



Clinical trial results:

A Phase IIa, randomized, double-blind, placebo-controlled study to evaluate multiple doses of GLPG2222 in subjects with Cystic Fibrosis who are homozygous for the F508del mutation

Summary

EudraCT number	2016-004477-40
Trial protocol	GB NL BE ES
Global end of trial date	19 October 2017

Results information

Result version number	v1 (current)
This version publication date	04 November 2018
First version publication date	04 November 2018

Trial information

Trial identification

Sponsor protocol code	GLPG2222-CL-202
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03119649
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 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	30 March 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 October 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary Objective:

- To evaluate the safety and tolerability of 4 different doses of GLPG2222 administered orally and q.d. for 29 days in adult subjects with CF who are homozygous for the F508del CFTR mutation.

Secondary Objectives:

- To assess changes in biomarkers of CFTR activity.
 - To assess changes in respiratory symptoms.
 - To assess the PK of GLPG2222.
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Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, the International Council for Harmonisation (ICH) Good Clinical Practice (GCP) Guideline E6 (R2) and with the applicable European and local regulatory requirements. Prior to the performance of any study-specific procedure, 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 participation was voluntary and 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: -

Evidence for comparator: -

Actual start date of recruitment	18 March 2017
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	Netherlands: 14
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	United Kingdom: 5
Country: Number of subjects enrolled	Belgium: 12
Country: Number of subjects enrolled	Serbia: 8
Country: Number of subjects enrolled	United States: 15
Worldwide total number of subjects	59
EEA total number of subjects	36

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)	59
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted from 18 March 2017 (date the first subject signed the ICF) to 19 October 2017 (date of last contact with the last subject). The study was conducted in 21 sites located in the United States of America (5), the Netherlands (4), Belgium (4), United Kingdom (4), Spain (3) and Serbia (1).

Pre-assignment

Screening details:

73 subjects were screened, 59 of which were enrolled and treated.

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, Monitor, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Pooled placebo from Cohort A and B

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

Dosage and administration details:

The matching placebo was provided as a tablet for oral use (cohort A: batch number 2016200079 and cohort B: batch number 0088/2017) and was administered q.d. for 29 days.

Arm title	GLPG2222 50 mg q.d.
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Arm description:

Cohort A

Arm type	Experimental
Investigational medicinal product name	GLPG2222
Investigational medicinal product code	G957389
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

GLPG2222 was provided as tablets for oral use, containing 50 mg (batch number 2016200080) or 100 mg (batch number 2016200081) active substance of G957389 (G957389 is the compound code for GLPG2222) and was administered q.d. for 29 days.

Arm title	GLPG2222 100 mg q.d.
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Arm description:

Cohort A

Arm type	Experimental
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Investigational medicinal product name	GLPG2222
Investigational medicinal product code	G957389
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

GLPG2222 was provided as tablets for oral use, containing 50 mg (batch number 2016200080) or 100 mg (batch number 2016200081) active substance of G957389 (G957389 is the compound code for GLPG2222) and was administered q.d. for 29 days.

Arm title	GLPG2222 200 mg q.d.
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Arm description:

Cohort B

Arm type	Experimental
Investigational medicinal product name	GLPG2222
Investigational medicinal product code	G957389
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

GLPG2222 was provided as tablets for oral use, containing 100 mg (batch number 0089/2017) or 150 mg (batch number 0090/2017) active substance of G957389 (G957389 is the compound code for GLPG2222) and was administered q.d. for 29 days.

Arm title	GLPG2222 400 mg q.d.
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Arm description:

Cohort B

Arm type	Experimental
Investigational medicinal product name	GLPG2222
Investigational medicinal product code	G957389
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

GLPG2222 was provided as tablets for oral use, containing 100 mg (batch number 0089/2017) or 150 mg (batch number 0090/2017) active substance of G957389 (G957389 is the compound code for GLPG2222) and was administered q.d. for 29 days.

Number of subjects in period 1	Placebo	GLPG2222 50 mg q.d.	GLPG2222 100 mg q.d.
Started	11	10	10
Completed	11	10	10

Number of subjects in period 1	GLPG2222 200 mg q.d.	GLPG2222 400 mg q.d.
Started	14	14
Completed	14	14

Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description: Pooled placebo from Cohort A and B	
Reporting group title	GLPG2222 50 mg q.d.
Reporting group description: Cohort A	
Reporting group title	GLPG2222 100 mg q.d.
Reporting group description: Cohort A	
Reporting group title	GLPG2222 200 mg q.d.
Reporting group description: Cohort B	
Reporting group title	GLPG2222 400 mg q.d.
Reporting group description: Cohort B	

Reporting group values	Placebo	GLPG2222 50 mg q.d.	GLPG2222 100 mg q.d.
Number of subjects	11	10	10
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)	11	10	10
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
median	27	26	24
full range (min-max)	21 to 58	20 to 37	18 to 35
Gender categorical Units: Subjects			
Female	4	3	6
Male	7	7	4
Race Units: Subjects			
White	11	9	10
Not allowed to ask per local regulations	0	1	0

BMI			
Units: kg/m ²			
median	22.20	21.05	20.75
full range (min-max)	16.3 to 25.7	18.7 to 25.1	14.1 to 23.3

Reporting group values	GLPG2222 200 mg q.d.	GLPG2222 400 mg q.d.	Total
Number of subjects	14	14	59
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	14	59
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
median	32	26	-
full range (min-max)	19 to 47	19 to 59	-
Gender categorical Units: Subjects			
Female	7	5	25
Male	7	9	34
Race Units: Subjects			
White	13	13	56
Not allowed to ask per local regulations	1	1	3
BMI Units: kg/m ²			
median	22.30	22.40	-
full range (min-max)	18.5 to 26.8	18.3 to 23.7	-

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Pooled placebo from Cohort A and B	
Reporting group title	GLPG2222 50 mg q.d.
Reporting group description:	
Cohort A	
Reporting group title	GLPG2222 100 mg q.d.
Reporting group description:	
Cohort A	
Reporting group title	GLPG2222 200 mg q.d.
Reporting group description:	
Cohort B	
Reporting group title	GLPG2222 400 mg q.d.
Reporting group description:	
Cohort B	

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

End point title	Safety - incidence of TEAE (Treatment-Emergent Adverse Events) ^[1]
End point description:	Safety and tolerability, assessed by the incidence of adverse events (AEs), as well as changes over time in weight, vital signs, oxygen saturation by pulse oximetry, 12-lead ECG, spirometry, and clinical safety laboratory data (hematology, chemistry, coagulation, and urinalysis).
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	Placebo	GLPG2222 50 mg q.d.	GLPG2222 100 mg q.d.	GLPG2222 200 mg q.d.
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	10	10	14
Units: Subjects				
Any TEAE	9	8	10	11
Severe TEAE	1	0	1	1
Serious TEAE	2	0	1	0
Treatment related TEAE	2	2	6	5
Discontinuation due to AE	0	0	0	0

End point values	GLPG2222 400 mg q.d.			
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Subject group type	Reporting group			
Number of subjects analysed	14			
Units: Subjects				
Any TEAE	9			
Severe TEAE	0			
Serious TEAE	0			
Treatment related TEAE	1			
Discontinuation due to AE	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Sweat Chloride Concentration by treatment group

End point title	Sweat Chloride Concentration by treatment group
End point description:	Change from baseline in sweat chloride concentration through 29 days.
End point type	Secondary
End point timeframe:	Sweat was collected at screening and pre-dose on Day 29 or early discontinuation (if applicable) with Last Observation Carried Forward (LOCF) imputation method.

End point values	Placebo	GLPG2222 50 mg q.d.	GLPG2222 100 mg q.d.	GLPG2222 200 mg q.d.
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	9	8	14
Units: mmol/L				
least squares mean (standard error)				
Day 29 (Change from Baseline)	-2.54 (± 2.787)	-5.84 (± 3.079)	-6.64 (± 3.286)	-18.30 (± 2.494)

End point values	GLPG2222 400 mg q.d.			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: mmol/L				
least squares mean (standard error)				
Day 29 (Change from Baseline)	-8.84 (± 2.494)			

Statistical analyses

Statistical analysis title	GLPG2222 50 mg q.d. versus placebo
Statistical analysis description:	
An analysis of covariance (ANCOVA) model on the changes from baseline at each time point, with treatment as factor and baseline value as covariate, was applied. Between-group comparisons was done for each GLPG2222 group versus the pooled placebo group with Last Observation Carried Forward (LOCF) imputation method.	
Comparison groups	Placebo v GLPG2222 50 mg q.d.
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4291
Method	ANCOVA
Parameter estimate	Least Square mean difference
Point estimate	-3.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.63
upper limit	5.02
Variability estimate	Standard error of the mean
Dispersion value	4.146

Statistical analysis title	GLPG2222 100 mg q.d. versus placebo
Statistical analysis description:	
An analysis of covariance (ANCOVA) model on the changes from baseline at each time point, with treatment as factor and baseline value as covariate, was applied. Between-group comparisons was done for each GLPG2222 group versus the pooled placebo group with Last Observation Carried Forward (LOCF) imputation method.	
Comparison groups	GLPG2222 100 mg q.d. v Placebo
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3477
Method	ANCOVA
Parameter estimate	Least Square mean difference
Point estimate	-4.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.79
upper limit	4.59
Variability estimate	Standard error of the mean
Dispersion value	4.324

Statistical analysis title	GLPG2222 200 mg q.d. versus placebo
Statistical analysis description:	
An analysis of covariance (ANCOVA) model on the changes from baseline at each time point, with treatment as factor and baseline value as covariate, was applied. Between-group comparisons was done	

for each GLPG2222 group versus the pooled placebo group with Last Observation Carried Forward (LOCF) imputation method.

Comparison groups	Placebo v GLPG2222 200 mg q.d.
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Least Square mean difference
Point estimate	-15.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.24
upper limit	-8.28
Variability estimate	Standard error of the mean
Dispersion value	3.723

Statistical analysis title	GLPG2222 400 mg q.d. versus placebo
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Statistical analysis description:

An analysis of covariance (ANCOVA) model on the changes from baseline at each time point, with treatment as factor and baseline value as covariate, was applied. Between-group comparisons was done for each GLPG2222 group versus the pooled placebo group with Last Observation Carried Forward (LOCF) imputation method.

Comparison groups	Placebo v GLPG2222 400 mg q.d.
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0995
Method	ANCOVA
Parameter estimate	Least Square mean difference
Point estimate	-6.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.85
upper limit	1.24
Variability estimate	Standard error of the mean
Dispersion value	3.757

Secondary: Pulmonary function by treatment group (ppFEV1)

End point title	Pulmonary function by treatment group (ppFEV1)
End point description:	
Change from baseline in percent predicted FEV1 through 29 days.	
End point type	Secondary

End point timeframe:

Between screening and pre-dose on Day 29 or early discontinuation (if applicable) with Last Observation Carried Forward (LOCF) imputation method.

End point values	Placebo	GLPG2222 50 mg q.d.	GLPG2222 100 mg q.d.	GLPG2222 200 mg q.d.
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	10	10	14
Units: Percent Predicted FEV1 (%)				
least squares mean (standard error)				
Day 29 (Change from Baseline)	-1.0 (± 1.45)	0.1 (± 1.50)	-0.3 (± 1.51)	0.0 (± 1.27)

End point values	GLPG2222 400 mg q.d.			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: Percent Predicted FEV1 (%)				
least squares mean (standard error)				
Day 29 (Change from Baseline)	1.3 (± 1.26)			

Statistical analyses

Statistical analysis title	GLPG2222 50 mg q.d versus placebo
Statistical analysis description:	
An analysis of covariance (ANCOVA) model on the changes from baseline at each time point, with treatment as factor and baseline value as covariate, was applied. Between-group comparisons was done for each GLPG2222 group versus the pooled placebo group with Last Observation Carried Forward (LOCF) imputation method.	
Comparison groups	Placebo v GLPG2222 50 mg q.d.
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.594
Method	ANCOVA
Parameter estimate	Least Square mean difference
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.1
upper limit	5.4
Variability estimate	Standard error of the mean
Dispersion value	2.11

Statistical analysis title	GLPG2222 100 mg q.d versus placebo
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Statistical analysis description:

An analysis of covariance (ANCOVA) model on the changes from baseline at each time point, with treatment as factor and baseline value as covariate, was applied. Between-group comparisons was done for each GLPG2222 group versus the pooled placebo group with Last Observation Carried Forward (LOCF) imputation method.

Comparison groups	Placebo v GLPG2222 100 mg q.d.
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7553
Method	ANCOVA
Parameter estimate	Least Square mean difference
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.5
upper limit	4.8
Variability estimate	Standard error of the mean
Dispersion value	2.06

Statistical analysis title

GLPG2222 200 mg q.d versus placebo

Statistical analysis description:

An analysis of covariance (ANCOVA) model on the changes from baseline at each time point, with treatment as factor and baseline value as covariate, was applied. Between-group comparisons was done for each GLPG2222 group versus the pooled placebo group with Last Observation Carried Forward (LOCF) imputation method.

Comparison groups	Placebo v GLPG2222 200 mg q.d.
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5958
Method	ANCOVA
Parameter estimate	Least Square mean difference
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.9
upper limit	4.9
Variability estimate	Standard error of the mean
Dispersion value	1.94

Statistical analysis title

GLPG2222 400 mg q.d versus placebo

Statistical analysis description:

An analysis of covariance (ANCOVA) model on the changes from baseline at each time point, with treatment as factor and baseline value as covariate, was applied. Between-group comparisons was done for each GLPG2222 group versus the pooled placebo group with Last Observation Carried Forward (LOCF) imputation method.

Comparison groups	Placebo v GLPG2222 400 mg q.d.
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2403
Method	ANCOVA
Parameter estimate	Least Square mean difference
Point estimate	2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	6.2
Variability estimate	Standard error of the mean
Dispersion value	1.94

Secondary: Cystic Fibrosis Questionnaire revised respiratory domain (CFQ-R)

End point title	Cystic Fibrosis Questionnaire revised respiratory domain (CFQ-R)
End point description:	Change from baseline in the respiratory domain of the Cystic Fibrosis Questionnaire- Revised (CFQ-R) through 29 days.
End point type	Secondary
End point timeframe:	Eligible subjects were asked to complete the adult version of the CFQ-R at screening, and Day 29 or at early discontinuation (if applicable) with Last Observation Carried Forward (LOCF) imputation method.

End point values	Placebo	GLPG2222 50 mg q.d.	GLPG2222 100 mg q.d.	GLPG2222 200 mg q.d.
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	10	10	14
Units: CFQ-R Score change from Baseline				
least squares mean (standard error)				
Day 29 (Change from Baseline)	-2.36 (± 3.318)	0.35 (± 3.469)	-0.74 (± 3.480)	4.48 (± 2.931)

End point values	GLPG2222 400 mg q.d.			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: CFQ-R Score change from Baseline				
least squares mean (standard error)				
Day 29 (Change from Baseline)	-0.77 (± 2.931)			

Statistical analyses

Statistical analysis title	GLPG2222 50 mg q.d. versus placebo
Statistical analysis description:	
An analysis of covariance (ANCOVA) model on the changes from baseline at each time point, with treatment as factor and baseline value as covariate, was applied. Between-group comparisons were done for each GLPG2222 group versus the pooled placebo group with Last Observation Carried Forward (LOCF) imputation method.	
Comparison groups	Placebo v GLPG2222 50 mg q.d.
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5749
Method	ANCOVA
Parameter estimate	Least Square mean difference
Point estimate	2.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.93
upper limit	12.35
Variability estimate	Standard error of the mean
Dispersion value	4.805

Statistical analysis title	GLPG2222 100 mg q.d. versus placebo
Statistical analysis description:	
An analysis of covariance (ANCOVA) model on the changes from baseline at each time point, with treatment as factor and baseline value as covariate, was applied. Between-group comparisons were done for each GLPG2222 group versus the pooled placebo group with Last Observation Carried Forward (LOCF) imputation method.	
Comparison groups	Placebo v GLPG2222 100 mg q.d.
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7381
Method	ANCOVA
Parameter estimate	Least Square mean difference
Point estimate	1.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.06
upper limit	11.3

Variability estimate	Standard error of the mean
Dispersion value	4.826

Statistical analysis title	GLPG2222 200 mg q.d. versus placebo
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Statistical analysis description:

An analysis of covariance (ANCOVA) model on the changes from baseline at each time point, with treatment as factor and baseline value as covariate, was applied. Between-group comparisons were done for each GLPG2222 group versus the pooled placebo group with Last Observation Carried Forward (LOCF) imputation method.

Comparison groups	Placebo v GLPG2222 200 mg q.d.
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1282
Method	ANCOVA
Parameter estimate	Least Square mean difference
Point estimate	6.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.04
upper limit	15.71
Variability estimate	Standard error of the mean
Dispersion value	4.425

Statistical analysis title	GLPG2222 400 mg q.d. versus placebo
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Statistical analysis description:

An analysis of covariance (ANCOVA) model on the changes from baseline at each time point, with treatment as factor and baseline value as covariate, was applied. Between-group comparisons were done for each GLPG2222 group versus the pooled placebo group with Last Observation Carried Forward (LOCF) imputation method.

Comparison groups	Placebo v GLPG2222 400 mg q.d.
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7212
Method	ANCOVA
Parameter estimate	Least Square mean difference
Point estimate	1.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.29
upper limit	10.47
Variability estimate	Standard error of the mean
Dispersion value	4.427

Secondary: PK - Cmax

End point title	PK - Cmax ^[2]
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End point description:

To assess the maximum observed plasma concentration of GLPG2222.

End point type	Secondary
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End point timeframe:

PK blood samples for GLPG2222 were taken pre-dose and 0.5, 1, 2, 3, 4, 6 and 8 hours post-dose on Day 15

(or on Day 29 if subject was not available for full PK profiling on Day 15), and pre-dose on Day 29.

Notes:

[2] - 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 pooled placebo arm has been excluded from PK analysis.

End point values	GLPG2222 50 mg q.d.	GLPG2222 100 mg q.d.	GLPG2222 200 mg q.d.	GLPG2222 400 mg q.d.
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	14	13
Units: ng/mL				
arithmetic mean (standard deviation)	478 (± 128)	1170 (± 395)	2490 (± 535)	5330 (± 2700)

Statistical analyses

No statistical analyses for this end point

Secondary: PK - AUC0-t

End point title	PK - AUC0-t ^[3]
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End point description:

To assess area under the plasma concentration-time curve from time zero till 24 hours following multiple dosing of GLPG2222

End point type	Secondary
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End point timeframe:

PK blood samples for GLPG2222 were taken pre-dose and 0.5, 1, 2, 3, 4, 6 and 8 hours post-dose on Day 15

(or on Day 29 if subject was not available for full PK profiling on Day 15), and pre-dose on Day 29.

Notes:

[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: The pooled placebo arm has been excluded from PK analysis.

End point values	GLPG2222 50 mg q.d.	GLPG2222 100 mg q.d.	GLPG2222 200 mg q.d.	GLPG2222 400 mg q.d.
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	14	13
Units: ng.h/mL				
arithmetic mean (standard deviation)	3850 (± 1670)	9670 (± 3770)	22900 (± 7530)	46400 (± 25500)

Statistical analyses

No statistical analyses for this end point

Secondary: PK - tmax

End point title	PK - tmax ^[4]
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End point description:

To assess time to occurrence of Cmax of GLPG2222

End point type	Secondary
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End point timeframe:

PK blood samples for GLPG2222 were taken pre-dose and 0.5, 1, 2, 3, 4, 6 and 8 hours post-dose on Day 15

(or on Day 29 if subject was not available for full PK profiling on Day 15), and pre-dose on Day 29.

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The pooled placebo arm has been excluded from PK analysis.

End point values	GLPG2222 50 mg q.d.	GLPG2222 100 mg q.d.	GLPG2222 200 mg q.d.	GLPG2222 400 mg q.d.
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	14	13
Units: hour				
median (full range (min-max))	2.0 (1.0 to 6.0)	2.0 (2.0 to 6.0)	3.0 (2.0 to 4.0)	2.0 (0.5 to 6.0)

Statistical analyses

No statistical analyses for this end point

Secondary: PK - CTrough

End point title	PK - CTrough ^[5]
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End point description:

To assess plasma concentration observed at pre-dose of GLPG2222 on the full PK profiling day (either Day 15 or Day 29 depending on the subject)

End point type	Secondary
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End point timeframe:

PK blood samples for GLPG2222 were taken pre-dose and 0.5, 1, 2, 3, 4, 6 and 8 hours post-dose on Day 15

(or on Day 29 if subject was not available for full PK profiling on Day 15), and pre-dose on Day 29.

Notes:

[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: The pooled placebo arm has been excluded from PK analysis.

End point values	GLPG2222 50 mg q.d.	GLPG2222 100 mg q.d.	GLPG2222 200 mg q.d.	GLPG2222 400 mg q.d.
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	14	14
Units: ng/mL				
arithmetic mean (standard deviation)	48.1 (± 33.7)	132 (± 87.2)	343 (± 204)	677 (± 659)

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 deaths or TEAEs leading to study drug discontinuation were reported during the study. A total of 4 (2 after GLPG2222, 2 after placebo) SAEs were reported in 2/11 (18.2%) and 1/10 (10.0%) subjects in the pooled placebo and GLPG2222 100 mg q.d. treatment groups, respectively.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.0
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Reporting groups

Reporting group title	Placebo
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Reporting group description: -

Reporting group title	GLPG2222 50 mg q.d.
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Reporting group description: -

Reporting group title	GLPG2222 100 mg q.d.
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Reporting group description: -

Reporting group title	GLPG2222 200 mg q.d.
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Reporting group description: -

Reporting group title	GLPG2222 400 mg q.d.
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Reporting group description: -

Serious adverse events	Placebo	GLPG2222 50 mg q.d.	GLPG2222 100 mg q.d.
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 11 (18.18%)	0 / 10 (0.00%)	1 / 10 (10.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Infections and infestations			
infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	2 / 11 (18.18%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	GLPG2222 200 mg q.d.	GLPG2222 400 mg q.d.	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

Infections and infestations			
infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	
occurrences causally related to treatment / all	0 / 0	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	Placebo	GLPG2222 50 mg q.d.	GLPG2222 100 mg q.d.
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 11 (81.82%)	8 / 10 (80.00%)	10 / 10 (100.00%)
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
Tooth extraction			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 11 (9.09%)	1 / 10 (10.00%)	2 / 10 (20.00%)
occurrences (all)	1	1	2
Pyrexia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	0	1	2
Adverse drug reaction			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Asthenia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Chest discomfort			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Catheter site related reaction			

subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Exercise tolerance increased subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Pain subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0
Reproductive system and breast disorders			
Azoospermia subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Menstruation irregular subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			
Cough subjects affected / exposed occurrences (all)	3 / 11 (27.27%) 3	5 / 10 (50.00%) 6	0 / 10 (0.00%) 0
Sputum increased subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	5 / 10 (50.00%) 7	1 / 10 (10.00%) 1
Dyspnoea subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	2 / 10 (20.00%) 2	1 / 10 (10.00%) 1
Epistaxis subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	1 / 10 (10.00%) 1	1 / 10 (10.00%) 1
Haemoptysis subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 10 (0.00%) 0	1 / 10 (10.00%) 1
Nasal congestion subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 10 (0.00%) 0	1 / 10 (10.00%) 1
Oropharyngeal pain			

subjects affected / exposed	1 / 11 (9.09%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Upper-airway cough syndrome			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Decreased bronchial secretion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dysphonia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Pleuritic pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pulmonary congestion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Pulmonary haemorrhage			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Respiratory depth decreased			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Respiratory tract congestion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Sputum decreased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Sputum discoloured			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1

Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood glucose decreased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood uric acid increased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Body temperature increased			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Neutrophil count increased			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Platelet count increased			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Red blood cells urine positive			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Thrombin time prolonged			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Urine leukocyte esterase positive			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Weight decreased			

subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
White blood cell count increased subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0
White blood cells urine positive subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Injury, poisoning and procedural complications Wound subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Nervous system disorders Headache subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	3 / 10 (30.00%) 3	3 / 10 (30.00%) 4
Dizziness subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Lethargy subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Loss of consciousness subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Memory impairment subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Retrograde amnesia subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 10 (0.00%) 0	1 / 10 (10.00%) 1
Eye disorders			

Blepharospasm subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Eye pruritus subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Gastrointestinal disorders			
Diarrhoea subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 10 (0.00%) 0	3 / 10 (30.00%) 3
Abdominal pain subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0
Nausea subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	1 / 10 (10.00%) 1	2 / 10 (20.00%) 2
Dyspepsia subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0
Constipation subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 10 (0.00%) 0	1 / 10 (10.00%) 1
Gastrointestinal motility disorder subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Gastrointestinal pain subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Tongue discolouration			

subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 10 (0.00%) 0	1 / 10 (10.00%) 1
Toothache subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Vomiting subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 10 (0.00%) 0	1 / 10 (10.00%) 1
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 10 (0.00%) 0	2 / 10 (20.00%) 3
Pruritus subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 10 (0.00%) 0	1 / 10 (10.00%) 1
Renal and urinary disorders Leukocyturia subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Renal colic subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0
Arthralgia subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Arthritis subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Neck pain subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 10 (0.00%) 0	1 / 10 (10.00%) 1
Infections and infestations			

Infected pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	1 / 11 (9.09%)	2 / 10 (20.00%)	1 / 10 (10.00%)
occurrences (all)	1	2	1
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 11 (9.09%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	1	1	1
Ear infection			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Enterovirus infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Pharyngitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Pseudomonas infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Purulent discharge			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection viral			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Skin candida			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Tooth abscess			

subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Tooth infection subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Urinary tract infection subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Diabetes mellitus inadequate control subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	1 / 10 (10.00%) 2	0 / 10 (0.00%) 0

Non-serious adverse events	GLPG2222 200 mg q.d.	GLPG2222 400 mg q.d.	
Total subjects affected by non-serious adverse events subjects affected / exposed	11 / 14 (78.57%)	9 / 14 (64.29%)	
Vascular disorders Hot flush subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	1 / 14 (7.14%) 1	
Surgical and medical procedures Tooth extraction subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1	0 / 14 (0.00%) 0	
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1	2 / 14 (14.29%) 3	
Pyrexia subjects affected / exposed occurrences (all)	2 / 14 (14.29%) 2	0 / 14 (0.00%) 0	
Adverse drug reaction			

subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	
occurrences (all)	2	0	
Asthenia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Chest discomfort			
subjects affected / exposed	1 / 14 (7.14%)	1 / 14 (7.14%)	
occurrences (all)	1	1	
Catheter site related reaction			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Exercise tolerance increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Reproductive system and breast disorders			
Azoospermia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Menstruation irregular			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 14 (21.43%)	4 / 14 (28.57%)	
occurrences (all)	3	4	
Sputum increased			
subjects affected / exposed	1 / 14 (7.14%)	1 / 14 (7.14%)	
occurrences (all)	1	1	
Dyspnoea			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Epistaxis			

subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0
Haemoptysis		
subjects affected / exposed	1 / 14 (7.14%)	1 / 14 (7.14%)
occurrences (all)	1	2
Nasal congestion		
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	1
Oropharyngeal pain		
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	1
Upper-airway cough syndrome		
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0
Decreased bronchial secretion		
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)
occurrences (all)	2	0
Dysphonia		
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0
Pleuritic pain		
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)
occurrences (all)	1	0
Pulmonary congestion		
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0
Pulmonary haemorrhage		
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0
Respiratory depth decreased		
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0
Respiratory tract congestion		
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	1
Sputum decreased		

subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Sputum discoloured			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Blood glucose decreased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Blood uric acid increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Body temperature increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Hepatic enzyme increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Lymphocyte count decreased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Neutrophil count increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Platelet count increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Red blood cells urine positive			

subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Thrombin time prolonged			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Urine leukocyte esterase positive			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Weight decreased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
White blood cell count increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
White blood cells urine positive			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Wound			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 14 (35.71%)	3 / 14 (21.43%)	
occurrences (all)	12	3	
Dizziness			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Lethargy			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Loss of consciousness			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Memory impairment			

subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	1 / 14 (7.14%) 1	
Retrograde amnesia subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 14 (0.00%) 0	
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 14 (0.00%) 0	
Eye disorders Blepharospasm subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1	0 / 14 (0.00%) 0	
Eye pruritus subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 14 (0.00%) 0	
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1	1 / 14 (7.14%) 1	
Abdominal pain subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 3	1 / 14 (7.14%) 2	
Abdominal pain upper subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1	2 / 14 (14.29%) 2	
Nausea subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 14 (0.00%) 0	
Dyspepsia subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	1 / 14 (7.14%) 1	
Constipation subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 14 (0.00%) 0	
Gastrointestinal motility disorder			

subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Tongue discolouration			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Toothache			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Pruritus			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Renal and urinary disorders			
Leukocyturia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Renal colic			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Arthralgia			

subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Arthritis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	
occurrences (all)	3	0	
Neck pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	2 / 14 (14.29%)	2 / 14 (14.29%)	
occurrences (all)	2	2	
Viral upper respiratory tract infection			
subjects affected / exposed	3 / 14 (21.43%)	1 / 14 (7.14%)	
occurrences (all)	3	1	
Ear infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Enterovirus infection			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Gastrointestinal infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Pharyngitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Pseudomonas infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Purulent discharge			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	
occurrences (all)	2	0	
Respiratory tract infection viral			

subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Sinusitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Skin candida			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Tooth abscess			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Tooth infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	
occurrences (all)	2	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	

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