Clinical trial results:
Randomized, Double-Blind, Parallel Group, Placebo-Controlled, Multicenter, Exploratory Phase IIa Study to Assess Safety, Tolerability, Pharmacokinetic and Pharmacodynamic Properties of GLPG1690 Administered for 12 Weeks in Subjects with Idiopathic Pulmonary Fibrosis (IPF).

Summary

EudraCT number	2015-004157-41
Trial protocol	GB IT
Global end of trial date	02 May 2017

Results information

Result version number	v1 (current)
This version publication date	13 May 2018
First version publication date	13 May 2018

Trial information

Trial identification

Sponsor protocol code	GLPG1690-CL-202

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02738801
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Galapagos NV
Sponsor organisation address	Generaal De Wittelaan L11 A3, Mechelen, Belgium,
Public contact	Clinical Trial Information Desk, Galapagos NV, +32 15 342 900, rd@glpg.com
Scientific contact	Clinical Trial Information Desk, Galapagos NV, +32 15 342 900, rd@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	07 December 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 May 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of the study were:
- to evaluate the safety and tolerability of GLPG1690.
- to characterize the PK and PD properties of GLPG1690.

The key secondary objectives of the study were:
- to evaluate the change from baseline in forced vital capacity (FVC).
- to evaluate the change in functional respiratory imaging (FRI) parameters.
- to evaluate the change in quality of life measures.

Protection of trial subjects:

This study was conducted in accordance with the current International Council on Harmonization (ICH) –Good Clinical Practice (GCP) Guideline E6.Compliance with this standard provides public assurance that the rights, safety, and well-being of study subjects are protected, consistent with the principles that have their origin in the Declaration of Helsinki, and that the clinical study data are credible.

The investigator or designated personnel had to explain the study and the implications of participation (e.g., objectives, methods, anticipated benefits, and possible risks) to potential subjects or their legally acceptable representatives prior to any study-related activity. Subjects were informed that their participation was voluntary and that they could withdraw from thestudy at any time. They were informed that choosing not to participate or to withdraw from the study would not have an impact on the care the subject received for the treatment of his/her disease. In case the subject was unable to read and write, an impartial witness had to confirm the informed consent.

The subject was given sufficient time to read the ICF and to ask additional questions. After this explanation and before entry in the study, consent had to be appropriately recorded by means of the subject's personally dated signature or by the signature of an independent witness who certified the subject's consent in writing. After having obtained the consent, a copy of the signed and dated informed consent had to be given to the subject.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 March 2016
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	United Kingdom: 4
Country: Number of subjects enrolled	Ukraine: 19
Worldwide total number of subjects	23
EEA total number of subjects	4

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)	8
From 65 to 84 years	15
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted from 24 Mar 2016 (first subject signed ICF) until 02 May 2017 (last contact with any subject in the study).
Three (3) countries (Italy, Ukraine, and the United Kingdom [UK]) participated in the study and 8 investigators (6 from Ukraine and 2 from the UK) enrolled subjects.

Pre-assignment

Screening details:

A total of 72 subjects were screened of whom 49 were not enrolled. Twenty three (23) subjects were randomized.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	GLPG1690 - 600 mg q.d.

Arm description: -

Arm type	Experimental
Investigational medicinal product name	GLPG1690
Investigational medicinal product code	G451990
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Oral doses of 600 mg GLPG1690 (3 capsules of 200 mg) were administered in the morning during 12 weeks.
GLPG1690 was presented as capsules for oral use (size 00), containing 200 mg G451990 (G451990 is the compound code for GLPG1690).

Arm title	Placebo

Arm description: -

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

Dosage and administration details:

Placebo to match (3 capsules) was administered in the morning during 12 weeks.
Placebo was presented as matching capsules for oral use (size 00).

Number of subjects in period 1	GLPG1690 - 600 mg q.d.	Placebo
Started	17	6
Completed	15	5
Not completed	2	1
Consent withdrawn by subject	1	-
Adverse event, non-fatal	1	1

Baseline characteristics

Reporting groups	
Reporting group title	GLPG1690 - 600 mg q.d.
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	GLPG1690 - 600 mg q.d.	Placebo	Total
Number of subjects	17	6	23
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	5	3	8
From 65-84 years	12	3	15
85 years and over	0	0	0
Age continuous Units: years			
median	67	64	
full range (min-max)	54 to 79	52 to 72	-
Gender categorical Units: Subjects			
Female	7	1	8
Male	10	5	15
Race Units: Subjects			
White	17	6	23
BMI Units: kg/m²			
median	28.00	32.20	
full range (min-max)	23.7 to 39.1	23.5 to 43.1	-

End points

End points reporting groups

Reporting group title	GLPG1690 - 600 mg q.d.
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Primary: Safety - TEAE (Treatment-Emergent Adverse Events)

End point title	Safety - TEAE (Treatment-Emergent Adverse Events)[1]

End point description:

Clinical safety was evaluated by assessing treatment-emergent AEs (TEAEs) and results of physical examinations, laboratory assessments, ECG, and vital signs in a descriptive manner.

End point type	Primary

End point timeframe:

From first study drug administration until the last follow-up visit.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive analysis only.

End point values	GLPG1690 - 600 mg q.d.	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	6		
Units: Subjects				
Any TEAE	11	4		
Severe TEAE	1	1		
Serious TEAE	1	2		
Treatment related TEAE	2	0		
Discontinuation due to AE	1	1		

Statistical analyses

No statistical analyses for this end point

Primary: PK - Cmax

End point title	PK - Cmax[2][3]

End point description:

Maximum observed plasma concentration.

End point type	Primary

End point timeframe:

PK samples were taken pre-dose at multiple timepoints. At Day 28, in addition to pre-dose, samples were taken 1.5h, 4h, and 6h postdose.
The PK parameter Week 4 (based on pre-dose and postdose samples) has been provided.

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive analysis only.

[3] - 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: Placebo arm has been excluded.

End point values	GLPG1690 - 600 mg q.d.			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: µg/mL				
arithmetic mean (standard deviation)	6.06 (± 4.92)			

Statistical analyses

No statistical analyses for this end point

Primary: PK - AUC0-τ

End point title	PK - AUC0-τ[4][5]

End point description:

Area under the plasma concentration time curve for the dosing interval (24 hours).

End point type	Primary

End point timeframe:

PK samples were taken pre-dose at multiple timepoints. At Day 28, in addition to pre-dose, samples were taken 1.5h, 4h, and 6h postdose.
The PK parameter Week 4 (based on pre-dose and postdose samples) has been provided.

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive analysis only.

[5] - 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: Placebo arm has been excluded.

End point values	GLPG1690 - 600 mg q.d.			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: µg.h/mL				
arithmetic mean (standard deviation)	55.6 (± 46.6)			

Statistical analyses

No statistical analyses for this end point

Primary: PD - LPA 18:2

End point title	PD - LPA 18:2[6]

End point description:

Plasma was collected for the evaluation of lipid lysophosphatidic acid (LPA) 18:2 for change from baseline. Observed case, intent-to-treat (ITT) population.

End point type	Primary

End point timeframe:

A 12-week treatment period. PD samples were taken pre-dose at multiple timepoints. At Day 28, in addition to pre-dose, samples were taken 1.5h and 6h postdose.

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive analysis only.

End point values	GLPG1690 - 600 mg q.d.	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16[7]	6[8]		
Units: Peak area ratio				
arithmetic mean (standard error)				
Week 4 - pre-dose	-0.1817 (± 0.0729)	-0.0875 (± 0.1085)		
Week 4 - 1.5h postdose	-0.2885 (± 0.0702)	-0.0454 (± 0.0619)		
Week 4 - 6h postdose	-03049 (± 0.00752)	-01123 (± 0.1608)		
Week 12 - pre-dose	-0.2466 (± 0.0724)	-0.010 (± 0.0688)		

Notes:

[7] - Week 4 (pre-dose) N=16
Week 4 (1.5h, 6h postdose) N=15
Week 12 (pre-dose) N=16
[8] - Week 4 (all time points) N=5
Week 12 (pre-dose) N=6

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in FVC

End point title	Change from baseline in FVC

End point description:

To evaluate the change from baseline in forced vital capacity. Last observation carried forward, ITT population.

End point type	Secondary

End point timeframe:

A 12-week treatment period. The parameter for Week 12 has been provided.

End point values	GLPG1690 - 600 mg q.d.	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	6		
Units: Liter				
arithmetic mean (standard error)	-0.1238 (± 0.08719)	-0.2588 (± 0.03447)		

Statistical analyses

No statistical analyses for this end point

Secondary: The change in FRI parameters - Specific Airway Volume

End point title	The change in FRI parameters - Specific Airway Volume

End point description:

To evaluate the change in functional respiratory imaging (FRI) parameters specific airway volume from baseline. Observed case, ITT population.

End point type	Secondary

End point timeframe:

A 12-week treatment period. The Parameter for Week 12 has been provided.

End point values	GLPG1690 - 600 mg q.d.	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	3		
Units: mL/L				
arithmetic mean (standard error)	0.0786 (± 0.49489)	3.0380 (± 1.37106)		

Statistical analyses

No statistical analyses for this end point

Secondary: The change in FRI parameters - Specific Airway Resistance

End point title	The change in FRI parameters - Specific Airway Resistance

End point description:

To evaluate the change in functional respiratory imaging (FRI) parameters specific airway resistance from baseline. Observed case, ITT population

End point type	Secondary

End point timeframe:

A 12-week treatment period. The parameter for Week 12 has been given.

End point values	GLPG1690 - 600 mg q.d.	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	3		
Units: kPa/sec				
arithmetic mean (standard error)	0.0044 (± 0.00820)	-0.0354 (± 0.01120)		

Statistical analyses

No statistical analyses for this end point

Secondary: The change in Quality of Life Measures (total SGQR score)

End point title	The change in Quality of Life Measures (total SGQR score)

End point description:

To evaluate the change in quality of life measures from baseline (St Georges Respiratory Questionnaire total score). Last observation carried forward, ITT population.

End point type	Secondary

End point timeframe:

A 12 week treatment period. The parameter for Week 12 has been provided.

End point values	GLPG1690 - 600 mg q.d.	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	6		
Units: Ratio				
arithmetic mean (standard error)	0.68 (± 2.820)	-0.37 (± 4.196)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AE: from the signature of ICF until the final follow-up visit.
TEAE: from first study drug administration until the final follow-up visit.

Adverse event reporting additional description:

No subjects died.Two subjects in the placebo group and 1 subject in the GLPG1690 group had a serious TEAE.
One subject in each group had a TEAE leading to the permanent discontinuation of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	GLPG1690 - 600 mg q.d.

Reporting group description: -

Reporting group title	Placebo

Reporting group description: -

Serious adverse events	GLPG1690 - 600 mg q.d.	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 17 (5.88%)	2 / 6 (33.33%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cholangiocarcinoma			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrioventricular block second degree			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infections and infestations			
Lower respiratory tract infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	GLPG1690 - 600 mg q.d.	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 17 (64.71%)	4 / 6 (66.67%)	
Investigations			
Blood creatine increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Electrocardiogram PR prolongation			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Vascular disorders			
Orthostatic hypotension			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Cardiac disorders			
Bradycardia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			

subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Loss of consciousness			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Peripheral swelling			
subjects affected / exposed	1 / 17 (5.88%)	1 / 6 (16.67%)	
occurrences (all)	1	1	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 17 (5.88%)	2 / 6 (33.33%)	
occurrences (all)	1	2	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 17 (11.76%)	1 / 6 (16.67%)	
occurrences (all)	2	1	
Dyspnoea			
subjects affected / exposed	2 / 17 (11.76%)	1 / 6 (16.67%)	
occurrences (all)	2	1	
Productive cough			
subjects affected / exposed	2 / 17 (11.76%)	0 / 6 (0.00%)	
occurrences (all)	2	0	
Idiopathic pulmonary fibrosis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Pulmonary congestion			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Haemothorax			

subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Pneumothorax spontaneous			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Dysuria			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	3	
Joint swelling			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Osteoarthritis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Pain in extremity			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Muscular weakness			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Lower respiratory tract infection			
subjects affected / exposed	2 / 17 (11.76%)	1 / 6 (16.67%)	
occurrences (all)	3	2	
Nasopharyngitis			
subjects affected / exposed	2 / 17 (11.76%)	1 / 6 (16.67%)	
occurrences (all)	2	1	
Infected cyst			

subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Pyelonephritis acute			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Respiratory tract infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Orchitis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Urinary tract infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported