EU Clinical Trials Register

Clinical trial results:
A Phase IIa, randomized, double-blind, placebo-controlled study to evaluate GLPG2737 in Orkambi-treated subjects with cystic fibrosis homozygous for the F508del mutation

Summary

EudraCT number	2017-002181-42
Trial protocol	DE
Global end of trial date	10 April 2018

Results information

Result version number	v1 (current)
This version publication date	16 March 2019
First version publication date	16 March 2019

Trial information

Trial identification

Sponsor protocol code	GLPG2737-CL-202

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03474042
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	Clinical Trial Information Desk, Galapagos NV, +32 15342 900, rd@glpg.com
Scientific contact	Clinical Trial Information Desk, Galapagos NV, +32 15342 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	27 September 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 April 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary objective:
To assess changes in sweat chloride concentration as a biomarker of CFTR ion channel function after administration of repeated doses of GLPG2737 compared to placebo in Orkambi-treated adult subjects with CF homozygous for the F508del mutation on Day 28.

Secondary Objectives:
- To evaluate safety and tolerability of GLPG2737.
- To assess changes in sweat chloride concentration.
- To assess changes in pulmonary function.
- To assess changes in respiratory symptoms.
- To characterize the pharmacokinetics (PK) of GLPG2737 and its active metabolite G1125498 (M4), ivacaftor, and lumacaftor.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Guideline for Good Clinical Practice (GCP) (Committee for Medicinal Products for Human Use [CHMP]/ICH/135/1995) and with the applicable local laws and regulatory requirements.

Prior to the performance of any study-specific procedures, written informed consent was obtained from each subject. The subject was informed about the nature and purpose of the study, as well as of its risks and benefits. It was explained that the subject could withdraw from the study at any time for any reason and that this would not have any effect on potential future medical care.

Background therapy:

Orkambi (lumacaftor 400 mg/ivacaftor 250 mg b.i.d.)

Evidence for comparator: -

Actual start date of recruitment	29 November 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 22
Worldwide total number of subjects	22
EEA total number of subjects	22

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)	22
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at seven study centers from 29 November 2017 (date the first subject signed the ICF) to 10 April 2018 (date of last visit/contact with any subject).

Pre-assignment

Screening details:

In total, 29 subjects were screened and 22 subjects were enrolled.

Period 1

Period 1 title	Overall period (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	GLPG2737 group

Arm description:

GLPG2737 75 mg b.i.d. in addition to a stable treatment with Orkambi (lumacaftor 400 mg/ivacaftor 250 mg b.i.d.)

Arm type	Experimental
Investigational medicinal product name	GLPG2737
Investigational medicinal product code	G1117337
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received GLPG2737 75 mg b.i.d.
GLPG2737 was provided as capsules for oral use, containing 75 mg G1117337 (G1117337 is the compound code for GLPG2737).

Arm title	Placebo group

Arm description:

Placebo b.i.d. in addition to a stable treatment with Orkambi (lumacaftor 400 mg/ivacaftor 250 mg b.i.d.)

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:

Subjects received matching placebo b.i.d.
Placebo was provided as capsules for oral use.

Number of subjects in period 1	GLPG2737 group	Placebo group
Started	14	8
Completed	14	7
Not completed	0	1
Subject request: medical emergency in family	-	1

Number of subjects in period 1	GLPG2737 group	Placebo group
Started	14	8
Completed	14	7
Not completed	0	1

Baseline characteristics

Reporting groups

Reporting group title	GLPG2737 group
Reporting group description:	
GLPG2737 75 mg b.i.d. in addition to a stable treatment with Orkambi (lumacaftor 400 mg/ivacaftor 250 mg b.i.d.)	
Reporting group title	Placebo group
Reporting group description:	
Placebo b.i.d. in addition to a stable treatment with Orkambi (lumacaftor 400 mg/ivacaftor 250 mg b.i.d.)	

Reporting group values	GLPG2737 group	Placebo group	Total
Number of subjects	14	8	22
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)	14	8	22
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
median	21.5	28.5	
full range (min-max)	19 to 42	19 to 38	-
Gender categorical			
Units: Subjects			
Female	5	3	8
Male	9	5	14
Race			
Units: Subjects			
White	14	8	22
BMI			
Units: kg/m2			
median	21.1	20.3	
full range (min-max)	18 to 29	17 to 24	-

End points

End points reporting groups

Reporting group title	GLPG2737 group
Reporting group description:	
GLPG2737 75 mg b.i.d. in addition to a stable treatment with Orkambi (lumacaftor 400 mg/ivacaftor 250 mg b.i.d.)	
Reporting group title	Placebo group
Reporting group description:	
Placebo b.i.d. in addition to a stable treatment with Orkambi (lumacaftor 400 mg/ivacaftor 250 mg b.i.d.)	

Primary: Efficacy - Sweat chloride concentration

End point title	Efficacy - Sweat chloride concentration
End point description:	
Change from baseline (pre-morning dose on Day 1) in sweat chloride concentration on Day 28 (primary endpoint) and on Day 14 (secondary endpoint) compared to placebo.	
End point type	Primary
End point timeframe:	
Baseline, Day 14 and Day 28	

End point values	GLPG2737 group	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	8[1]		
Units: mmol/l				
arithmetic mean (standard error)				
Baseline (actual value)	86.0 (± 4.50)	84.3 (± 4.85)		
Day 14	-18.9 (± 5.11)	0.6 (± 6.97)		
Day 28	-22.1 (± 3.79)	-6.3 (± 4.28)		

Notes:

[1] - N=7 on Day 14; N=6 on Day 28

Statistical analyses

Statistical analysis title	GLPG2737 vs Placebo - Day 28 (Primary endpoint)
Statistical analysis description:	
A mixed-effect model approach with treatment and day (Day 14 and Day 28) as fixed effects, treatment*day as interaction, subjects as random effect and baseline as covariate.	
Comparison groups	GLPG2737 group v Placebo group
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.021
Method	Mixed models analysis
Parameter estimate	LS-mean
Point estimate	-19.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	-36
upper limit	-3.2
Variability estimate	Standard error of the mean
Dispersion value	7.99

Statistical analysis title	GLPG2737 vs Placebo - Day 14 (Secondary endpoint)

Statistical analysis description:

A mixed-effect model approach with treatment and day (Day 14 and Day 28) as fixed effects, treatment*day as interaction, subjects as random effect and baseline as covariate.

Comparison groups	GLPG2737 group v Placebo group
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0191
Method	Mixed models analysis
Parameter estimate	LS-mean
Point estimate	-19.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-35.3
upper limit	-3.5
Variability estimate	Standard error of the mean
Dispersion value	7.72

Secondary: Safety - AEs

End point title	Safety - AEs

End point description:

Safety and tolerability, assessed by the number of subjects with adverse events (AEs). An analysis of the treatment-emergent adverse events (TEAEs) was performed, selecting only those AEs that started on or after the first dose of IMP. AEs emerging prior to the first dose (during the screening period) were only listed. The safety assessments were based on adverse events, laboratory assessments, 12-lead ECG, vital signs, spirometry, oxygen saturation by pulse oximetry, and weight were summarized using descriptive statistics. Physical examination data were only listed.

End point type	Secondary

End point timeframe:

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

End point values	GLPG2737 group	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	8		
Units: Subjects				
Any TEAE	10	8		
Severe TEAE	0	0		
Serious TEAE	0	0		
Treatment related TEAE	3	1		
Discontinuation due to AE	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Efficacy - %pFEV1

End point title	Efficacy - %pFEV1

End point description:

Change from baseline (pre-morning dose on Day 1) in percent predicted forced expiratory volume in 1 second (%pFEV1) through 28 days.

End point type	Secondary

End point timeframe:

Baseline, Day 14 and Day 28.

End point values	GLPG2737 group	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14[2]	8[3]		
Units: percent				
arithmetic mean (standard error)				
Baseline (actual value)	55.7 (± 4.49)	68.8 (± 6.20)		
Day 14	4.4 (± 1.51)	1.0 (± 1.05)		
Day 28	1.8 (± 1.20)	-1.8 (± 1.01)		

Notes:

[2] - N=12 at Day 14 and 28

[3] - N=7 at Day 14; N=6 at Day 28

Statistical analyses

Statistical analysis title	GLPG2737 vs Placebo - Day 14

Statistical analysis description:

A mixed-effects model approach. P-values were provided for the point estimates (PEs) of the difference in change from baseline in %pFEV1 between the GLPG2737 and placebo group.

Comparison groups	GLPG2737 group v Placebo group

Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0617
Method	Mixed models analysis
Parameter estimate	LS-mean
Point estimate	3.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	7.4
Variability estimate	Standard error of the mean
Dispersion value	1.87

Statistical analysis title	GLPG2737 vs Placebo - Day 28

Statistical analysis description:

A mixed-effects model approach. P-values were provided for the point estimates (PEs) of the difference in change from baseline in %pFEV1 between the GLPG2737 and placebo group.

Comparison groups	GLPG2737 group v Placebo group
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0848
Method	Mixed models analysis
Parameter estimate	LS-mean
Point estimate	3.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	7.3
Variability estimate	Standard error of the mean
Dispersion value	1.92

Secondary: CFQ-R

End point title	CFQ-R

End point description:

Change from baseline (pre-morning dose on Day 1) in the respiratory domain of the cystic fibrosis questionnaire-revised (CFQ-R) on Day 28.

End point type	Secondary

End point timeframe:

Baseline and Day 28.

End point values	GLPG2737 group	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	8[4]		
Units: percent				
arithmetic mean (standard error)				
Baseline (actual value)	68.0 (± 4.83)	69.4 (± 5.26)		
Day 28	-1.3 (± 6.48)	-0.7 (± 1.30)		

Notes:

[4] - N=7 at Day 28

Statistical analyses

Statistical analysis title	GLPG2737 vs Placebo

Statistical analysis description:

An analysis of covariance (ANCOVA) model on the changes from baseline on Day 28, with treatment as factor and baseline value as covariate, was applied.

Comparison groups	Placebo group v GLPG2737 group
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9125
Method	ANCOVA
Parameter estimate	LS-mean
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21
upper limit	18.9
Variability estimate	Standard error of the mean
Dispersion value	9.48

Secondary: PK - Cmax

End point title	PK - Cmax

End point description:

Determine Cmax on Day 14 of GLPG2737, its active metabolite G1125498 (M4), ivacaftor, and lumacaftor.

End point type	Secondary

End point timeframe:

Day 14

End point values	GLPG2737 group	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	7		
Units: ng/ml				
arithmetic mean (standard deviation)				
GLPG2737	293 (± 113)	0 (± 0)		
G1125498	422 (± 155)	0 (± 0)		
ivacaftor	720 (± 237)	714 (± 726)		
lumacaftor	24000 (± 8010)	17000 (± 2950)		

Statistical analyses

Statistical analysis title	GLPG2737 vs Placebo - Ivacaftor
Statistical analysis description:	
An analysis of variance (ANOVA) model with treatment arm (GLPG2737 group and placebo group) as a factor. The PEs were calculated as the geometric mean ratio of GLPG2737 group relative to placebo group with corresponding 90% CI.	
Comparison groups	Placebo group v GLPG2737 group
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS-geometric means
Point estimate	1.396
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.834
upper limit	2.337

Statistical analysis title	GLPG2737 vs Placebo - Lumacaftor
Statistical analysis description:	
An analysis of variance (ANOVA) model with treatment arm (GLPG2737 group and placebo group) as a factor. The PEs were calculated as the geometric mean ratio of GLPG2737 group relative to placebo group with corresponding 90% CI.	
Comparison groups	GLPG2737 group v Placebo group
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS-geometric means
Point estimate	1.349
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.042
upper limit	1.745

Secondary: PK - AUC0-8h

End point title	PK - AUC0-8h
End point description:	
Determine AUC0-8h on Day 14 of GLPG2737, its active metabolite G1125498 (M4), ivacaftor, and lumacaftor.	
End point type	Secondary
End point timeframe:	
Day 14	

End point values	GLPG2737 group	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	7		
Units: ng.h/ml				
arithmetic mean (standard deviation)				
GLPG2737	1510 (± 551)	0 (± 0)		
G1125498	2740 (± 1100)	0 (± 0)		
ivacaftor	3230 (± 986)	3720 (± 4040)		
lumacaftor	141000 (± 52100)	97800 (± 23500)		

Statistical analyses

Statistical analysis title	GLPG2737 vs Placebo - Ivacaftor
Statistical analysis description:	
An analysis of variance (ANOVA) model with treatment arm (GLPG2737 group and placebo group) as a factor. The PEs were calculated as the geometric mean ratio of GLPG2737 group relative to placebo group with corresponding 90% CI.	
Comparison groups	GLPG2737 group v Placebo group
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS-geometric means
Point estimate	1.205
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.733
upper limit	1.981

Statistical analysis title	GLPG2737 vs Placebo - Lumacaftor

Statistical analysis description:

An analysis of variance (ANOVA) model with treatment arm (GLPG2737 group and placebo group) as a factor. The PEs were calculated as the geometric mean ratio of GLPG2737 group relative to placebo group with corresponding 90% CI.

Comparison groups	GLPG2737 group v Placebo group
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS-geometric means
Point estimate	1.371
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.025
upper limit	1.834

Secondary: PK - Ctrough

End point title	PK - Ctrough

End point description:

Determine Ctrough through 28 days of GLPG2737, its active metabolite G1125498 (M4), ivacaftor, and lumacaftor.

End point type	Secondary

End point timeframe:

Days 1, 14 and 28.

End point values	GLPG2737 group	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	8[5]		
Units: ng/ml				
arithmetic mean (standard deviation)				
GLPG2737 - Day 14	83.8 (± 68.0)	0 (± 0)		
GLPG2737 - Day 28	93.2 (± 60.3)	0 (± 0)		
G1125498 - Day 14	259 (± 150)	0 (± 0)		
G1125498 - Day 28	294 (± 153)	0 (± 0)		
ivacaftor - Day 1	192 (± 197)	53.2 (± 47.7)		
ivacaftor - Day 14	84.2 (± 62.5)	74.3 (± 53.2)		
ivacaftor - Day 28	108 (± 73)	66.8 (± 37.6)		
lumacaftor - Day 1	17000 (± 14200)	6950 (± 4050)		
lumacaftor - Day 14	11600 (± 6970)	7290 (± 4980)		
lumacaftor - Day 28	13500 (± 7110)	7600 (± 2750)		

Notes:

[5] - N=7 at Days 14 and 28

Statistical analyses

Statistical analysis title	Day 14 vs Day 1 - Ivacaftor

Statistical analysis description:

A mixed effect model with subject as random effect and day as fixed effect. The PEs were calculated as the geometric mean ratio of Day 28 (coadministration of Orkambi+GLPG2737) relative to Day 1 (Orkambi alone) and Day 14 (coadministration of Orkambi+GLPG2737) relative to Day 1 (Orkambi alone), with corresponding 90% confidence interval (CI).

Comparison groups	GLPG2737 group v Placebo group
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS-geometric mean ratio
Point estimate	0.489
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.264
upper limit	0.906

Statistical analysis title	Day 28 vs Day 1 - Ivacaftor

Statistical analysis description:

A mixed-effects model with subject as random effect and day as fixed effect. The PEs were calculated as the geometric mean ratio of Day 28 (coadministration of Orkambi+GLPG2737) relative to Day 1 (Orkambi alone) and Day 14 (coadministration of Orkambi+GLPG2737) relative to Day 1 (Orkambi alone), with corresponding 90% confidence interval (CI).

Comparison groups	GLPG2737 group v Placebo group
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS-geometric mean ratio
Point estimate	0.787
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.425
upper limit	1.458

Statistical analysis title	Day 14 vs Day 1 - Lumacaftor

Statistical analysis description:

A mixed-effects model with subject as random effect and day as fixed effect. The PEs were calculated as the geometric mean ratio of Day 28 (coadministration of Orkambi+GLPG2737) relative to Day 1 (Orkambi alone) and Day 14 (coadministration of Orkambi+GLPG2737) relative to Day 1 (Orkambi alone), with corresponding 90% confidence interval (CI).

Comparison groups	GLPG2737 group v Placebo group

Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS-geometric mean ratio
Point estimate	0.919
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.521
upper limit	1.619

Statistical analysis title	Day 28 vs Day 1

Statistical analysis description:

A mixed-effects model with subject as random effect and day as fixed effect. The PEs were calculated as the geometric mean ratio of Day 28 (coadministration of Orkambi+GLPG2737) relative to Day 1 (Orkambi alone) and Day 14 (coadministration of Orkambi+GLPG2737) relative to Day 1 (Orkambi alone), with corresponding 90% confidence interval (CI).

Comparison groups	GLPG2737 group v Placebo group
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS-geometric mean ratio
Point estimate	1.309
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.742
upper limit	2.306

Adverse events

Adverse events information

Timeframe for reporting adverse events:

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

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	GLPG2737 group

Reporting group description:

Subjects received GLPG2737 mg b.i.d.

Reporting group title	Placebo group

Reporting group description:

Subjects received placebo b.i.d.

Serious adverse events	GLPG2737 group	Placebo group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 14 (0.00%)	0 / 8 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	GLPG2737 group	Placebo group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 14 (71.43%)	8 / 8 (100.00%)	
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	1 / 14 (7.14%)	1 / 8 (12.50%)	
occurrences (all)	3	1	
Fatigue			
subjects affected / exposed	1 / 14 (7.14%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
Pyrexia			

subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)
occurrences (all)	1	0

Reproductive system and breast disorders

Testicular pain

subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)
occurrences (all)	1	0

Respiratory, thoracic and mediastinal disorders

Haemoptysis

subjects affected / exposed	1 / 14 (7.14%)	1 / 8 (12.50%)
occurrences (all)	2	2

Oropharyngeal pain

subjects affected / exposed	2 / 14 (14.29%)	0 / 8 (0.00%)
occurrences (all)	2	0

Sputum increased

subjects affected / exposed	1 / 14 (7.14%)	1 / 8 (12.50%)
occurrences (all)	1	1

Cough

subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)
occurrences (all)	1	0

Dysphonia

subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)
occurrences (all)	1	0

Nasal dryness

subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	1

Painful respiration

subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)
occurrences (all)	1	0

Rales

subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)
occurrences (all)	1	0

Sputum retention

subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	1

Psychiatric disorders

Insomnia		
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)
occurrences (all)	1	0
Investigations		
C-reactive protein increased		
subjects affected / exposed	1 / 14 (7.14%)	1 / 8 (12.50%)
occurrences (all)	1	1
Alanine aminotransferase increased		
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	1
Aspartate aminotransferase increased		
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	1
Blood albumin decreased		
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	1
Blood alkaline phosphatase increased		
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	1
Blood calcium decreased		
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	1
Blood calcium increased		
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	1
Blood creatine phosphokinase increased		
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)
occurrences (all)	1	0
Blood creatinine decreased		
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	1
Blood urea increased		
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	1
Crystal urine present		

subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	1
Eosinophil count abnormal		
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	1
High density lipoprotein decreased		
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	1
Lymphocyte percentage decreased		
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	1
Neutrophil count increased		
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	1
Platelet count increased		
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	1
Protein total decreased		
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	1
Prothrombin time prolonged		
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	1
White blood cell count decreased		
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)
occurrences (all)	1	0
White blood cell count increased		
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	1
Injury, poisoning and procedural complications		
Chest injury		
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)
occurrences (all)	1	0
Fall		

subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)
occurrences (all)	1	0
Limb injury		
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)
occurrences (all)	1	0
Skin abrasion		
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)
occurrences (all)	1	0
Nervous system disorders		
Headache		
subjects affected / exposed	1 / 14 (7.14%)	2 / 8 (25.00%)
occurrences (all)	1	2
Ear and labyrinth disorders		
Ear pain		
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)
occurrences (all)	1	0
Eye disorders		
Blepharospasm		
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	1
Gastrointestinal disorders		
Abdominal pain		
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)
occurrences (all)	1	0
Dyspepsia		
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	1
Flatulence		
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)
occurrences (all)	1	0
Nausea		
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)
occurrences (all)	1	0
Toothache		
subjects affected / exposed	0 / 14 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	1
Skin and subcutaneous tissue disorders		

Pruritus			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 14 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			
Viral upper respiratory tract infection			
subjects affected / exposed	3 / 14 (21.43%)	4 / 8 (50.00%)	
occurrences (all)	3	5	
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	0 / 14 (0.00%)	2 / 8 (25.00%)	
occurrences (all)	0	2	
Upper respiratory tract infection			
subjects affected / exposed	1 / 14 (7.14%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
Epididymitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Rhinitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 8 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 October 2017	The initially proposed dose regimen was changed from 150 mg GLPG2737 q.d. to 75 mg GLPG2737 b.i.d. The lower bound for heart rate range was changed from 40 to 50 bpm.
24 October 2017	Erratum: The lower bound for heart rate range was changed from 40 to 50 bpm for the ECG parameter 'heart rate'.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

 None reported