG1690 (ziritaxestat) matching placebo tablets for oral use once daily (mean GLPG1690 exposure was up to 353.4 days)

Number of subjects in period 1	GLPG1690 600 mg	GLPG1690 200 mg	Placebo
Started	174	175	174
Completed	0	0	0
Not completed	174	175	174
Consent withdrawn by subject	17	10	10
Physician decision	-	2	-
Adverse Event	5	2	4
Death	11	7	8
Miscellaneous	1	2	2
Protocol specified withdrawal criteria met	-	-	1
Study Terminated by Sponsor	139	152	146
Lost to follow-up	1	-	1
Lack of efficacy	-	-	2

Baseline characteristics

Reporting groups	
Reporting group title	GLPG1690 600 mg
Reporting group description:	
Participants received GLPG1690 (ziritaxestat) 600 milligrams (mg), film-coated tablets orally once daily (mean GLPG1690 exposure was up to 325.3 days) in addition to local standard of care. Standard of care included either pirfenidone or nintedanib at a stable dose for at least 2 months before screening, and during screening; or neither pirfenidone or nintedanib (for any reason).	
Reporting group title	GLPG1690 200 mg
Reporting group description:	
Participants received GLPG1690 (ziritaxestat) 200 mg as film-coated tablet for oral use once daily (mean GLPG1690 exposure was up to 356.0 days) in addition to local standard of care. Standard of care included either pirfenidone or nintedanib at a stable dose for at least 2 months before screening, and during screening; or neither pirfenidone or nintedanib (for any reason).	
Reporting group title	Placebo
Reporting group description:	
Participants received GLPG1690 (ziritaxestat) matching placebo tablets for oral use once daily (mean GLPG1690 exposure was up to 353.4 days) in addition to local standard of care. Standard of care included either pirfenidone or nintedanib at a stable dose for at least 2 months before screening, and during screening; or neither pirfenidone or nintedanib (for any reason).	

Reporting group values	GLPG1690 600 mg	GLPG1690 200 mg	Placebo
Number of subjects	174	175	174
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	69.4	70.0	70.6
standard deviation	± 7.2	± 6.7	± 7.7
Gender categorical Units: Subjects			
Female	32	32	28
Male	142	143	146
Race Units: Subjects			
American Indian or Alaska native	10	6	6
Asian	11	9	9
Black or African American	1	0	0
Multiple	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
White	152	160	159
Ethnicity Units: Subjects			
Hispanic or Latino	44	27	26
Not Hispanic or Latino	129	145	148
Not Reported	1	2	0
Unknown	0	1	0

Forced Vital Capacity (FVC)			
FVC (in milliliter (mL)) is the maximum amount of air exhaled from lungs by a participant after taking their deepest possible breath, as measured by spirometry.			
Units: mL			
arithmetic mean	2947.0	2873.2	2943.3
standard deviation	± 820.8	± 815.8	± 738.7

Reporting group values	Total		
Number of subjects	523		
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	92		
Male	431		
Race			
Units: Subjects			
American Indian or Alaska native	22		
Asian	29		
Black or African American	1		
Multiple	0		
Native Hawaiian or Other Pacific Islander	0		
White	471		
Ethnicity			
Units: Subjects			
Hispanic or Latino	97		
Not Hispanic or Latino	422		
Not Reported	3		
Unknown	1		
Forced Vital Capacity (FVC)			
FVC (in milliliter (mL)) is the maximum amount of air exhaled from lungs by a participant after taking their deepest possible breath, as measured by spirometry.			
Units: mL			
arithmetic mean			
standard deviation	-		

End points

End points reporting groups

Reporting group title	GLPG1690 600 mg

Reporting group description:

Participants received GLPG1690 (ziritaxestat) 600 milligrams (mg), film-coated tablets orally once daily (mean GLPG1690 exposure was up to 325.3 days) in addition to local standard of care. Standard of care included either pirfenidone or nintedanib at a stable dose for at least 2 months before screening, and during screening; or neither pirfenidone or nintedanib (for any reason).

Reporting group title	GLPG1690 200 mg

Reporting group description:

Participants received GLPG1690 (ziritaxestat) 200 mg as film-coated tablet for oral use once daily (mean GLPG1690 exposure was up to 356.0 days) in addition to local standard of care. Standard of care included either pirfenidone or nintedanib at a stable dose for at least 2 months before screening, and during screening; or neither pirfenidone or nintedanib (for any reason).

Reporting group title	Placebo

Reporting group description:

Participants received GLPG1690 (ziritaxestat) matching placebo tablets for oral use once daily (mean GLPG1690 exposure was up to 353.4 days) in addition to local standard of care. Standard of care included either pirfenidone or nintedanib at a stable dose for at least 2 months before screening, and during screening; or neither pirfenidone or nintedanib (for any reason).

Subject analysis set title	GLPG1690 200 mg/Nintedanib
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received GLPG1690 (ziritaxestat) 200 mg, film-coated tablets orally once daily (mean GLPG1690 exposure was up to 325.3 days) in addition to local standard of care. Standard of care included nintedanib at a stable dose for at least 2 months before screening, and during screening.

Subject analysis set title	GLPG1690 600 mg/Nintedanib
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received GLPG1690 (ziritaxestat) 600 mg, film-coated tablets orally once daily (mean GLPG1690 exposure was up to 325.3 days) in addition to local standard of care. Standard of care included nintedanib at a stable dose for at least 2 months before screening, and during screening.

Subject analysis set title	GLPG1690 200 mg/Pirfenidone
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received GLPG1690 (ziritaxestat) 200 mg, film-coated tablets orally once daily (mean GLPG1690 exposure was up to 325.3 days) in addition to local standard of care. Standard of care included pirfenidone at a stable dose for at least 2 months before screening, and during screening.

Subject analysis set title	GLPG1690 600 mg/Pirfenidone
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received GLPG1690 (ziritaxestat) 600 mg, film-coated tablets orally once daily (mean GLPG1690 exposure was up to 325.3 days) in addition to local standard of care. Standard of care included pirfenidone at a stable dose for at least 2 months before screening, and during screening.

Primary: Annual Rate of Decline in FVC up to Week 52

End point title	Annual Rate of Decline in FVC up to Week 52

End point description:

FVC (in mL) is the maximum amount of air exhaled from lungs by a participant after taking their deepest possible breath, as measured by spirometry.

Analysis Population: Full Analysis Set – Efficacy (FAS-EF) included all randomized participants who received at least 1 dose of investigational product and excluded participants from the site found to have

serious GCP-noncompliance issues.

End point type	Primary

End point timeframe:

Baseline up to week 52

End point values	GLPG1690 600 mg	GLPG1690 200 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	169	171	164	
Units: mL				
least squares mean (standard error)	-124.6 (± 27.15)	-173.9 (± 26.31)	-147.3 (± 26.72)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	GLPG1690 600 mg v Placebo
Number of subjects included in analysis	333
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.5525 [2]
Method	Coefficient Regression Model
Parameter estimate	Least Squares (LS) mean difference
Point estimate	22.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-52.3
upper limit	97.6
Variability estimate	Standard error of the mean
Dispersion value	38.12

Notes:

[1] - Treatment effect determined by using estimated slopes for each treatment group on basis of time-by-treatment
interaction term from the mixed model.

[2] - P-value:based on random coefficient regression model(linear slope model) on FVC values.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v GLPG1690 200 mg

Number of subjects included in analysis	335
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.4776 [4]
Method	Coefficient Regression Model
Parameter estimate	LS mean difference
Point estimate	-26.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-100.5
upper limit	47.1
Variability estimate	Standard error of the mean
Dispersion value	37.53

Notes:

[3] - Treatment effect determined by using estimated slopes for each treatment group on basis of time-by-treatment
interaction term from the mixed model.

[4] - P-value: based on random coefficient regression model (linear slope model) on FVC.

Secondary: Percentage of Participants With Disease Progression Up to Week 52

End point title	Percentage of Participants With Disease Progression Up to Week 52

End point description:

Disease progression was defined as the composite occurrence of more than or equal to (>=)10 percent (%) absolute decline in percent predicted forced vital capacity (%FVC) or all-cause mortality. FVC (in mL) is the maximum amount of air exhaled from lungs by a participant after taking their deepest possible breath, as measured by spirometry.

Analysis Population: Full Analysis Set - Efficacy

End point type	Secondary

End point timeframe:

Up to week 52

End point values	GLPG1690 600 mg	GLPG1690 200 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	169	171	164	
Units: Percentage of participants				
number (not applicable)	17.8	18.7	18.3	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v GLPG1690 600 mg

Number of subjects included in analysis	333
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9648
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.56
upper limit	1.74

Statistical analysis title	Statistical Analysis 2
Comparison groups	GLPG1690 200 mg v Placebo
Number of subjects included in analysis	335
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.853
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	1.84

Secondary: Percentage of Participants With Respiratory-Related Hospitalization Until End of Study (EoS)

End point title	Percentage of Participants With Respiratory-Related Hospitalization Until End of Study (EoS)

End point description:

Percentage of participants with respiratory related hospitalization were reported in this measure.

Analysis Population: Full Analysis Set – Efficacy

End point type	Secondary

End point timeframe:

Up to EoS (week 121)

End point values	GLPG1690 600 mg	GLPG1690 200 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	169	171	164	
Units: Percentage of participants				
number (not applicable)	9.5	9.4	9.8	

Statistical analyses

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v GLPG1690 200 mg
Number of subjects included in analysis	335
Analysis specification	Pre-specified
Analysis type	superiority[5]
Parameter estimate	Hazard ratio (HR)
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.47
upper limit	1.88

Notes:

[5] - Hazard ratio and 95% confidence interval originated from a Cox proportional hazards for time to respiratory-related hospitalization.

Statistical analysis title	Statistical Analysis 1
Comparison groups	GLPG1690 600 mg v Placebo
Number of subjects included in analysis	333
Analysis specification	Pre-specified
Analysis type	superiority[6]
Parameter estimate	Hazard ratio (HR)
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	2.05

Notes:

[6] - Hazard ratio and 95% confidence interval originated from a Cox proportional hazards for time to respiratory-related hospitalization.

Secondary: Change From Baseline in St.George's Respiratory Questionnaire (SGRQ) Total Score at Week 52

End point title	Change From Baseline in St.George's Respiratory Questionnaire (SGRQ) Total Score at Week 52

End point description:

SGRQ is a 50-item paper questionnaire designed to measure and quantify the impact of chronic respiratory disease on health-related quality of life (QOL) and well-being, split into 3 domains: symptoms score assessing the frequency and severity of respiratory symptoms (Items 1-8), activity score assessing the effects of breathlessness on mobility and physical activity (Items 11-17 and 36 to 44), and impacts score assessing the psychosocial impact of the disease (Items 9-10, 18-35 and 45-50). Each item has a specific weight.

Domain scores = 100 * summed weights from positive items in that component/sum of maximum weights for all non-missing items in that component

Total score = 100 * summed weights from positive items in the questionnaire/sum of maximum weights for all non-missing items in the questionnaire

Scores were weighted such that each domain score ranged from 0 to 100 and the total score ranged from 0 to 100, with higher scores indicating the poorer health-related QOL.

End point type	Secondary

End point timeframe:

Baseline, week 52

Analysis Population: Full Analysis Set- Efficacy

End point values	GLPG1690 600 mg	GLPG1690 200 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	169	171	164	
Units: Score on a scale				
least squares mean (standard error)	3.3 (± 1.41)	4.1 (± 1.32)	3.8 (± 1.36)	

Statistical analyses

Statistical analysis title	Statistical Analysis 2
Comparison groups	GLPG1690 200 mg v Placebo
Number of subjects included in analysis	335
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8617 [7]
Method	Mixed models analysis
Parameter estimate	LS mean difference
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	4.1

Notes:

[7] - LS mean difference(95% CI) per treatment group with treatment, time (categorical), treatment-by-time interaction, stratum and baseline SGRQ total score as fixed effects and participant as random effect.

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v GLPG1690 600 mg

Number of subjects included in analysis	333
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.785 [8]
Method	Mixed models analysis
Parameter estimate	LS mean difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.4
upper limit	3.3

Notes:

[8] - LS mean difference (95% CI) per treatment group with treatment, time (categorical), treatment-by-time interaction, stratum and baseline SGRQ total score as fixed effects and participant as random effect.

Secondary: Annual Rate of Decline in FVC Until EoS

End point title	Annual Rate of Decline in FVC Until EoS

End point description:

FVC (in mL) is the maximum amount of air exhaled from lungs by a participant after taking their deepest possible breath, as measured by spirometry.

Analysis Population: Full Analysis Set - Efficacy

End point type	Secondary

End point timeframe:

Baseline up to EoS (week 121)

End point values	GLPG1690 600 mg	GLPG1690 200 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	169	171	164	
Units: mL				
arithmetic mean (standard deviation)	-127.0 (± 24.01)	-175.5 (± 22.97)	-146.4 (± 23.59)	

Statistical analyses

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v GLPG1690 200 mg
Number of subjects included in analysis	335
Analysis specification	Pre-specified
Analysis type	superiority[9]
Parameter estimate	LS Mean difference
Point estimate	-29.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-93.9
upper limit	35.8
Variability estimate	Standard error of the mean
Dispersion value	32.95

Notes:

[9] - The treatment effect was determined by using estimated slopes for each study group on the basis of the time-by-treatment interaction term from the mixed model.

Statistical analysis title	Statistical Analysis 1
Comparison groups	GLPG1690 600 mg v Placebo
Number of subjects included in analysis	333
Analysis specification	Pre-specified
Analysis type	superiority[10]
Parameter estimate	LS Mean difference
Point estimate	19.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-46.9
upper limit	85.7
Variability estimate	Standard error of the mean
Dispersion value	33.68

Notes:

[10] - The treatment effect was determined by using estimated slopes for each study group on the basis of the time-by-treatment interaction term from the mixed model.

Secondary: Percentage of Participants With Disease Progression Until EoS

End point title	Percentage of Participants With Disease Progression Until EoS

End point description:

Disease progression was defined as the composite occurrence of >=10% absolute decline in percent predicted %FVC or all-cause mortality.

Analysis Population: Full Analysis Set - Efficacy

End point type	Secondary

End point timeframe:

Up to EoS (week 121)

End point values	GLPG1690 600 mg	GLPG1690 200 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	169	171	164	
Units: Percentage of participants				
number (not applicable)	23.1	24.6	21.3	

Statistical analyses

Statistical analysis title	Statistical Analysis 2
Comparison groups	GLPG1690 200 mg v Placebo
Number of subjects included in analysis	335
Analysis specification	Pre-specified
Analysis type	superiority[11]
Parameter estimate	Odds ratio (OR)
Point estimate	1.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	2.09

Notes:

[11] - Odds ratio and 95% confidence interval originated from a logistic regression.

Statistical analysis title	Statistical Analysis 1
Comparison groups	GLPG1690 600 mg v Placebo
Number of subjects included in analysis	333
Analysis specification	Pre-specified
Analysis type	superiority[12]
Parameter estimate	Odds ratio (OR)
Point estimate	1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	1.95

Notes:

[12] - Odds ratio and 95% confidence interval originated from a logistic regression.

Secondary: Change From Baseline in St.George's Respiratory Questionnaire (SGRQ) Total Score at Week 100

End point title	Change From Baseline in St.George's Respiratory Questionnaire (SGRQ) Total Score at Week 100

End point description:

SGRQ is a 50-item paper questionnaire designed to measure and quantify the impact of chronic respiratory disease on health-related quality of life (QOL) and well-being, split into 3 domains: symptoms score assessing the frequency and severity of respiratory symptoms (Items 1-8), activity score assessing the effects of breathlessness on mobility and physical activity (Items 11-17 and 36 to 44), and impacts score assessing the psychosocial impact of the disease (Items 9-10, 18-35 and 45-50). Each item has a specific weight.

Domain scores = 100 * summed weights from positive items in that component/sum of maximum weights for all non-missing items in that component

Total score = 100 * summed weights from positive items in the questionnaire/sum of maximum weights for all non-missing items in the questionnaire

Scores were weighted such that each domain score ranged from 0 to 100 and the total score ranged from 0 to 100, with higher scores indicating the poorer health-related QOL.

End point type	Secondary

End point timeframe:

Baseline, week 100

Analysis Population: Full Analysis Set - Efficacy

End point values	GLPG1690 600 mg	GLPG1690 200 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	169	171	164	
Units: Score on a scale				
least squares mean (confidence interval 95%)	11.4 (0.3 to 22.6)	10.5 (1.1 to 20.0)	7.7 (-2.7 to 18.0)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	GLPG1690 600 mg v Placebo
Number of subjects included in analysis	333
Analysis specification	Pre-specified
Analysis type	superiority[13]
Parameter estimate	LS mean difference
Point estimate	3.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.5
upper limit	19

Notes:

[13] - The treatment effect was determined by using estimated least square mean difference between each active treatment group and placebo from the mixed model.

Statistical analysis title	Statistical Analysis 2
Comparison groups	GLPG1690 200 mg v Placebo
Number of subjects included in analysis	335
Analysis specification	Pre-specified
Analysis type	superiority[14]
Parameter estimate	LS mean difference
Point estimate	2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.1
upper limit	16.8

Notes:

[14] - The treatment effect was determined by using estimated least square mean difference between each active treatment group and placebo from the mixed model.

Secondary: Percentage of Participants With All Cause Hospitalization Until EoS

End point title	Percentage of Participants With All Cause Hospitalization Until EoS

End point description:

Percentage of participants with all cause hospitalization were reported for this measure.

Analysis Population: Full Analysis Set - Efficacy

End point type	Secondary

End point timeframe:

Up to EoS (week 121)

End point values	GLPG1690 600 mg	GLPG1690 200 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	169	171	164	
Units: Percentage of participants				
number (not applicable)	18.3	21.6	18.9	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	GLPG1690 600 mg v Placebo
Number of subjects included in analysis	333
Analysis specification	Pre-specified
Analysis type	superiority[15]
Parameter estimate	Hazard ratio (HR)
Point estimate	1.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	1.78

Notes:

[15] - Hazard ratio and 95% confidence interval originated from a cox proportional hazards model for time to first all cause hospitalization.

Statistical analysis title	Statistical Analysis 2
Comparison groups	GLPG1690 200 mg v Placebo

Number of subjects included in analysis	335
Analysis specification	Pre-specified
Analysis type	superiority[16]
Parameter estimate	Hazard ratio (HR)
Point estimate	1.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	1.98

Notes:

[16] - Hazard ratio and 95% confidence interval originated from a cox proportional hazards model for time to first all cause hospitalization.

Secondary: Percentage of Participants With Respiratory Related Mortality Until EoS

End point title	Percentage of Participants With Respiratory Related Mortality Until EoS

End point description:

Percentage of participants with respiratory related mortality until end of study were reported for this study.

Analysis Population: Full Analysis Set - Efficacy

End point type	Secondary

End point timeframe:

Up to EoS (week 121)

End point values	GLPG1690 600 mg	GLPG1690 200 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	169	171	164	
Units: Percentage of Participants				
number (not applicable)	3.6	4.1	1.8	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Hospitalized for Non-Elective Lung Transplant Until EoS

End point title	Percentage of Participants Hospitalized for Non-Elective Lung Transplant Until EoS

End point description:

Percentage of participants who were hospitalized for Non-Elective lung transplant were reported for this measure.

Analysis Population: Full Analysis Set - Efficacy

End point type	Secondary

End point timeframe:

Up to EoS (week 121)

End point values	GLPG1690 600 mg	GLPG1690 200 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	169	171	164	
Units: Percentage of Participants				
number (not applicable)	0.0	0.0	0.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With First Acute IPF Exacerbation Until EoS

End point title	Percentage of Participants With First Acute IPF Exacerbation Until EoS

End point description:

Percentage of participants with first acute IPF exacerbation until end of study were reported for this measure.

Analysis Population: Full Analysis Set - Efficacy

End point type	Secondary

End point timeframe:

Up to EoS (week 121)

End point values	GLPG1690 600 mg	GLPG1690 200 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	169	171	164	
Units: Percentage of Participants				
number (not applicable)	4.7	4.7	3.7	

Statistical analyses

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v GLPG1690 200 mg

Number of subjects included in analysis	335
Analysis specification	Pre-specified
Analysis type	superiority[17]
Parameter estimate	Hazard ratio (HR)
Point estimate	1.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.42
upper limit	3.5

Notes:

[17] - Hazard ratio and 95% confidence interval originated from a Cox proportional hazards model for time to first acute IPF exacerbation.

Statistical analysis title	Statistical Analysis 1
Comparison groups	GLPG1690 600 mg v Placebo
Number of subjects included in analysis	333
Analysis specification	Pre-specified
Analysis type	superiority[18]
Parameter estimate	Hazard ratio (HR)
Point estimate	1.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.44
upper limit	3.81

Notes:

[18] - Hazard ratio and 95% confidence interval originated from a Cox proportional hazards model for time to first acute IPF exacerbation.

Secondary: Percentage of Participants With All Cause Mortality or Hospitalization for non-elective Lung Transplant Until EoS

End point title	Percentage of Participants With All Cause Mortality or Hospitalization for non-elective Lung Transplant Until EoS

End point description:

Percentage of participants with all-cause mortality or hospitalization for non-elective lung transplant were reported for this measure.

Analysis Population: Full Analysis Set - Efficacy

End point type	Secondary

End point timeframe:

Up to EoS (week 121)

End point values	GLPG1690 600 mg	GLPG1690 200 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	161	171	164	
Units: Percentage of Participants				
number (not applicable)	7.1	4.7	4.9	

Statistical analyses

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v GLPG1690 200 mg
Number of subjects included in analysis	335
Analysis specification	Pre-specified
Analysis type	superiority[19]
Parameter estimate	Hazard ratio (HR)
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.36
upper limit	2.61

Notes:

[19] - Hazard ratio and 95% confidence interval originated from a Cox proportional hazards model for time to first all cause mortality or hospitalization for non-elective lung transplant.

Statistical analysis title	Statistical Analysis 1
Comparison groups	GLPG1690 600 mg v Placebo
Number of subjects included in analysis	325
Analysis specification	Pre-specified
Analysis type	superiority[20]
Parameter estimate	Hazard ratio (HR)
Point estimate	1.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	4.08

Notes:

[20] - Hazard ratio and 95% confidence interval originated from a Cox proportional hazards model for time to first all cause mortality or hospitalization for non-elective lung transplant.

Secondary: Percentage of Participants With All Cause Mortality, Hospitalization for Non-elective Lung Transplant, Or Qualifying For Lung Transplant Until EoS

End point title	Percentage of Participants With All Cause Mortality, Hospitalization for Non-elective Lung Transplant, Or Qualifying For Lung Transplant Until EoS

End point description:

Percentage of participants with all-cause mortality or hospitalization for non-elective lung transplant or hospitalization for qualifying for lung transplant were reported for this measure.

Analysis Population: Full Analysis Set - Efficacy

End point type	Secondary

End point timeframe:

Up to EoS (week 121)

End point values	GLPG1690 600 mg	GLPG1690 200 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	169	171	164	
Units: Percentage of participants				
number (not applicable)	7.1	4.7	4.9	

Statistical analyses

Statistical analysis title	Statistical Analysis 2
Comparison groups	GLPG1690 200 mg v Placebo
Number of subjects included in analysis	335
Analysis specification	Pre-specified
Analysis type	superiority[21]
Parameter estimate	Hazard ratio (HR)
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.36
upper limit	2.61

Notes:

[21] - Hazard ratio and 95% confidence interval originated from a Cox proportional hazards model for time to first all cause mortality, hospitalization for non-elective lung transplant or hospitalization for qualifying for lung transplant.

Statistical analysis title	Statistical Analysis 1
Comparison groups	GLPG1690 600 mg v Placebo
Number of subjects included in analysis	333
Analysis specification	Pre-specified
Analysis type	superiority[22]
Parameter estimate	Hazard ratio (HR)
Point estimate	1.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	4.08

Notes:

[22] - Hazard ratio and 95% confidence interval originated from a Cox proportional hazards model for time to first all cause mortality, hospitalization for non-elective lung transplant or hospitalization for qualifying for lung transplant.

Secondary: Percentage of Participants With All-Cause Mortality or Hospitalization that Meets >=10% Absolute Decline in %FVC or Respiratory-Related Hospitalization Until EoS

End point title	Percentage of Participants With All-Cause Mortality or

	Hospitalization that Meets >=10% Absolute Decline in %FVC or Respiratory-Related Hospitalization Until EoS

End point description:

Percentage of participants with all-cause mortality or respiratory related hospitalization that meets >=10% absolute decline in %FVC or respiratory-related hospitalization were reported for this measure.

Analysis Population: Full Analysis Set - Efficacy

End point type	Secondary

End point timeframe:

Up to EoS (week 121)

End point values	GLPG1690 600 mg	GLPG1690 200 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	169	171	164	
Units: Percentage of participants				
number (not applicable)	13.6	11.1	14.0	

Statistical analyses

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v GLPG1690 200 mg
Number of subjects included in analysis	335
Analysis specification	Pre-specified
Analysis type	superiority[23]
Parameter estimate	Hazard ratio (HR)
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.43
upper limit	1.46

Notes:

[23] - Hazard ratio and 95% confidence interval originated from a Cox proportional hazards model or time to first all-cause mortality or hospitalization that meets >=10% absolute decline in %FVC or respiratory-related hospitalization.

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v GLPG1690 600 mg
Number of subjects included in analysis	333
Analysis specification	Pre-specified
Analysis type	superiority[24]
Parameter estimate	Hazard ratio (HR)
Point estimate	1.06

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	1.91

Notes:

[24] - Hazard ratio and 95% confidence interval originated from a Cox proportional hazards model or time to first all-cause mortality or hospitalization that meets >=10% absolute decline in %FVC or respiratory-related hospitalization.

Secondary: Percentage of Participants With All-Cause Mortality or Respiratory-Related Hospitalizations Until EoS

End point title	Percentage of Participants With All-Cause Mortality or Respiratory-Related Hospitalizations Until EoS

End point description:

Percentage of participants with all-cause mortality or respiratory related hospitalization were reported for this measure.

Analysis Population: Full Analysis Set - Efficacy

End point type	Secondary

End point timeframe:

Up to EoS (week 121)

End point values	GLPG1690 600 mg	GLPG1690 200 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	169	171	164	
Units: Percentage of participants				
number (not applicable)	13.6	11.1	14.0	

Statistical analyses

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v GLPG1690 200 mg
Number of subjects included in analysis	335
Analysis specification	Pre-specified
Analysis type	superiority[25]
Parameter estimate	Hazard ratio (HR)
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.43
upper limit	1.46

Notes:

[25] - Hazard ratio and 95% confidence interval originated from a Cox proportional hazards model for time to all-cause mortality or respiratory-related hospitalizations.

Statistical analysis title	Statistical Analysis 1

Comparison groups	GLPG1690 600 mg v Placebo
Number of subjects included in analysis	333
Analysis specification	Pre-specified
Analysis type	superiority[26]
Parameter estimate	Hazard ratio (HR)
Point estimate	1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	1.91

Notes:

[26] - Hazard ratio and 95% confidence interval originated from a Cox proportional hazards model for time to all-cause mortality or respiratory-related hospitalizations.

Secondary: FVC at Week 52

End point title	FVC at Week 52

End point description:

FVC (in mL) is the maximum amount of air exhaled from lungs by a participant after taking their deepest possible breath, as measured by spirometry.

Analysis Population: FAS-EF with available data at specified time point.

End point type	Secondary

End point timeframe:

Week 52

End point values	GLPG1690 600 mg	GLPG1690 200 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	82	97	94	
Units: mL				
arithmetic mean (standard error)	2886.20 (± 83.969)	2662.90 (± 79.056)	3021.99 (± 78.415)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in FVC at Week 52

End point title	Change From Baseline in FVC at Week 52

End point description:

FVC (in mL) is the maximum amount of air exhaled from lungs by a participant after taking their deepest possible breath, as measured by spirometry.

Analysis Population: FAS-EF with available data at specified time point.

End point type	Secondary

End point timeframe:

Baseline, week 52

End point values	GLPG1690 600 mg	GLPG1690 200 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	82	97	94	
Units: mL				
arithmetic mean (standard error)	-145.94 (± 31.799)	-182.29 (± 30.286)	-133.24 (± 31.819)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in FVC at Week 52

End point title	Percent Change From Baseline in FVC at Week 52

End point description:

FVC (in mL) is the maximum amount of air exhaled from lungs by a participant after taking their deepest possible breath, as measured by spirometry.

Analysis Population: FAS-EF with available data at specified time point.
.

End point type	Secondary

End point timeframe:

Baseline, week 52

End point values	GLPG1690 600 mg	GLPG1690 200 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	82	97	94	
Units: Percent change				
arithmetic mean (standard error)	-4.57 (± 0.992)	-6.46 (± 1.115)	-4.48 (± 0.978)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in FVC at Week 112

End point title	Change From Baseline in FVC at Week 112[27]

End point description:

FVC (in mL) is the maximum amount of air exhaled from lungs by a participant after taking their deepest possible breath, as measured by spirometry.

Analysis Population: FAS - EF with available data at specified time point. No participant was available for analysis at Week 112 for arm "GLPG1690 200 mg" and "Placebo".

End point type	Secondary

End point timeframe:

Baseline, week 112

Notes:

[27] - 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: No participant was available for analysis at Week 112 for arms "GLPG1690 200 mg" and "Placebo".

End point values	GLPG1690 600 mg			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: mL				
arithmetic mean (standard error)	-55.75 (± 277.750)			

Statistical analyses

No statistical analyses for this end point

Secondary: FVC at Week 112

End point title	FVC at Week 112[28]

End point description:

FVC (in mL) is the maximum amount of air exhaled from lungs by a participant after taking their deepest possible breath, as measured by spirometry.

Analysis Population: FAS-EF with available data at specified time point. No participant was available for analysis at Week 112 for arm "GLPG1690 200 mg" and "Placebo".

End point type	Secondary

End point timeframe:

Week 112

Notes:

[28] - 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: No participant was available for analysis at Week 112 for arms "GLPG1690 200 mg" and "Placebo".

End point values	GLPG1690 600 mg			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: mL				
arithmetic mean (standard error)	3262.00 (± 15.000)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Absolute Categorical Change From Baseline in Percent FVC at Week 52: FVC Change Within ≤5

End point title	Percentage of Participants With Absolute Categorical Change From Baseline in Percent FVC at Week 52: FVC Change Within ≤5

End point description:

FVC (in mL) is the maximum amount of air exhaled from lungs by a participant after taking their deepest possible breath, as measured by spirometry.

Analysis Population: FAS - EF with available data at specified time point.

End point type	Secondary

End point timeframe:

Baseline, week 52

End point values	GLPG1690 600 mg	GLPG1690 200 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	169	171	164	
Units: Percentage of participants				
number (not applicable)	90.2	92.8	89.4	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in FVC at Week 112

End point title	Percent Change From Baseline in FVC at Week 112[29]

End point description:

FVC (in mL) is the maximum amount of air exhaled from lungs by a participant after taking their deepest possible breath, as measured by spirometry.

Analysis Population: FAS-EF with available data at specified time point. No participant was available for analysis at Week 112 for arm "GLPG1690 200 mg" and "Placebo".

End point type	Secondary

End point timeframe:

Baseline, week 112

Notes:

[29] - 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: No participant was available for analysis at Week 112 for arms "GLPG1690 200 mg" and "Placebo".

End point values	GLPG1690 600 mg			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: Percent change				
arithmetic mean (standard error)	-0.95 (± 8.288)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Absolute Categorical Change From Baseline in Percent FVC at Week 112: FVC Change Within ≤5

End point title	Percentage of Participants With Absolute Categorical Change From Baseline in Percent FVC at Week 112: FVC Change Within ≤5[30]

End point description:

FVC (in mL) is the maximum amount of air exhaled from lungs by a participant after taking their deepest possible breath, as measured by spirometry.

Analysis Population: FAS - EF with available data at specified time point. No participant was available for analysis at Week 112 for arms "GLPG1690 200 mg" and "Placebo".

End point type	Secondary

End point timeframe:

Baseline, week 112

Notes:

[30] - 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: No participant was available for analysis at Week 112 for arms "GLPG1690 200 mg" and "Placebo".

End point values	GLPG1690 600 mg			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: Percentage of participants				
number (not applicable)	50.0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Absolute Categorical Change From Baseline in Percent FVC at Week 52: FVC Change Within ≤10

End point title	Percentage of Participants With Absolute Categorical Change From Baseline in Percent FVC at Week 52: FVC Change Within ≤10

End point description:

FVC (in mL) is the maximum amount of air exhaled from lungs by a participant after taking their deepest possible breath, as measured by spirometry.

Analysis Population: FAS - EF with available data at specified time point.

End point type	Secondary

End point timeframe:

Baseline, week 52

End point values	GLPG1690 600 mg	GLPG1690 200 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	169	171	164	
Units: Percentage of participants				
number (not applicable)	97.6	97.9	96.8	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Absolute Categorical Change From Baseline in Percent FVC Until Week 112: FVC Change Within ≤10

End point title	Percentage of Participants With Absolute Categorical Change From Baseline in Percent FVC Until Week 112: FVC Change Within ≤10[31]

End point description:

FVC (in mL) is the maximum amount of air exhaled from lungs by a participant after taking their deepest possible breath, as measured by spirometry.

Analysis Population: Full Analysis Set - Efficacy. No participant was available for analysis at Week 112 for arm "GLPG1690 200 mg" and "Placebo".

End point type	Secondary

End point timeframe:

Baseline, week 112

Notes:

[31] - 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: No participant was available for analysis at Week 112 for arms "GLPG1690 200 mg" and "Placebo".

End point values	GLPG1690 600 mg			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: Percentage of participants				
number (not applicable)	100			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Treatment Emergent Adverse Events (TEAEs) and Serious TEAEs

End point title	Percentage of Participants With Treatment Emergent Adverse Events (TEAEs) and Serious TEAEs

End point description:

Safety was assessed by adverse events (AEs), which included abnormalities identified during a medical test (e.g. laboratory tests, vital signs, electrocardiogram, etc.) if the abnormality induced clinical signs or symptoms, needed active intervention, interruption or discontinuation of study drug or was clinically significant. A Treatment emergent AE (TEAE) was defined as any AE that started or worsened after the first dose of study drug up to 30 days after the last dose of study drug. AEs were considered serious (SAEs) if the AE resulted in death, was life-threatening, resulted in persistent or significant disability/incapacity or substantial disruption of the ability to conduct normal life functions, resulted in congenital anomaly, or birth defect or required inpatient hospitalization or led to prolongation of hospitalization.
Analysis Population: FAS consisted of all randomized participants who received at least 1 dose of investigational product.

End point type	Secondary

End point timeframe:

Baseline Up to 30 days after the last dose (up to week 121)

End point values	GLPG1690 600 mg	GLPG1690 200 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	174	175	174	
Units: Percentage of participants				
number (not applicable)				
TEAE	78.7	84.6	84.5	
Serious TEAE	21.8	21.7	20.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Leicester Cough Questionnaire (LCQ) Total Score and Individual Domain Score at Week 52 and Until EoS

End point title	Change From Baseline in Leicester Cough Questionnaire (LCQ)

	Total Score and Individual Domain Score at Week 52 and Until EoS

End point description:

Cough was evaluated using the LCQ. The LCQ was a 19-item questionnaire split into three domains: physical, psychological, and social. Scores were calculated by domain (range from 1 to 7, higher scores indicated a better health status) and then the total score was calculated by adding the individual domain score. Total score ranged from 3 to 21, where higher scores indicated a better health status.

Analysis Population: Due to change in planned analysis, this endpoint was not analyzed.

End point type	Secondary

End point timeframe:

Baseline, week 52, EoS (week 121)

End point values	GLPG1690 600 mg	GLPG1690 200 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[32]	0[33]	0[34]	
Units: Score on a scale				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[32] - Due to change in planned analysis, this endpoint was not analyzed.

[33] - Due to change in planned analysis, this endpoint was not analyzed.

[34] - Due to change in planned analysis, this endpoint was not analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Visual Analogue Score (VAS): Cough at Week 52 and Until EoS

End point title	Change From Baseline in Visual Analogue Score (VAS): Cough at Week 52 and Until EoS

End point description:

Cough was assessed using VAS scale, ranged from 0 (no cough) to 100 millimeter (mm) (worst possible cough).

Analysis Population: Due to change in planned analysis, this endpoint was not analyzed.

End point type	Secondary

End point timeframe:

Baseline, week 52, EoS (week 121)

End point values	GLPG1690 600 mg	GLPG1690 200 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[35]	0[36]	0[37]	
Units: Score on a scale				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[35] - Due to change in planned analysis, this endpoint was not analyzed

[36] - Due to change in planned analysis, this endpoint was not analyzed

[37] - Due to change in planned analysis, this endpoint was not analyzed

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in VAS Score: Urge to Cough at Week 52 and Until EoS

End point title	Change From Baseline in VAS Score: Urge to Cough at Week 52 and Until EoS

End point description:

Urge to Cough was assessed using VAS scale, ranged from 0 (no urge to cough) to of 100 mm (highest urge to cough).

Analysis Population: Due to change in planned analysis, this endpoint was not analysed.

End point type	Secondary

End point timeframe:

Baseline, week 52, EoS (week 121)

End point values	GLPG1690 600 mg	GLPG1690 200 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[38]	0[39]	0[40]	
Units: Score on a scale				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[38] - Due to change in planned analysis, this endpoint was not analyzed

[39] - Due to change in planned analysis, this endpoint was not analyzed

[40] - Due to change in planned analysis, this endpoint was not analyzed

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in European Quality Of Life (EQ) VAS at Week 52 and Until EoS

End point title	Change From Baseline in European Quality Of Life (EQ) VAS at Week 52 and Until EoS

End point description:

EuroQol outcome measurements was a printed 20 centimeter (cm) EQ VAS that appears somewhat like a thermometer, on which a score from 0 (worst imaginable health state or death) to 100 (best imaginable health state) was marked by the participant (or, when necessary, their proxy) with the scale in view.

Analysis Population: Due to change in planned analysis, this endpoint was not analysed.

End point type	Secondary

End point timeframe:

Baseline, week 52, EoS (week 121)

End point values	GLPG1690 600 mg	GLPG1690 200 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[41]	0[42]	0[43]	
Units: Score on a scale				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[41] - Due to change in planned analysis, this endpoint was not analyzed

[42] - Due to change in planned analysis, this endpoint was not analyzed

[43] - Due to change in planned analysis, this endpoint was not analyzed

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in King's Brief Interstitial Lung Disease (K-BILD) at Week 52 and EoS

End point title	Change From Baseline in King's Brief Interstitial Lung Disease (K-BILD) at Week 52 and EoS

End point description:

The K-BILD questionnaire was specifically developed to analyze the health status of participants with ILD. The questionnaire consists of 15 items (assessed by the patients on a scale ranging from 1 to 7, where 1 and 7 represent worst and best health status). Items are compiled into 3 domains: breathlessness and activities (range: 0-21), psychological (range: 0-34), and chest symptoms (range: 0-8). To score the K-BILD, the Likert response scale weightings for individual items are combined and scores are transformed to a range of 0-100 by using logit values (higher scores indicate better health status).

Analysis Population: Due to change in planned analysis, this endpoint was not analysed.

End point type	Secondary

End point timeframe:

Baseline, week 52, EoS (week 121)

End point values	GLPG1690 600 mg	GLPG1690 200 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[44]	0[45]	0[46]	
Units: Score on a scale				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[44] - Due to change in planned analysis, this endpoint was not analyzed

[45] - Due to change in planned analysis, this endpoint was not analyzed

[46] - Due to change in planned analysis, this endpoint was not analyzed

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under The Concentration Time Curve (AUC) of Ziritaxtestat

End point title	Area Under The Concentration Time Curve (AUC) of Ziritaxtestat[47]

End point description:

Area under the concentration time curve of ziritaxtestat was reported.

Analysis Population: Pharmacokinetic Analysis Set: All randomized participants who received at least one dose of IP and for whom evaluable PK data were available.

End point type	Secondary

End point timeframe:

Sparse samples collected on day 1 pre-dose, day 85 post-dose, day 237 post-dose, day 183 pre-dose, day 365 pre-dose

Notes:

[47] - 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: Endpoint was analyzed only in the arms who received study drug.

End point values	GLPG1690 600 mg	GLPG1690 200 mg	GLPG1690 200 mg/Nintedanib	GLPG1690 600 mg/Nintedanib
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	18	24	24	26
Units: Nanogram * milliliter per hour (ng*mL/h)				
median (confidence interval 90%)	51136 (40132.9 to 62139.1)	10367 (7960.4 to 12773.6)	7095 (6411.3 to 7778.7)	33796 (29021.56 to 38570.44)

End point values	GLPG1690 200 mg/Pirfenidone	GLPG1690 600 mg/Pirfenidone		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	27		
Units: Nanogram * milliliter per hour (ng*mL/h)				
median (confidence interval 90%)	6375 (5907.28 to 6842.72)	21188 (16847.76 to 25528.24)		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Concentration (Cmax) of Ziritaxtestat

End point title	Maximum Observed Plasma Concentration (Cmax) of Ziritaxtestat[48]

End point description:

Maximum Observed Plasma Concentration of Ziritaxtestat was reported.

Analysis Population: Pharmacokinetic Analysis Set

End point type	Secondary

End point timeframe:

Sparse samples collected on day 1 pre-dose, day 85 post-dose, day 237 post-dose, day 183 pre-dose, day 365 pre-dose

Notes:

[48] - 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: Endpoint was analyzed only in the arms who received study drug.

End point values	GLPG1690 600 mg	GLPG1690 200 mg	GLPG1690 200 mg/Nintedanib	GLPG1690 600 mg/Nintedanib
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	18	24	24	26
Units: Nanogram per milliliter (ng/mL)				
median (confidence interval 90%)	864 (721.42 to 1006.58)	3962 (3330.09 to 4593.91)	583 (541.55 to 624.45)	2686 (2414.7 to 2957.3)

End point values	GLPG1690 200 mg/Pirfenidone	GLPG1690 600 mg/Pirfenidone		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	27		
Units: Nanogram per milliliter (ng/mL)				
median (confidence interval 90%)	591 (556.46 to 625.54)	2009 (1692.94 to 2325.06)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Functional Exercise Capacity Assessed by Total Distance Walked in Six-minute Walk Test (6MWT) at Week 52 and 100

End point title	Change From Baseline in Functional Exercise Capacity Assessed by Total Distance Walked in Six-minute Walk Test (6MWT) at Week 52 and 100

End point description:

The 6-MWT depicts the total distance covered by a participant during 6 minutes of walking.

Analysis Population: FAS-EF with available data at specified time point.

End point type	Secondary

End point timeframe:

Baseline, week 52, week 100

End point values	GLPG1690 600 mg	GLPG1690 200 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	67[49]	73[50]	80[51]	
Units: Meter				
arithmetic mean (standard error)				
Change at Week 52	-36.34 (± 7.805)	-15.65 (± 9.865)	-34.75 (± 11.546)	
Change at Week 100	-83.00 (± 17.521)	-79.00 (± 13.00)	-137.87 (± 93.135)	

Notes:

[49] - n = 67, 3

[50] - n = 73, 2

[51] - n = 80, 2

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Diffusing Capacity of Lung for Carbon Monoxide (DLCO) (corrected for hemoglobin [Hb]) at Week 52 and Week 100

End point title	Change From Baseline in Diffusing Capacity of Lung for Carbon Monoxide (DLCO) (corrected for hemoglobin [Hb]) at Week 52 and Week 100

End point description:

Change from baseline in DLCO (percent predicted hemoglobin level corrected) was reported for this measure.

Analysis Population: FAS - EF with available data at specified time point.

mmol/min/kPa: Millimole per minute per kilopascal

End point type	Secondary

End point timeframe:

Baseline, week 52, week 100

End point values	GLPG1690 600 mg	GLPG1690 200 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	60[52]	77[53]	73[54]	
Units: mmol/min/kPa				
arithmetic mean (standard error)				
Change at Week 52	-0.640 (± 0.1205)	-0.137 (± 0.1288)	-0.193 (± 0.0907)	
Change at Week 100	-0.215 (± 0.6737)	-1.670 (± 99999)	-2.134 (± 1.9836)	

Notes:
[52] - n = 60, 3
[53] - n = 77, 1
[54] - n = 73, 2

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline up to 30 days after the last dose (Up to week 121)	
Adverse event reporting additional description:	
FAS consisted of all randomized participants who received at least 1 dose of investigational product.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received GLPG1690 (ziritaxestat) matching placebo tablets for oral use once daily (mean GLPG1690 exposure was 50.48 weeks) in addition to local standard of care. Standard of care included either pirfenidone or nintedanib at a stable dose for at least 2 months before screening, and during screening; or neither pirfenidone or nintedanib (for any reason).	
Reporting group title	GLPG1690 600 mg
Reporting group description:	
Participants received GLPG1690 (ziritaxestat) 600 mg, film-coated tablets orally once daily (mean GLPG1690 exposure was 46.47 weeks) in addition to local standard of care. Standard of care included either pirfenidone or nintedanib at a stable dose for at least 2 months before screening, and during screening; or neither pirfenidone or nintedanib (for any reason).	
Reporting group title	GLPG1690 200 mg
Reporting group description:	
Participants received GLPG1690 (ziritaxestat) 200 mg as film-coated tablet for oral use once daily (mean GLPG1690 exposure was 50.85 weeks) in addition to local standard of care. Standard of care included either pirfenidone or nintedanib at a stable dose for at least 2 months before screening, and during screening; or neither pirfenidone or nintedanib (for any reason).	

Serious adverse events	Placebo	GLPG1690 600 mg	GLPG1690 200 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	36 / 174 (20.69%)	38 / 174 (21.84%)	38 / 175 (21.71%)
number of deaths (all causes)	9	12	8
number of deaths resulting from adverse events	8	9	6
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign lung neoplasm			
subjects affected / exposed	0 / 174 (0.00%)	1 / 174 (0.57%)	0 / 175 (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
Colon neoplasm			

subjects affected / exposed	0 / 174 (0.00%)	1 / 174 (0.57%)	0 / 175 (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
Lymphoproliferative disorder			
subjects affected / exposed	1 / 174 (0.57%)	0 / 174 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	0 / 174 (0.00%)	0 / 174 (0.00%)	1 / 175 (0.57%)
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	0 / 174 (0.00%)	0 / 174 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Aortic stenosis			
subjects affected / exposed	0 / 174 (0.00%)	0 / 174 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 174 (0.00%)	0 / 174 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orthostatic hypotension			
subjects affected / exposed	0 / 174 (0.00%)	0 / 174 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 174 (0.00%)	0 / 174 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Drug intolerance			
subjects affected / exposed	0 / 174 (0.00%)	0 / 174 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	0 / 174 (0.00%)	0 / 174 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 174 (0.00%)	0 / 174 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Idiopathic pulmonary fibrosis			
subjects affected / exposed	12 / 174 (6.90%)	12 / 174 (6.90%)	7 / 175 (4.00%)
occurrences causally related to treatment / all	0 / 19	1 / 20	0 / 16
deaths causally related to treatment / all	0 / 3	0 / 4	0 / 1
Acute respiratory failure			
subjects affected / exposed	1 / 174 (0.57%)	0 / 174 (0.00%)	2 / 175 (1.14%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 5
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Epistaxis			
subjects affected / exposed	1 / 174 (0.57%)	0 / 174 (0.00%)	0 / 175 (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 arterial hypertension			
subjects affected / exposed	0 / 174 (0.00%)	0 / 174 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 174 (0.00%)	4 / 174 (2.30%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	2 / 5	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0

Pneumothorax spontaneous			
subjects affected / exposed	0 / 174 (0.00%)	0 / 174 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	2 / 174 (1.15%)	2 / 174 (1.15%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 174 (0.00%)	0 / 174 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	0 / 174 (0.00%)	0 / 174 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device loosening			
subjects affected / exposed	0 / 174 (0.00%)	0 / 174 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood bilirubin increased			
subjects affected / exposed	1 / 174 (0.57%)	1 / 174 (0.57%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 1	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet morphology abnormal			
subjects affected / exposed	0 / 174 (0.00%)	0 / 174 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			

subjects affected / exposed	0 / 174 (0.00%)	1 / 174 (0.57%)	0 / 175 (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
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	0 / 174 (0.00%)	1 / 174 (0.57%)	0 / 175 (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
Foot fracture			
subjects affected / exposed	1 / 174 (0.57%)	0 / 174 (0.00%)	0 / 175 (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
Joint dislocation			
subjects affected / exposed	0 / 174 (0.00%)	0 / 174 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 174 (0.00%)	1 / 174 (0.57%)	0 / 175 (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
Congenital, familial and genetic disorders			
Hydrocele			
subjects affected / exposed	0 / 174 (0.00%)	1 / 174 (0.57%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 174 (0.00%)	1 / 174 (0.57%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			

subjects affected / exposed	1 / 174 (0.57%)	2 / 174 (1.15%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 174 (0.00%)	0 / 174 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic valve incompetence			
subjects affected / exposed	1 / 174 (0.57%)	0 / 174 (0.00%)	0 / 175 (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
Atrioventricular block complete			
subjects affected / exposed	1 / 174 (0.57%)	0 / 174 (0.00%)	0 / 175 (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 failure congestive			
subjects affected / exposed	0 / 174 (0.00%)	0 / 174 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Coronary artery disease			
subjects affected / exposed	0 / 174 (0.00%)	2 / 174 (1.15%)	0 / 175 (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
Coronary artery stenosis			
subjects affected / exposed	1 / 174 (0.57%)	0 / 174 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiomyopathy			
subjects affected / exposed	0 / 174 (0.00%)	1 / 174 (0.57%)	0 / 175 (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
Myocardial infarction			

subjects affected / exposed	2 / 174 (1.15%)	1 / 174 (0.57%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Myocardial rupture			
subjects affected / exposed	1 / 174 (0.57%)	0 / 174 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pericardial haemorrhage			
subjects affected / exposed	1 / 174 (0.57%)	0 / 174 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 174 (0.00%)	0 / 174 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carotid artery stenosis			
subjects affected / exposed	1 / 174 (0.57%)	0 / 174 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 174 (0.00%)	0 / 174 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cubital tunnel syndrome			
subjects affected / exposed	0 / 174 (0.00%)	0 / 174 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Limbic encephalitis			
subjects affected / exposed	1 / 174 (0.57%)	0 / 174 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Encephalopathy			

subjects affected / exposed	0 / 174 (0.00%)	0 / 174 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 174 (0.00%)	1 / 174 (0.57%)	0 / 175 (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
Status epilepticus			
subjects affected / exposed	1 / 174 (0.57%)	0 / 174 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	1 / 174 (0.57%)	0 / 174 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Leukocytosis			
subjects affected / exposed	0 / 174 (0.00%)	0 / 174 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	1 / 174 (0.57%)	0 / 174 (0.00%)	0 / 175 (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			
Cataract			
subjects affected / exposed	1 / 174 (0.57%)	0 / 174 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Visual impairment			
subjects affected / exposed	0 / 174 (0.00%)	1 / 174 (0.57%)	0 / 175 (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

Gastrointestinal disorders			
Gastrointestinal disorder			
subjects affected / exposed	0 / 174 (0.00%)	0 / 174 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 174 (0.00%)	1 / 174 (0.57%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral hernia strangulated			
subjects affected / exposed	0 / 174 (0.00%)	1 / 174 (0.57%)	0 / 175 (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
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 174 (0.00%)	1 / 174 (0.57%)	0 / 175 (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
Haemorrhoids			
subjects affected / exposed	1 / 174 (0.57%)	0 / 174 (0.00%)	0 / 175 (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
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 174 (0.00%)	0 / 174 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 174 (0.57%)	0 / 174 (0.00%)	0 / 175 (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
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	1 / 174 (0.57%)	0 / 174 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cholecystitis			
subjects affected / exposed	1 / 174 (0.57%)	0 / 174 (0.00%)	0 / 175 (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
Cholecystitis acute			
subjects affected / exposed	0 / 174 (0.00%)	1 / 174 (0.57%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	0 / 174 (0.00%)	0 / 174 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 174 (0.00%)	1 / 174 (0.57%)	2 / 175 (1.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	1 / 174 (0.57%)	0 / 174 (0.00%)	0 / 175 (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
Calculus bladder			
subjects affected / exposed	1 / 174 (0.57%)	0 / 174 (0.00%)	0 / 175 (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
Musculoskeletal and connective tissue disorders			
Spinal pain			
subjects affected / exposed	0 / 174 (0.00%)	0 / 174 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 174 (0.00%)	0 / 174 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Spinal osteoarthritis			
subjects affected / exposed	1 / 174 (0.57%)	0 / 174 (0.00%)	0 / 175 (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			
Appendicitis			
subjects affected / exposed	0 / 174 (0.00%)	0 / 174 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial infection			
subjects affected / exposed	0 / 174 (0.00%)	1 / 174 (0.57%)	0 / 175 (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
COVID-19			
subjects affected / exposed	2 / 174 (1.15%)	2 / 174 (1.15%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 174 (0.00%)	1 / 174 (0.57%)	3 / 175 (1.71%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Campylobacter gastroenteritis			
subjects affected / exposed	0 / 174 (0.00%)	0 / 174 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 174 (0.00%)	0 / 174 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 174 (0.00%)	1 / 174 (0.57%)	0 / 175 (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
Lower respiratory tract infection			

subjects affected / exposed	2 / 174 (1.15%)	1 / 174 (0.57%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 174 (0.00%)	1 / 174 (0.57%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 174 (0.57%)	4 / 174 (2.30%)	2 / 175 (1.14%)
occurrences causally related to treatment / all	0 / 1	1 / 7	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 174 (0.00%)	1 / 174 (0.57%)	0 / 175 (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
Scrotal abscess			
subjects affected / exposed	0 / 174 (0.00%)	0 / 174 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 174 (0.57%)	0 / 174 (0.00%)	0 / 175 (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
Suspected COVID-19			
subjects affected / exposed	1 / 174 (0.57%)	0 / 174 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 174 (0.00%)	1 / 174 (0.57%)	0 / 175 (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

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

Non-serious adverse events	Placebo	GLPG1690 600 mg	GLPG1690 200 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	82 / 174 (47.13%)	91 / 174 (52.30%)	99 / 175 (56.57%)
Nervous system disorders			
Dizziness			
subjects affected / exposed	9 / 174 (5.17%)	8 / 174 (4.60%)	4 / 175 (2.29%)
occurrences (all)	9	10	4
Headache			
subjects affected / exposed	10 / 174 (5.75%)	9 / 174 (5.17%)	13 / 175 (7.43%)
occurrences (all)	11	14	15
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	6 / 174 (3.45%)	10 / 174 (5.75%)	9 / 175 (5.14%)
occurrences (all)	7	10	12
Gastrointestinal disorders			
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 174 (1.15%)	9 / 174 (5.17%)	3 / 175 (1.71%)
occurrences (all)	2	10	3
Diarrhoea			
subjects affected / exposed	20 / 174 (11.49%)	51 / 174 (29.31%)	40 / 175 (22.86%)
occurrences (all)	33	111	84
Nausea			
subjects affected / exposed	10 / 174 (5.75%)	16 / 174 (9.20%)	14 / 175 (8.00%)
occurrences (all)	14	18	20
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	16 / 174 (9.20%)	16 / 174 (9.20%)	21 / 175 (12.00%)
occurrences (all)	18	18	25
Idiopathic pulmonary fibrosis			
subjects affected / exposed	13 / 174 (7.47%)	13 / 174 (7.47%)	12 / 175 (6.86%)
occurrences (all)	18	15	15
Dyspnoea			
subjects affected / exposed	10 / 174 (5.75%)	10 / 174 (5.75%)	17 / 175 (9.71%)
occurrences (all)	10	12	25

Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	9 / 174 (5.17%)	3 / 174 (1.72%)	9 / 175 (5.14%)
occurrences (all)	10	3	13
Infections and infestations			
Bronchitis			
subjects affected / exposed	4 / 174 (2.30%)	8 / 174 (4.60%)	11 / 175 (6.29%)
occurrences (all)	4	10	13
Upper respiratory tract infection			
subjects affected / exposed	11 / 174 (6.32%)	10 / 174 (5.75%)	12 / 175 (6.86%)
occurrences (all)	14	10	15
Nasopharyngitis			
subjects affected / exposed	10 / 174 (5.75%)	11 / 174 (6.32%)	7 / 175 (4.00%)
occurrences (all)	11	14	10

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 October 2018	Amendment 1: Changes to accommodate requests made under the Voluntary Harmonization Procedure (VHP).
11 February 2019	Amendment 2: to change and clarify inclusion criteria regarding diagnosis and background standard of care medication for IPF, to clarify screening procedures, to include new drug-drug interaction information for investigational medicinal product (IMP) with pirfenidone and nintedanib, and to update the information and guidance reflecting new data from nonclinical fertility studies. Additionally, the multiple testing approach as recommended in Health Authority feedback has been included in the statistical analysis section.
12 November 2019	Amendment 3: to add new data from the GLPG1690-CL-113 drug-drug interaction study on interaction of GLPG1690 with nintedanib, and to change the IMP intake time for all subjects taking nintedanib to approximately 4 hours after the morning nintedanib dose.
17 December 2019	Amendment 4: Update of the exclusion criteria, and addition of the possibility to receive IMP in an extension study.
08 June 2020	Amendment 5: To implement the urgent safety measures (USMs) for protection of subjects during the Coronavirus disease (COVID-19) pandemic.

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.

Study was prematurely terminated based on recommendations of the Independent Data Monitoring Committee.

Notes: