# 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 |

**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. |

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. |

Arm description:

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

| | |
|---|---|
| Arm type | Placebo |

| | |
|---|---|
| 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<br>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<br>Units: years | | | |
| median | 29 | 29 | 46 |
| full range (min-max) | 19 to 42 | 18 to 35 | 19 to 53 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 4 | 8 | 4 |
| Male | 12 | 6 | 3 |
| Race<br>Units: Subjects | | | |
| White | 16 | 14 | 7 |
| BMI<br>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<br>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).<br>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 (± 2.08) | 2.4 (± 2.08) | 1.4 (± 2.29) | |

## 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 |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 19.1 |

### Reporting groups

| | |
|---|---|
| Reporting group title | GLPG2222 - 150 mg q.d. |
| Reporting group description: - | |
| Reporting group title | GLPG2222 - 300 mg q.d. |
| Reporting group description: - | |
| Reporting group title | Placebo q.d. |

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 | 0 / 16 (0.00%) | 1 / 14 (7.14%) | 0 / 7 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Chest pain | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 14 (7.14%) | 0 / 7 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Chills | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 14 (0.00%) | 0 / 7 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Immune system disorders | | | |
| Seasonal allergy | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 14 (0.00%) | 0 / 7 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Reproductive system and breast disorders | | | |
| Dysmenorrhoea | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 14 (0.00%) | 1 / 7 (14.29%) |
| occurrences (all) | 0 | 0 | 1 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 3 / 16 (18.75%) | 2 / 14 (14.29%) | 1 / 7 (14.29%) |
| occurrences (all) | 3 | 2 | 1 |
| Cough | | | |
| subjects affected / exposed | 2 / 16 (12.50%) | 2 / 14 (14.29%) | 1 / 7 (14.29%) |
| occurrences (all) | 2 | 2 | 1 |
| Sputum increased | | | |
| subjects affected / exposed | 2 / 16 (12.50%) | 1 / 14 (7.14%) | 1 / 7 (14.29%) |
| occurrences (all) | 2 | 1 | 1 |
| Haemoptysis | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 1 / 14 (7.14%) | 1 / 7 (14.29%) |
| occurrences (all) | 1 | 7 | 1 |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 1 / 14 (7.14%) | 0 / 7 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Hypoventilation | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 14 (7.14%) | 0 / 7 (0.00%) |
| occurrences (all) | 0 | 1 | 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 | 0 / 16 (0.00%) | 1 / 14 (7.14%) | 0 / 7 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Liver function test abnormal | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 14 (0.00%) | 1 / 7 (14.29%) |
| occurrences (all) | 0 | 0 | 1 |
| Liver function test increased | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 14 (0.00%) | 1 / 7 (14.29%) |
| occurrences (all) | 0 | 0 | 1 |
| Weight increased | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 14 (7.14%) | 0 / 7 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 14 (0.00%) | 1 / 7 (14.29%) |
| occurrences (all) | 0 | 0 | 1 |
| Joint injury | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 14 (0.00%) | 1 / 7 (14.29%) |
| occurrences (all) | 0 | 0 | 1 |
| Limb injury | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 14 (0.00%) | 0 / 7 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Congenital, familial and genetic disorders | | | |
| Cystic fibrosis related diabetes | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 14 (0.00%) | 1 / 7 (14.29%) |
| occurrences (all) | 0 | 0 | 1 |
| Cardiac disorders | | | |
| Angina pectoris | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 14 (0.00%) | 0 / 7 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Palpitations | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 14 (7.14%) | 0 / 7 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| sinus arrhytmia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 14 (7.14%) | 0 / 7 (0.00%) |
| occurrences (all) | 0 | 1 | 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 | 0 / 16 (0.00%) | 1 / 14 (7.14%) | 0 / 7 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 14 (7.14%) | 0 / 7 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Infections and infestations | | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 2 / 14 (14.29%) | 1 / 7 (14.29%) |
| occurrences (all) | 1 | 2 | 1 |
| Rhinitis | | | |
| subjects affected / exposed | 2 / 16 (12.50%) | 1 / 14 (7.14%) | 0 / 7 (0.00%) |
| occurrences (all) | 3 | 1 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 14 (7.14%) | 0 / 7 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Metabolism and nutrition disorders | | | |
| Gout | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 14 (0.00%) | 1 / 7 (14.29%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypoglycaemia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 14 (7.14%) | 0 / 7 (0.00%) |
| occurrences (all) | 0 | 1 | 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