Clinical trial results:
A Phase II Randomized, Double-Blind, Placebo-Controlled, 26-Week Study to Evaluate the Efficacy, Safety and Tolerability of GLPG1205 in Subjects with Idiopathic Pulmonary Fibrosis

Summary

EudraCT number	2017-004302-18
Trial protocol	SK SE FR BG FI HR RO
Global end of trial date	14 August 2020

Results information

Result version number	v1 (current)
This version publication date	30 July 2021
First version publication date	30 July 2021

Trial information

Trial identification

Sponsor protocol code	GLPG1205-CL-220

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03725852
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	14 August 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 August 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of GLPG1205 treatment in participants with idiopathic pulmonary fibrosis (IPF) on pulmonary function as evaluated by forced vital capacity (FVC) compared to placebo over 26 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 Harmonisation Guideline for Good Clinical Practice (ICH-GCP) E6 (R2), and local ethical and legal requirements. The investigator informed the participants of the risks and benefits of the study. The participants 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 review. The participants were covered by the sponsor's insurance according to local legal requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 September 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	Slovakia: 2
Country: Number of subjects enrolled	Sweden: 6
Country: Number of subjects enrolled	Croatia: 1
Country: Number of subjects enrolled	Bulgaria: 13
Country: Number of subjects enrolled	Finland: 3
Country: Number of subjects enrolled	France: 17
Country: Number of subjects enrolled	Oman: 2
Country: Number of subjects enrolled	Romania: 8
Country: Number of subjects enrolled	Ukraine: 16
Worldwide total number of subjects	68
EEA total number of subjects	50

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)	12
From 65 to 84 years	56
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Bulgaria, Croatia, Finland, France, Oman, Romania, Slovakia, Sweden, and Ukraine. The first participant was screened on 27 Sep 2018. The last study visit occurred on 14 Aug 2020.

Pre-assignment

Screening details:

A total of 155 participants were screened, of which 86 participants were considered ineligible. Out of 69 enrolled participants, 1 participant met an exclusion criterion pre-dose and was therefore excluded.

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, Subject, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	GLPG1205 100 mg

Arm description:

Participants received GLPG1205 100 milligrams (mg) (2 capsules x 50 mg), orally once daily for 26 weeks in addition to the local standard of care. Standard of care included nintedanib, pirfenidone, or neither nintedanib nor pirfenidone.

Arm type	Experimental
Investigational medicinal product name	GLPG1205
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

GLPG1205 was administered per dose and schedule specified in the arm description.

Arm title	Placebo

Arm description:

Participants received GLPG1205 matching placebo, orally once daily (as 2 capsules) for 26 weeks in addition to the local standard of care. Standard of care included nintedanib, pirfenidone, or neither nintedanib nor pirfenidone.

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

Dosage and administration details:

Placebo matching GLPG1205 was administered per dose and schedule specified in the arm description.

Number of subjects in period 1	GLPG1205 100 mg	Placebo
Started	45	23
Completed	41	23
Not completed	4	0
Consent withdrawn by subject	1	-
Death	1	-
Travel restrictions due to COVID-19	2	-

Baseline characteristics

Reporting groups	
Reporting group title	GLPG1205 100 mg
Reporting group description:	
Participants received GLPG1205 100 milligrams (mg) (2 capsules x 50 mg), orally once daily for 26 weeks in addition to the local standard of care. Standard of care included nintedanib, pirfenidone, or neither nintedanib nor pirfenidone.	
Reporting group title	Placebo
Reporting group description:	
Participants received GLPG1205 matching placebo, orally once daily (as 2 capsules) for 26 weeks in addition to the local standard of care. Standard of care included nintedanib, pirfenidone, or neither nintedanib nor pirfenidone.	

Reporting group values	GLPG1205 100 mg	Placebo	Total
Number of subjects	45	23	68
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	70.5	68.3	
standard deviation	± 6.8	± 5.5	-
Gender categorical Units: Subjects			
Female	12	6	18
Male	33	17	50
Race Units: Subjects			
Asian	2	0	2
White	32	17	49
Unknown or Not Reported	11	6	17
Ethnicity Units: Subjects			
Not Hispanic or Latino	45	23	68

End points

End points reporting groups

Reporting group title	GLPG1205 100 mg

Reporting group description:

Participants received GLPG1205 100 milligrams (mg) (2 capsules x 50 mg), orally once daily for 26 weeks in addition to the local standard of care. Standard of care included nintedanib, pirfenidone, or neither nintedanib nor pirfenidone.

Reporting group title	Placebo

Reporting group description:

Participants received GLPG1205 matching placebo, orally once daily (as 2 capsules) for 26 weeks in addition to the local standard of care. Standard of care included nintedanib, pirfenidone, or neither nintedanib nor pirfenidone.

Subject analysis set title	All Participants
Subject analysis set type	Full analysis

Subject analysis set description:

Participants who received either GLPG1205 100 mg (2 capsules x 50 mg), or GLPG1205 matching placebo, orally once daily for 26 weeks in addition to the local standard of care. Standard of care included nintedanib, pirfenidone, or neither nintedanib nor pirfenidone.

Primary: Change From Baseline in Forced Vital Capacity (FVC) at Week 26

End point title	Change From Baseline in Forced Vital Capacity (FVC) at Week 26

End point description:

Forced vital capacity (FVC) (milliliter [mL]) is the maximum amount of air exhaled from lungs by a participant after taking their deepest possible breath, as measured by spirometry. Participants in the full analysis set (FAS) (consisted of all randomized participants who received at least 1 dose of the study drug) with available data were analyzed.

End point type	Primary

End point timeframe:

Baseline, Week 26

End point values	GLPG1205 100 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	23		
Units: mL				
arithmetic mean (standard error)				
Baseline (n=45,23)	2865.43 (± 103.544)	2817.08 (± 167.773)		
Change at Week 26 (n=29,20)	-31.29 (± 42.398)	-79.47 (± 32.838)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	GLPG1205 100 mg v Placebo

Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.495 [2]
Method	ANCOVA
Parameter estimate	Least square (LS) mean difference
Point estimate	42.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-81.84
upper limit	166.49
Variability estimate	Standard error of the mean
Dispersion value	61.483

Notes:

[1] - This analysis included 49 participants.

[2] - P-value was based on an analysis of covariance (ANCOVA) model at each time point including treatment, sex, stratum (nintedanib, pirfenidone or neither), age, height, and baseline value as covariates.

Secondary: Number of Participants With Treatment-Emergent Adverse Events (TEAEs), Serious TEAEs, TEAEs Related to Study Drug, and TEAEs Leading to Study Drug Discontinuation

End point title	Number of Participants With Treatment-Emergent Adverse Events (TEAEs), Serious TEAEs, TEAEs Related to Study Drug, and TEAEs Leading to Study Drug Discontinuation

End point description:

An adverse event (AE) was any untoward medical occurrence in a participant administered study drug and which did not necessarily have a causal relationship with study drug. A TEAE was any AE with an onset date on or after the start of study drug intake and no later than 30 days after last dose of study drug, or any worsening of any AE on or after the start of study drug intake. A serious AE was defined as an AE that resulted in death, was life-threatening, required hospitalization or prolongation of existing hospitalization, resulted in persistent or significant disability/incapacity, was a congenital anomaly/birth defect, or was medically significant. Participants in the FAS population were analyzed.

End point type	Secondary

End point timeframe:

First dose date up to 30 days after the last dose of study drug (maximum up to 263 days)

End point values	GLPG1205 100 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	23		
Units: participants				
TEAEs	36	18		
Serious TEAEs	9	1		
TEAEs related to study drug	20	3		
TEAEs leading to study drug discontinuation	10	0		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: TEAEs	
Comparison groups	GLPG1205 100 mg v Placebo
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	superiority[3]
Parameter estimate	Difference in Percentage
Point estimate	1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.3
upper limit	24.5

Notes:

[3] - 95% CI for difference calculated using the method of Miettinen and Nurminen.

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Serious TEAEs	
Comparison groups	GLPG1205 100 mg v Placebo
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	superiority[4]
Parameter estimate	Difference in Percentage
Point estimate	15.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	30.7

Notes:

[4] - 95% CI for difference calculated using the method of Miettinen and Nurminen.

Statistical analysis title	Statistical Analysis 3
Statistical analysis description: TEAEs related to study drug	
Comparison groups	GLPG1205 100 mg v Placebo
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	superiority[5]
Parameter estimate	Difference in Percentage
Point estimate	31.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.2
upper limit	49.4

Notes:

[5] - 95% CI for difference calculated using the method of Miettinen and Nurminen.

Statistical analysis title	Statistical Analysis 4
Statistical analysis description:	
TEAEs leading to study drug discontinuation	
Comparison groups	GLPG1205 100 mg v Placebo
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	superiority[6]
Parameter estimate	Difference in Percentage
Point estimate	22.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.7
upper limit	36.4

Notes:

[6] - 95% CI for difference calculated using the method of Miettinen and Nurminen.

Secondary: Time to Any Major Events Depicted by Cumulative Percentage of Participants With All-cause Deaths, Respiratoryrelated Deaths, All-cause Hospitalizations, and Respiratory-related Hospitalizations

End point title	Time to Any Major Events Depicted by Cumulative Percentage of Participants With All-cause Deaths, Respiratoryrelated Deaths, All-cause Hospitalizations, and Respiratory-related Hospitalizations

End point description:

Treatment effect on time to death (all-cause and respiratory-related)/hospitalization (all-cause and respiratory-related) were assessed using the log-rank test. Kaplan-Meier estimates were derived for the probability of death (all-cause and respiratory-related)/hospitalization (all-cause and respiratory-related). Cumulative percentage of participants with all-cause deaths, respiratory-related deaths, all-cause hospitalizations, and respiratory-related hospitalizations were reported. Participants in the FAS population were analyzed. Here, the value '999999' signifies that 95% CI could not be estimated for the placebo group for deaths as all participants in this group were censored.

End point type	Secondary

End point timeframe:

Day 1 up to Week 30

End point values	GLPG1205 100 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	23		
Units: percentage of participants				
number (confidence interval 95%)				
All-cause deaths	3.1 (0.4 to 20.2)	0 (-999999 to 999999)		
Respiratory-related deaths	3.1 (0.4 to 20.2)	0 (-999999 to 999999)		
All-cause hospitalizations	16.6 (8.3 to 31.9)	4.3 (0.6 to 27.1)		

Respiratory-related hospitalizations	2.8 (0.4 to 18.1)	4.3 (0.6 to 27.1)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: All-cause deaths	
Comparison groups	GLPG1205 100 mg v Placebo
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.397
Method	Logrank

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Respiratory-related deaths	
Comparison groups	GLPG1205 100 mg v Placebo
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.397
Method	Logrank

Statistical analysis title	Statistical Analysis 3
Statistical analysis description: All-cause hospitalizations	
Comparison groups	GLPG1205 100 mg v Placebo
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.131
Method	Logrank

Statistical analysis title	Statistical Analysis 4
Statistical analysis description: Respiratory-related hospitalizations	
Comparison groups	GLPG1205 100 mg v Placebo

Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.762
Method	Logrank

Secondary: Change From Baseline in Total Distance Walked in Six-minute Walk Test (6MWT) at Week 26

End point title	Change From Baseline in Total Distance Walked in Six-minute Walk Test (6MWT) at Week 26

End point description:

The 6-MWT depicts the total distance covered by a participant during 6 minutes of walking. Participants in the FAS population with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	GLPG1205 100 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	23		
Units: meters				
arithmetic mean (standard error)				
Baseline (n=45,23)	412.6 (± 18.53)	391.8 (± 25.72)		
Change at Week 26 (n=26,19)	-16.6 (± 10.56)	-8.7 (± 10.43)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	GLPG1205 100 mg v Placebo
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	superiority[7]
P-value	= 0.565 [8]
Method	ANCOVA
Parameter estimate	Weighted LS mean difference
Point estimate	-9.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-40.87
upper limit	22.64
Variability estimate	Standard error of the mean
Dispersion value	15.713

Notes:

[7] - This analysis included 45 participants.

[8] - P-value was based on an ANCOVA model at Week 26 including treatment, stratum (nintedanib, pirfenidone or neither) and baseline 6MWT distance as covariates.

Secondary: Change From Baseline in St.George's Respiratory Questionnaire (SGRQ) Total Score at Week 26

End point title	Change From Baseline in St.George's Respiratory Questionnaire (SGRQ) Total Score at Week 26

End point description:

The 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 (assessing the frequency and severity of respiratory symptoms), activity (assessing the effects of breathlessness on mobility and physical activity), and impact (assessing the psychosocial impact of the disease). Scores were weighted such that each domain score and the total score ranged from 0 to 100, with higher scores indicating the poorer health-related QOL. Participants in the FAS population with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	GLPG1205 100 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	23		
Units: units on a scale				
arithmetic mean (standard error)				
Baseline (n=45,23)	45.363 (± 2.8518)	48.599 (± 3.9497)		
Change at Week 26 (n=29,19)	-3.797 (± 2.6683)	-1.424 (± 2.7151)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	GLPG1205 100 mg v Placebo
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	superiority[9]
P-value	= 0.673 [10]
Method	ANCOVA
Parameter estimate	Weighted LS mean difference
Point estimate	-1.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.06
upper limit	5.91
Variability estimate	Standard error of the mean
Dispersion value	3.71

Notes:

[9] - This analysis included 48 participants.

[10] - P-value was based on an ANCOVA model at Week 26 including treatment, stratum (nintedanib, pirfenidone or neither) and baseline SGRQ value as covariates.

Secondary: Change From Baseline in SGRQ Domain Score at Week 26

End point title	Change From Baseline in SGRQ Domain Score at Week 26

End point description:

The SGRQ is a 50-item paper questionnaire designed to measure and quantify the impact of chronic respiratory disease on health-related QOL and well-being, split into 3 domains: symptoms (assessing the frequency and severity of respiratory symptoms), activity (assessing the effects of breathlessness on mobility and physical activity), and impact (assessing the psychosocial impact of the disease). Scores were weighted such that each domain score ranged from 0 to 100, with higher scores indicating the poorer health-related QOL. Participants in the FAS population with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	GLPG1205 100 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	23		
Units: units on a scale				
arithmetic mean (standard error)				
Baseline (symptoms score) (n=45,23)	49.454 (± 3.7439)	56.059 (± 4.3333)		
Change at Week 26 (symptoms score) (n=29,19)	-3.135 (± 2.6281)	-3.437 (± 4.4017)		
Baseline (activity score) (n=45,23)	58.243 (± 3.0224)	59.454 (± 4.6140)		
Change at Week 26 (activity score) (n=29,20)	-4.387 (± 3.5367)	1.156 (± 3.6228)		
Baseline (impacts score) (n=45,23)	36.409 (± 3.1765)	40.064 (± 4.2897)		
Change at Week 26 (impacts score) (n=29,20)	-3.460 (± 3.1330)	-1.412 (± 3.2971)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Symptoms score

Comparison groups	GLPG1205 100 mg v Placebo
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	superiority[11]
P-value	= 0.875 [12]
Method	ANCOVA
Parameter estimate	Weighted LS mean difference
Point estimate	-0.72

Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.98
upper limit	8.53
Variability estimate	Standard error of the mean
Dispersion value	4.591

Notes:

[11] - This analysis included 48 participants.

[12] - P-value was based on an ANCOVA model at Week 26 including treatment, stratum (nintedanib, pirfenidone or neither) and baseline SGRQ value as covariates.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Activity score

Comparison groups	GLPG1205 100 mg v Placebo
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	superiority[13]
P-value	= 0.416 [14]
Method	ANCOVA
Parameter estimate	Weighted LS mean difference
Point estimate	-4.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.29
upper limit	6.02
Variability estimate	Standard error of the mean
Dispersion value	5.038

Notes:

[13] - This analysis included 49 participants.

[14] - P-value was based on an ANCOVA model at Week 26 including treatment, stratum (nintedanib, pirfenidone or neither) and baseline SGRQ value as covariates.

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

Impacts score

Comparison groups	GLPG1205 100 mg v Placebo
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	superiority[15]
P-value	= 0.961 [16]
Method	ANCOVA
Parameter estimate	Weighted LS mean difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.32
upper limit	7.92
Variability estimate	Standard error of the mean
Dispersion value	4.029

Notes:

[15] - This analysis included 49 participants.

[16] - P-value was based on an ANCOVA model at Week 26 including treatment, stratum (nintedanib, pirfenidone or neither) and baseline SGRQ value as covariates.

Secondary: Percentage of SGRQ Responders

End point title	Percentage of SGRQ Responders

End point description:

The SGRQ is a 50-item paper questionnaire designed to measure and quantify the impact of chronic respiratory disease on health-related QOL and well-being, split into 3 domains: symptoms (assessing the frequency and severity of respiratory symptoms), activity (assessing the effects of breathlessness on mobility and physical activity), and impact (assessing the psychosocial impact of the disease). Scores were weighted such that each domain score and total score ranged from 0 to 100, with higher scores indicating the poorer health-related QOL. SGRQ responders are those with absolute change from baseline in SGRQ total score less than or equal to -4 percent (%) at least once. Participants in the FAS population with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline up to Week 26

End point values	GLPG1205 100 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	22		
Units: percentage of participants				
number (not applicable)	40.0	40.9		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	GLPG1205 100 mg v Placebo
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1
Method	Fisher exact

Secondary: Pre-dose Plasma Concentration (Ctrough) of GLPG1205 at Week 26

End point title	Pre-dose Plasma Concentration (Ctrough) of GLPG1205 at Week 26[17]

End point description:

GLPG1205 pre-dose plasma concentration (Ctrough) at Week 26 was reported applying the exclusion rules (e.g. dose reduction, discontinuation, samples flagged). Participants in the pharmacokinetic (PK) analysis set (a subset of the FAS, including all participants who had available and evaluable plasma concentration data, excluding all protocol deviations or AEs that may have had an impact on the PK analysis) with available data were analyzed.

End point type	Secondary

End point timeframe:

Week 26 (pre-dose)

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The results for this endpoint were not reported for the placebo group as the participants in the placebo group did not receive GLPG1205.

End point values	GLPG1205 100 mg			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: nanograms per milliliter (ng/mL)				
arithmetic mean (standard deviation)	4979.9 (± 2279.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Pre-dose Plasma Concentration (Ctrough) of Nintedanib at Week 20

End point title	Pre-dose Plasma Concentration (Ctrough) of Nintedanib at Week 20

End point description:

Nintedanib pre-dose plasma concentration (Ctrough) at Week 20 was reported applying the exclusion rules (e.g. dose reduction, discontinuation, samples flagged). Participants in the PK analysis set with available data were analyzed.

End point type	Secondary

End point timeframe:

Week 20 (pre-dose)

End point values	All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	8			
Units: ng/mL				
arithmetic mean (standard deviation)	14.37 (± 12.97)			

Statistical analyses

No statistical analyses for this end point

Secondary: Pre-dose Plasma Concentration (Ctrough) of Pirfenidone at Week 20

End point title	Pre-dose Plasma Concentration (Ctrough) of Pirfenidone at Week 20

End point description:

Pirfenidone pre-dose plasma concentration (Ctrough) at Week 20 was reported applying the exclusion rules (e.g. dose reduction, discontinuation, samples flagged). Participants in the PK analysis set with available data were analyzed.

End point type	Secondary

End point timeframe:

Week 20 (pre-dose)

End point values	All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: ng/mL				
arithmetic mean (standard deviation)	2868.2 (± 2630.8)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
First dose date up to 30 days after the last dose of study drug (maximum up to 263 days)	
Adverse event reporting additional description:	
Full analysis set (FAS) consisted of all randomized participants who received at least 1 dose of study drug.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups	
Reporting group title	GLPG1205 100 mg
Reporting group description:	
Participants received GLPG1205 100 mg (2 capsules x 50 mg), orally once daily for 26 weeks in addition to the local standard of care. Standard of care included nintedanib, pirfenidone, or neither nintedanib nor pirfenidone.	
Reporting group title	Placebo
Reporting group description:	
Participants received GLPG1205 matching placebo, orally once daily (as 2 capsules) for 26 weeks in addition to the local standard of care. Standard of care included nintedanib, pirfenidone, or neither nintedanib nor pirfenidone.	

Serious adverse events	GLPG1205 100 mg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 45 (20.00%)	1 / 23 (4.35%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	1	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			

subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (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			
Headache			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Normocytic anaemia			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
General physical health deterioration			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Interstitial lung disease			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neck pain			

subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (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 / 45 (0.00%)	1 / 23 (4.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal viral infection			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural infection			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	GLPG1205 100 mg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	36 / 45 (80.00%)	18 / 23 (78.26%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 45 (6.67%)	1 / 23 (4.35%)	
occurrences (all)	10	10	
Surgical and medical procedures			
Tooth extraction			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	9 / 45 (20.00%)	0 / 23 (0.00%)	
occurrences (all)	16	0	
Chest pain			

subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	3	0	
Fatigue			
subjects affected / exposed	6 / 45 (13.33%)	0 / 23 (0.00%)	
occurrences (all)	7	0	
Hunger			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Malaise			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Pyrexia			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	3	0	
Thirst			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 23 (4.35%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	6 / 45 (13.33%)	2 / 23 (8.70%)	
occurrences (all)	10	2	
Dyspnoea			
subjects affected / exposed	5 / 45 (11.11%)	2 / 23 (8.70%)	
occurrences (all)	5	2	
Epistaxis			
subjects affected / exposed	0 / 45 (0.00%)	2 / 23 (8.70%)	
occurrences (all)	0	2	
Idiopathic pulmonary fibrosis			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	2	0	
Interstitial lung disease			

subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal pain			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Rhinitis allergic			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 45 (4.44%)	0 / 23 (0.00%)	
occurrences (all)	2	0	
Depression			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Hallucination			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	2	0	
Insomnia			
subjects affected / exposed	2 / 45 (4.44%)	0 / 23 (0.00%)	
occurrences (all)	3	0	
Irritability			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 45 (6.67%)	0 / 23 (0.00%)	
occurrences (all)	7	0	
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 45 (6.67%)	0 / 23 (0.00%)	
occurrences (all)	5	0	
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	2	0	
Blood bilirubin increased			

subjects affected / exposed	2 / 45 (4.44%)	0 / 23 (0.00%)	
occurrences (all)	3	0	
Blood lactate dehydrogenase increased			
subjects affected / exposed	2 / 45 (4.44%)	0 / 23 (0.00%)	
occurrences (all)	2	0	
Blood pressure increased			
subjects affected / exposed	2 / 45 (4.44%)	0 / 23 (0.00%)	
occurrences (all)	2	0	
Brain natriuretic peptide increased			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	3 / 45 (6.67%)	0 / 23 (0.00%)	
occurrences (all)	5	0	
Neutrophil count increased			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Weight decreased			
subjects affected / exposed	6 / 45 (13.33%)	1 / 23 (4.35%)	
occurrences (all)	6	1	
White blood cell count increased			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Radius fracture			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Rib fracture			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Thermal burn			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			

Burning sensation			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Dizziness			
subjects affected / exposed	6 / 45 (13.33%)	2 / 23 (8.70%)	
occurrences (all)	16	2	
Dyskinesia			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	11 / 45 (24.44%)	4 / 23 (17.39%)	
occurrences (all)	20	11	
Paraesthesia			
subjects affected / exposed	0 / 45 (0.00%)	1 / 23 (4.35%)	
occurrences (all)	0	1	
Parkinson's disease			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Somnolence			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Tremor			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Immune thrombocytopenia			
subjects affected / exposed	0 / 45 (0.00%)	1 / 23 (4.35%)	
occurrences (all)	0	1	
Leukocytosis			
subjects affected / exposed	2 / 45 (4.44%)	0 / 23 (0.00%)	
occurrences (all)	2	0	
Neutrophilia			
subjects affected / exposed	2 / 45 (4.44%)	0 / 23 (0.00%)	
occurrences (all)	2	0	
Normocytic anaemia			

subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Diplopia			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Panophthalmitis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 23 (4.35%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	5 / 45 (11.11%)	0 / 23 (0.00%)	
occurrences (all)	5	0	
Abdominal pain upper			
subjects affected / exposed	3 / 45 (6.67%)	0 / 23 (0.00%)	
occurrences (all)	4	0	
Chronic gastritis			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	1 / 45 (2.22%)	1 / 23 (4.35%)	
occurrences (all)	1	1	
Diarrhoea			
subjects affected / exposed	12 / 45 (26.67%)	3 / 23 (13.04%)	
occurrences (all)	22	4	
Dry mouth			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Dyspepsia			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Gastric ulcer			

subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 45 (0.00%)	1 / 23 (4.35%)	
occurrences (all)	0	2	
Mucous stools			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	13 / 45 (28.89%)	2 / 23 (8.70%)	
occurrences (all)	19	2	
Toothache			
subjects affected / exposed	0 / 45 (0.00%)	1 / 23 (4.35%)	
occurrences (all)	0	3	
Vomiting			
subjects affected / exposed	4 / 45 (8.89%)	0 / 23 (0.00%)	
occurrences (all)	5	0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Hepatic mass			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Hepatic steatosis			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Hyperbilirubinaemia			
subjects affected / exposed	0 / 45 (0.00%)	1 / 23 (4.35%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 45 (0.00%)	1 / 23 (4.35%)	
occurrences (all)	0	1	
Papule			

subjects affected / exposed	0 / 45 (0.00%)	1 / 23 (4.35%)	
occurrences (all)	0	1	
Photosensitivity reaction			
subjects affected / exposed	0 / 45 (0.00%)	1 / 23 (4.35%)	
occurrences (all)	0	2	
Pruritus			
subjects affected / exposed	3 / 45 (6.67%)	0 / 23 (0.00%)	
occurrences (all)	3	0	
Rash			
subjects affected / exposed	2 / 45 (4.44%)	1 / 23 (4.35%)	
occurrences (all)	2	1	
Renal and urinary disorders			
Polyuria			
subjects affected / exposed	2 / 45 (4.44%)	0 / 23 (0.00%)	
occurrences (all)	2	0	
Renal pain			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Back pain			
subjects affected / exposed	3 / 45 (6.67%)	1 / 23 (4.35%)	
occurrences (all)	3	3	
Intervertebral disc protrusion			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Muscular weakness			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	2 / 45 (4.44%)	1 / 23 (4.35%)	
occurrences (all)	2	1	
Neck pain			

subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Osteoarthritis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 23 (4.35%)	
occurrences (all)	0	1	
Pain in extremity			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			
Bronchitis			
subjects affected / exposed	3 / 45 (6.67%)	3 / 23 (13.04%)	
occurrences (all)	3	3	
Diarrhoea infectious			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Erythema migrans			
subjects affected / exposed	0 / 45 (0.00%)	1 / 23 (4.35%)	
occurrences (all)	0	1	
Gastroenteritis			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal viral infection			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Gingival abscess			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Kidney infection			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Laryngitis			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			
subjects affected / exposed	6 / 45 (13.33%)	4 / 23 (17.39%)	
occurrences (all)	6	5	

Oral candidiasis			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Oral fungal infection			
subjects affected / exposed	0 / 45 (0.00%)	1 / 23 (4.35%)	
occurrences (all)	0	1	
Oral herpes			
subjects affected / exposed	0 / 45 (0.00%)	1 / 23 (4.35%)	
occurrences (all)	0	1	
Pneumonia			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Respiratory tract infection			
subjects affected / exposed	0 / 45 (0.00%)	1 / 23 (4.35%)	
occurrences (all)	0	2	
Sinusitis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 23 (4.35%)	
occurrences (all)	0	1	
Tracheitis			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 45 (0.00%)	1 / 23 (4.35%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Appetite disorder			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Decreased appetite			
subjects affected / exposed	5 / 45 (11.11%)	0 / 23 (0.00%)	
occurrences (all)	5	0	
Dyslipidaemia			
subjects affected / exposed	1 / 45 (2.22%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Hyperkalaemia			

subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1	0 / 23 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 January 2019	− The secondary objective/endpoints evaluating time to major events were modified. − Eligibility criteria were modified. − Prohibition of medications known to prolong QT interval was removed. Instead, chronic use or initiation of such medications needed to be evaluated on a case-by-case basis. − Conditions leading to treatment discontinuation or withdrawal from the study were revised. − Conditions for rescreening were revised. − Timing for efficacy assessments (SGRQ and functional respiratory imaging [FRI]) were revised. − Safety assessments and normal ranges/thresholds for abnormalities were revised to better reflect the IPF participant population. − Definitions of populations for analyses were revised. − Definition of an acute IPF exacerbation was updated and contraindications for the 6MWT were corrected in the respective appendices.
30 April 2020	Urgent safety measures were included to mitigate the impact of the COVID-19 pandemic for the participating IPF participants. The urgent safety measures were implemented in compliance with local country and study center restrictions and regulations, which included an extension of certain visit windows, unscheduled virtual phone call or remote visits, alternative visit approach, shipment of the study drug to the participants etc.

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 not powered to detect statistical significance and was limited by its small sample size, high variability of the primary endpoint (FVC), and a high rate of early treatment discontinuations.

Notes: