



Clinical trial results:

A phase IIa, randomized, double-blind, placebo-controlled study to evaluate GLPG2222 in ivacaftor-treated subjects with Cystic Fibrosis harbouring one F508del CFTR mutation and a second gating (class III) mutation.

Summary

EudraCT number	2016-002837-31
Trial protocol	IE GB DE BE CZ
Global end of trial date	24 August 2017

Results information

Result version number	v1 (current)
This version publication date	26 August 2018
First version publication date	26 August 2018

Trial information

Trial identification

Sponsor protocol code	GLPG2222-CL-201
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03045523
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Galapagos NV
Sponsor organisation address	Industriepark Mechelen Noord 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	27 March 2018
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	24 August 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 two doses of orally administered GLPG2222 in ivacaftor-treated adult subjects with CF harboring one F508del CFTR mutation and a second gating (Class III) mutation.

Secondary Objectives:

- To assess changes in sweat chloride as a biomarker of CFTR ion channel function.
- To assess changes in pulmonary function (forced expiratory volume in 1 second [FEV1]).
- To assess changes in the Respiratory Domain of the Cystic Fibrosis Questionnaire – Revised (CFQ-R).

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 Harmonization (ICH) Note for Guidance on Good Clinical Practice (GCP) (Committee for Proprietary Medicinal Products [CPMP]/ICH/135/95) and with applicable local requirements.

Prior to the performance of any study-specific procedure, written informed consent was obtained from each subject. He or she 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 he or she could withdraw from the study at any time for any reason and that this would not have any effect on his or her potential future medical care.

Background therapy:

Ivacaftor (Kalydeco) 150 mg twice daily (b.i.d.)

Evidence for comparator: -

Actual start date of recruitment	23 January 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	United Kingdom: 10
Country: Number of subjects enrolled	Belgium: 7
Country: Number of subjects enrolled	Czech Republic: 2
Country: Number of subjects enrolled	Germany: 5
Country: Number of subjects enrolled	Ireland: 8
Country: Number of subjects enrolled	Australia: 5
Worldwide total number of subjects	37
EEA total number of subjects	32

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)	37
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted from 23-Jan-2017 (date the first subject signed the ICF) to 24-Aug-2017 (date of last contact with last subject). The last visit of last subject occurred on 11-Aug-2017. Subjects were effectively enrolled in sites located in Australia(4), Belgium (3), Czech Republic (1), Germany (3), United Kingdom (7), and Ireland (3).

Pre-assignment

Screening details:

In total, 47 subjects were screened, 37 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, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	GLPG2222 - 150 mg q.d.

Arm description:

GLPG2222 was administered in addition to a stable ivacaftor regimen (150 mg b.i.d.)

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

Dosage and administration details:

A dose of 150 mg GLPG2222 corresponding to 3.0 mL of the oral suspension containing 50 mg G957389/mL was administered as a ready-to-use oral suspension, once daily (q.d.) for 29 days. GLPG2222 was presented as a ready-to-use oral suspension, containing 50 or 100 mg G957389/mL (G957389 is the compound code for GLPG2222).

Arm title	GLPG2222 - 300 mg q.d.
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Arm description:

GLPG2222 was administered in addition to a stable ivacaftor regimen (150 mg b.i.d.)

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

Dosage and administration details:

A dose of 300 mg GLPG2222 corresponding to 3.0 mL of the oral suspension containing 100 mg G957389/mL was administered as a ready-to-use oral suspension, once daily (q.d.) for 29 days. GLPG2222 was presented as a ready-to-use oral suspension, containing 50 or 100 mg G957389/mL.

Arm title	Placebo q.d.
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Arm description:

Placebo to match was administered in addition to a stable ivacaftor regimen (150 mg b.i.d.)

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

Dosage and administration details:

Placebo to match corresponding to 3.0 mL of the oral suspension was administered daily.

Number of subjects in period 1	GLPG2222 - 150 mg q.d.	GLPG2222 - 300 mg q.d.	Placebo q.d.
Started	16	14	7
Completed	15	13	7
Not completed	1	1	0
Wrong study drug kit provided	1	-	-
Lost to follow-up	-	1	-

Baseline characteristics

Reporting groups

Reporting group title	GLPG2222 - 150 mg q.d.
Reporting group description: GLPG2222 was administered in addition to a stable ivacaftor regimen (150 mg b.i.d.)	
Reporting group title	GLPG2222 - 300 mg q.d.
Reporting group description: GLPG2222 was administered in addition to a stable ivacaftor regimen (150 mg b.i.d.)	
Reporting group title	Placebo q.d.
Reporting group description: Placebo to match was administered in addition to a stable ivacaftor regimen (150 mg b.i.d.)	

Reporting group values	GLPG2222 - 150 mg q.d.	GLPG2222 - 300 mg q.d.	Placebo q.d.
Number of subjects	16	14	7
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)	16	14	7
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
median	29	29	46
full range (min-max)	19 to 42	18 to 35	19 to 53
Gender categorical Units: Subjects			
Female	4	8	4
Male	12	6	3
Race Units: Subjects			
White	16	14	7
BMI Units: kg/m2			
median	23.95	22.00	25.30
full range (min-max)	19.9 to 31.5	18.4 to 34.3	21.2 to 33.6

Reporting group values	Total		
Number of subjects	37		
Age categorical Units: Subjects			
In utero	0		

Preterm newborn infants (gestational age < 37 wks)	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)	37		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: years			
median			
full range (min-max)	-		
Gender categorical			
Units: Subjects			
Female	16		
Male	21		
Race			
Units: Subjects			
White	37		
BMI			
Units: kg/m2			
median			
full range (min-max)	-		

End points

End points reporting groups

Reporting group title	GLPG2222 - 150 mg q.d.
Reporting group description: GLPG2222 was administered in addition to a stable ivacaftor regimen (150 mg b.i.d.)	
Reporting group title	GLPG2222 - 300 mg q.d.
Reporting group description: GLPG2222 was administered in addition to a stable ivacaftor regimen (150 mg b.i.d.)	
Reporting group title	Placebo q.d.
Reporting group description: Placebo to match was administered in addition to a stable ivacaftor regimen (150 mg b.i.d.)	

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

End point title	Safety - TEAE (Treatment-Emergent Adverse Events) ^[1]
End point description: The number of subjects with treatment-emergent adverse events (TEAEs). An analysis of the TEAEs was performed. Laboratory assessments, 12-lead ECG, vital signs, physical examinations, oxygen saturation by pulse oximetry and spirometry were analyzed descriptively.	
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	GLPG2222 - 150 mg q.d.	GLPG2222 - 300 mg q.d.	Placebo q.d.	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	14	7	
Units: Subjects				
Any TEAE	12	13	7	
Severe TEAE	1	0	0	
Serious TEAE	0	0	0	
Treatment related TEAE	4	8	5	
Discontinuation due to AE	0	0	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: The statistical evaluation of the mean sweat chloride concentration changes from baseline per time point for the modified ITT (intent to treat) Population, based on the arm with the greatest volume.	

End point type	Secondary
End point timeframe:	
Sweat was collected at screening and pre-dose on Days 1, 15 and 29, early discontinuation (if applicable) and follow-up.	

End point values	GLPG2222 - 150 mg q.d.	GLPG2222 - 300 mg q.d.	Placebo q.d.	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	7	
Units: mmol/L				
arithmetic mean (standard error)				
Baseline	45.8 (± 5.21)	52.2 (± 6.45)	43.1 (± 9.23)	
Day 15	-2.8 (± 3.57)	-6.3 (± 3.31)	1.0 (± 5.37)	
Day 29	-2.5 (± 3.09)	-6.5 (± 2.97)	6.3 (± 5.78)	

Statistical analyses

No statistical analyses for this end point

Secondary: Pulmonary function by treatment group (mean absolute FEV1)

End point title	Pulmonary function by treatment group (mean absolute FEV1)
End point description:	
The statistical evaluation of the mean FEV1 changes from baseline per time point for the modified ITT population.	
End point type	Secondary
End point timeframe:	
Between screening and pre-dose on Days 1, 15 and 29, early discontinuation (if applicable) and follow-up.	

End point values	GLPG2222 - 150 mg q.d.	GLPG2222 - 300 mg q.d.	Placebo q.d.	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	7	
Units: Liter				
arithmetic mean (standard error)				
Baseline	3.029 (± 0.2450)	2.385 (± 0.2452)	2.637 (± 0.4390)	
Day 15	0.097 (± 0.0576)	0.096 (± 0.0288)	0.060 (± 0.0548)	
Day 29	-0.008 (± 0.0605)	0.076 (± 0.0295)	-0.023 (± 0.0378)	

Statistical analyses

No statistical analyses for this end point

Secondary: Pulmonary function by treatment group (ppFEV1)

End point title	Pulmonary function by treatment group (ppFEV1)
End point description: The statistical evaluation of the mean percent predicted forced expiratory volume in 1 second (ppFEV1) changes from baseline per time point.	
End point type	Secondary
End point timeframe: Between screening and pre-dose on Days 1, 15 and 29, early discontinuation (if applicable) and follow-up.	

End point values	GLPG2222 - 150 mg q.d.	GLPG2222 - 300 mg q.d.	Placebo q.d.	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	7	
Units: Liter				
arithmetic mean (standard error)				
Baseline	71.0 (± 8.01)	72.2 (± 4.40)	62.9 (± 4.77)	
Day 15	2.0 (± 1.65)	2.3 (± 1.39)	2.6 (± 0.87)	
Day 29	-0.7 (± 1.11)	-0.5 (± 1.58)	1.9 (± 0.95)	

Statistical analyses

No statistical analyses for this end point

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

End point title	Cystic Fibrosis Questionnaire revised respiratory domain (CFQ-R)
End point description: The statistical evaluation of the mean CFQ-R Respiratory domain score changes from baseline per time point for modified ITT population.	
End point type	Secondary
End point timeframe: Eligible subjects were asked to complete the adult version of the CFQ-R at screening, Days 1, 15 and 29, early discontinuation (if applicable) and follow-up.	

End point values	GLPG2222 - 150 mg q.d.	GLPG2222 - 300 mg q.d.	Placebo q.d.	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	7	
Units: percentage				
arithmetic mean (standard error)				
Baseline	79.6 (± 5.22)	81.3 (± 3.17)	81.7 (± 6.50)	
Day 15	3.3 (± 1.78)	1.6 (± 2.13)	1.4 (± 0.91)	

Day 29	1.9 (\pm 2.08)	2.4 (\pm 2.08)	1.4 (\pm 2.29)	
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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, serious adverse events or TEAEs leading to study drug discontinuation were reported during the study. Twelve (12) Treatment-emergent AEs were considered related to the study drug by the investigator.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.1
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Reporting groups

Reporting group title	GLPG2222 - 150 mg q.d.
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Reporting group description: -

Reporting group title	GLPG2222 - 300 mg q.d.
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Reporting group description: -

Reporting group title	Placebo q.d.
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Reporting group description: -

Serious adverse events	GLPG2222 - 150 mg q.d.	GLPG2222 - 300 mg q.d.	Placebo q.d.
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 16 (0.00%)	0 / 14 (0.00%)	0 / 7 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	GLPG2222 - 150 mg q.d.	GLPG2222 - 300 mg q.d.	Placebo q.d.
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 16 (75.00%)	13 / 14 (92.86%)	7 / 7 (100.00%)
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 16 (12.50%)	4 / 14 (28.57%)	0 / 7 (0.00%)
occurrences (all)	3	4	0
Chest discomfort			

subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 14 (7.14%) 2	0 / 7 (0.00%) 0
Chest pain subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 14 (7.14%) 1	0 / 7 (0.00%) 0
Chills subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 2	0 / 14 (0.00%) 0	0 / 7 (0.00%) 0
Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 14 (0.00%) 0	0 / 7 (0.00%) 0
Reproductive system and breast disorders Dysmenorrhoea subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 14 (0.00%) 0	1 / 7 (14.29%) 1
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all)	3 / 16 (18.75%) 3	2 / 14 (14.29%) 2	1 / 7 (14.29%) 1
Cough subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 2	2 / 14 (14.29%) 2	1 / 7 (14.29%) 1
Sputum increased subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 2	1 / 14 (7.14%) 1	1 / 7 (14.29%) 1
Haemoptysis subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	1 / 14 (7.14%) 7	1 / 7 (14.29%) 1
Dyspnoea subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 2	1 / 14 (7.14%) 1	0 / 7 (0.00%) 0
Hypoventilation subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 14 (7.14%) 1	0 / 7 (0.00%) 0
Nasal congestion			

subjects affected / exposed	0 / 16 (0.00%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Nasal polyps			
subjects affected / exposed	0 / 16 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Painful respiration			
subjects affected / exposed	1 / 16 (6.25%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Productive cough			
subjects affected / exposed	1 / 16 (6.25%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Throat irritation			
subjects affected / exposed	0 / 16 (0.00%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Emotional disorder			
subjects affected / exposed	0 / 16 (0.00%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Blood glucose decreased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Blood glucose fluctuation			
subjects affected / exposed	0 / 16 (0.00%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Blood uric acid increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Glucose urine			
subjects affected / exposed	1 / 16 (6.25%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Glucose urine present			

subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 14 (7.14%) 1	0 / 7 (0.00%) 0
Liver function test abnormal subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 14 (0.00%) 0	1 / 7 (14.29%) 1
Liver function test increased subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 14 (0.00%) 0	1 / 7 (14.29%) 1
Weight increased subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 14 (7.14%) 1	0 / 7 (0.00%) 0
Injury, poisoning and procedural complications			
Fall subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 14 (0.00%) 0	1 / 7 (14.29%) 1
Joint injury subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 14 (0.00%) 0	1 / 7 (14.29%) 1
Limb injury subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 14 (0.00%) 0	0 / 7 (0.00%) 0
Congenital, familial and genetic disorders			
Cystic fibrosis related diabetes subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 14 (0.00%) 0	1 / 7 (14.29%) 1
Cardiac disorders			
Angina pectoris subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 14 (0.00%) 0	0 / 7 (0.00%) 0
Palpitations subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 14 (7.14%) 1	0 / 7 (0.00%) 0
sinus arrhythmia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 14 (7.14%) 1	0 / 7 (0.00%) 0
Nervous system disorders			

Headache			
subjects affected / exposed	3 / 16 (18.75%)	7 / 14 (50.00%)	2 / 7 (28.57%)
occurrences (all)	6	13	2
Paraesthesia			
subjects affected / exposed	0 / 16 (0.00%)	2 / 14 (14.29%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Dizziness			
subjects affected / exposed	0 / 16 (0.00%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Tremor			
subjects affected / exposed	1 / 16 (6.25%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Eye pruritus			
subjects affected / exposed	0 / 16 (0.00%)	0 / 14 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	5 / 16 (31.25%)	3 / 14 (21.43%)	1 / 7 (14.29%)
occurrences (all)	5	4	1
Abdominal pain			
subjects affected / exposed	2 / 16 (12.50%)	3 / 14 (21.43%)	0 / 7 (0.00%)
occurrences (all)	2	5	0
Nausea			
subjects affected / exposed	2 / 16 (12.50%)	2 / 14 (14.29%)	0 / 7 (0.00%)
occurrences (all)	2	3	0
Constipation			
subjects affected / exposed	0 / 16 (0.00%)	1 / 14 (7.14%)	2 / 7 (28.57%)
occurrences (all)	0	1	2
Abdominal pain upper			
subjects affected / exposed	1 / 16 (6.25%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Faeces soft			
subjects affected / exposed	0 / 16 (0.00%)	1 / 14 (7.14%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Flatulence			

subjects affected / exposed	1 / 16 (6.25%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Abdominal distension			
subjects affected / exposed	1 / 16 (6.25%)	0 / 14 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Steatorrhoea			
subjects affected / exposed	0 / 16 (0.00%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 16 (6.25%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Hyperhidrosis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 16 (0.00%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 16 (0.00%)	2 / 14 (14.29%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Neck pain			
subjects affected / exposed	0 / 16 (0.00%)	2 / 14 (14.29%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Arthralgia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Metatarsalgia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Muscle twitching			
subjects affected / exposed	0 / 16 (0.00%)	1 / 14 (7.14%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal pain			

subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 14 (7.14%) 1	0 / 7 (0.00%) 0
Myalgia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 14 (7.14%) 1	0 / 7 (0.00%) 0
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	2 / 14 (14.29%) 2	1 / 7 (14.29%) 1
Rhinitis subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 3	1 / 14 (7.14%) 1	0 / 7 (0.00%) 0
Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 14 (7.14%) 1	0 / 7 (0.00%) 0
Metabolism and nutrition disorders Gout subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 14 (0.00%) 0	1 / 7 (14.29%) 1
Hypoglycaemia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 14 (7.14%) 1	0 / 7 (0.00%) 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