



## 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 |
|-----------------------|-----------------|

#### 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:

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**Results analysis stage**

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|  |               |
|--|---------------|
| 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:

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**General information about the trial**

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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.

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:

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**Population of trial subjects**

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**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     |
| <b>Arm title</b>             | 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.

|                  |                     |
|------------------|---------------------|
| <b>Arm title</b> | GLPG2222 50 mg q.d. |
|------------------|---------------------|

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.

|                  |                      |
|------------------|----------------------|
| <b>Arm title</b> | GLPG2222 100 mg q.d. |
|------------------|----------------------|

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.

|                  |                      |
|------------------|----------------------|
| <b>Arm title</b> | GLPG2222 200 mg q.d. |
|------------------|----------------------|

**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.

|                  |                      |
|------------------|----------------------|
| <b>Arm title</b> | GLPG2222 400 mg q.d. |
|------------------|----------------------|

**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.

| <b>Number of subjects in period 1</b> | Placebo | GLPG2222 50 mg q.d. | GLPG2222 100 mg q.d. |
|---------------------------------------|---------|---------------------|----------------------|
| Started                               | 11      | 10                  | 10                   |
| Completed                             | 11      | 10                  | 10                   |

| <b>Number of subjects in period 1</b> | 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:<br>Pooled placebo from Cohort A and B |                      |
| Reporting group title  | GLPG2222 50 mg q.d.  |
| Reporting group description:<br>Cohort A                           |                      |
| Reporting group title  | GLPG2222 100 mg q.d. |
| Reporting group description:<br>Cohort A                           |                      |
| Reporting group title  | GLPG2222 200 mg q.d. |
| Reporting group description:<br>Cohort B                           |                      |
| Reporting group title  | GLPG2222 400 mg q.d. |
| Reporting group description:<br>Cohort B                           |                      |

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

|                          |              |              |              |
|--------------------------|--------------|--------------|--------------|
| BMI                      |              |              |              |
| Units: kg/m <sup>2</sup> |              |              |              |
| 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 |

| <b>Reporting group values</b>                         | GLPG2222 200 mg<br>q.d. | GLPG2222 400 mg<br>q.d. | Total |
|---|-------------------------|-------------------------|-------|
| Number of subjects                                    | 14                      | 14                      | 59    |
| Age categorical                                       |                         |                         |       |
| Units: Subjects                                       |                         |                         |       |
| In utero  | 0                       | 0                       | 0     |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0                       | 0                       | 0     |
| Newborns (0-27 days)                                  | 0                       | 0                       | 0     |
| Infants and toddlers (28 days-23<br>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<br>regulations           | 1                       | 1                       | 3     |
| BMI   |                         |                         |       |
| Units: kg/m <sup>2</sup>                              |                         |                         |       |
| 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:<br>Pooled placebo from Cohort A and B |                      |
| Reporting group title  | GLPG2222 50 mg q.d.  |
| Reporting group description:<br>Cohort A                           |                      |
| Reporting group title  | GLPG2222 100 mg q.d. |
| Reporting group description:<br>Cohort A                           |                      |
| Reporting group title  | GLPG2222 200 mg q.d. |
| Reporting group description:<br>Cohort B                           |                      |
| Reporting group title  | GLPG2222 400 mg q.d. |
| Reporting group description:<br>Cohort B                           |                      |

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

|  |   |
|--|---|
| End point title  | Safety - incidence of TEAE (Treatment-Emergent Adverse Events) <sup>[1]</sup> |
| End point description:<br>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:<br>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. |  |  |  |
|------------------|----------------------|--|--|--|

|                             |                 |  |  |  |
|-----------------------------|-----------------|--|--|--|
| 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

|   |                                    |
|---|------------------------------------|
| <b>Statistical analysis title</b>   | 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                              |

|   |                                     |
|---|-------------------------------------|
| <b>Statistical analysis title</b>   | 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                               |

|   |                                     |
|---|-------------------------------------|
| <b>Statistical analysis title</b>   | 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

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.

| <b>End point values</b>             | 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)         |

| <b>End point values</b>             | 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

| <b>Statistical analysis title</b>   | 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                              |

| <b>Statistical analysis title</b> | 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                       | 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

|  |                                    |
|--|------------------------------------|
| <b>Statistical analysis title</b>  | 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                              |

|  |                                     |
|--|-------------------------------------|
| <b>Statistical analysis title</b>  | 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                      |

|                                   |                                     |
|-----------------------------------|-------------------------------------|
| <b>Statistical analysis title</b> | 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 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                          |

|                                   |                                     |
|-----------------------------------|-------------------------------------|
| <b>Statistical analysis title</b> | 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 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                          |

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**Secondary: PK - Cmax**

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|                 |                          |
|-----------------|--------------------------|
| End point title | PK - Cmax <sup>[2]</sup> |
|-----------------|--------------------------|

End point description:

To assess the maximum observed plasma concentration of GLPG2222.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

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)        |

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**Statistical analyses**

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No statistical analyses for this end point

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**Secondary: PK - AUC0-t**

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|                 |                            |
|-----------------|----------------------------|
| End point title | PK - AUC0-t <sup>[3]</sup> |
|-----------------|----------------------------|

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 |
|----------------|-----------|

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<sup>[4]</sup>

End point description:

To assess time to occurrence of Cmax of GLPG2222

End point type Secondary

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<sup>[5]</sup>

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

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.

| <b>End point values</b>              | GLPG2222 50<br>mg q.d. | GLPG2222 100<br>mg q.d. | GLPG2222 200<br>mg q.d. | GLPG2222 400<br>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 |
|-----------------|------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 20.0 |
|--------------------|------|

### Reporting groups

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description: -

|                       |                     |
|-----------------------|---------------------|
| Reporting group title | GLPG2222 50 mg q.d. |
|-----------------------|---------------------|

Reporting group description: -

|                       |                      |
|-----------------------|----------------------|
| Reporting group title | GLPG2222 100 mg q.d. |
|-----------------------|----------------------|

Reporting group description: -

|                       |                      |
|-----------------------|----------------------|
| Reporting group title | GLPG2222 200 mg q.d. |
|-----------------------|----------------------|

Reporting group description: -

|                       |                      |
|-----------------------|----------------------|
| Reporting group title | GLPG2222 400 mg q.d. |
|-----------------------|----------------------|

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 %

| <b>Non-serious adverse events</b>                     | 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<br>occurrences (all)                                 | 0 / 11 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Exercise tolerance increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 11 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Pain<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 11 (0.00%)<br>0  | 1 / 10 (10.00%)<br>1 | 0 / 10 (0.00%)<br>0  |
| Reproductive system and breast disorders   |                      |                      |                      |
| Azoospermia<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 11 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Menstruation irregular<br>subjects affected / exposed<br>occurrences (all)       | 1 / 11 (9.09%)<br>1  | 0 / 10 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Respiratory, thoracic and mediastinal disorders                                  |                      |                      |                      |
| Cough<br>subjects affected / exposed<br>occurrences (all)                        | 3 / 11 (27.27%)<br>3 | 5 / 10 (50.00%)<br>6 | 0 / 10 (0.00%)<br>0  |
| Sputum increased<br>subjects affected / exposed<br>occurrences (all)             | 1 / 11 (9.09%)<br>1  | 5 / 10 (50.00%)<br>7 | 1 / 10 (10.00%)<br>1 |
| Dyspnoea<br>subjects affected / exposed<br>occurrences (all)                     | 1 / 11 (9.09%)<br>1  | 2 / 10 (20.00%)<br>2 | 1 / 10 (10.00%)<br>1 |
| Epistaxis<br>subjects affected / exposed<br>occurrences (all)                    | 1 / 11 (9.09%)<br>1  | 1 / 10 (10.00%)<br>1 | 1 / 10 (10.00%)<br>1 |
| Haemoptysis<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 11 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  | 1 / 10 (10.00%)<br>1 |
| Nasal congestion<br>subjects affected / exposed<br>occurrences (all)             | 1 / 11 (9.09%)<br>1  | 0 / 10 (0.00%)<br>0  | 1 / 10 (10.00%)<br>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<br>occurrences (all)  | 1 / 11 (9.09%)<br>1 | 0 / 10 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| White blood cell count increased<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 11 (0.00%)<br>0 | 1 / 10 (10.00%)<br>1 | 0 / 10 (0.00%)<br>0  |
| White blood cells urine positive<br>subjects affected / exposed<br>occurrences (all)                        | 1 / 11 (9.09%)<br>1 | 0 / 10 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Injury, poisoning and procedural complications<br>Wound<br>subjects affected / exposed<br>occurrences (all) | 1 / 11 (9.09%)<br>1 | 0 / 10 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Nervous system disorders<br>Headache<br>subjects affected / exposed<br>occurrences (all)                    | 1 / 11 (9.09%)<br>1 | 3 / 10 (30.00%)<br>3 | 3 / 10 (30.00%)<br>4 |
| Dizziness<br>subjects affected / exposed<br>occurrences (all)   | 1 / 11 (9.09%)<br>1 | 0 / 10 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Lethargy<br>subjects affected / exposed<br>occurrences (all)  | 0 / 11 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Loss of consciousness<br>subjects affected / exposed<br>occurrences (all)                                   | 1 / 11 (9.09%)<br>1 | 0 / 10 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Memory impairment<br>subjects affected / exposed<br>occurrences (all)                                       | 0 / 11 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Retrograde amnesia<br>subjects affected / exposed<br>occurrences (all)                                      | 1 / 11 (9.09%)<br>1 | 0 / 10 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Blood and lymphatic system disorders<br>Anaemia<br>subjects affected / exposed<br>occurrences (all)         | 0 / 11 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  | 1 / 10 (10.00%)<br>1 |
| Eye disorders   |                     |                      |                      |

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

|  |                     |                      |                      |
|--|---------------------|----------------------|----------------------|
| subjects affected / exposed<br>occurrences (all)   | 0 / 11 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  | 1 / 10 (10.00%)<br>1 |
| Toothache<br>subjects affected / exposed<br>occurrences (all)  | 0 / 11 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)   | 0 / 11 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  | 1 / 10 (10.00%)<br>1 |
| Skin and subcutaneous tissue disorders<br>Rash<br>subjects affected / exposed<br>occurrences (all)               | 0 / 11 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  | 2 / 10 (20.00%)<br>3 |
| Pruritus<br>subjects affected / exposed<br>occurrences (all)   | 0 / 11 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  | 1 / 10 (10.00%)<br>1 |
| Renal and urinary disorders<br>Leukocyturia<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 11 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Renal colic<br>subjects affected / exposed<br>occurrences (all)  | 0 / 11 (0.00%)<br>0 | 1 / 10 (10.00%)<br>1 | 0 / 10 (0.00%)<br>0  |
| Musculoskeletal and connective tissue disorders<br>Back pain<br>subjects affected / exposed<br>occurrences (all) | 1 / 11 (9.09%)<br>1 | 1 / 10 (10.00%)<br>1 | 0 / 10 (0.00%)<br>0  |
| Arthralgia<br>subjects affected / exposed<br>occurrences (all)   | 0 / 11 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Arthritis<br>subjects affected / exposed<br>occurrences (all)  | 0 / 11 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Neck pain<br>subjects affected / exposed<br>occurrences (all)  | 0 / 11 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  | 1 / 10 (10.00%)<br>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<br>occurrences (all)   | 0 / 11 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0 |
| Tooth infection<br>subjects affected / exposed<br>occurrences (all)  | 0 / 11 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0 |
| Urinary tract infection<br>subjects affected / exposed<br>occurrences (all)                                  | 0 / 11 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0 |
| Metabolism and nutrition disorders<br>Decreased appetite<br>subjects affected / exposed<br>occurrences (all) | 1 / 11 (9.09%)<br>1 | 0 / 10 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0 |
| Diabetes mellitus inadequate control<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 11 (0.00%)<br>0 | 1 / 10 (10.00%)<br>2 | 0 / 10 (0.00%)<br>0 |

| <b>Non-serious adverse events</b>  | GLPG2222 200 mg<br>q.d. | GLPG2222 400 mg<br>q.d. |  |
|--|-------------------------|-------------------------|--|
| Total subjects affected by non-serious<br>adverse events<br>subjects affected / exposed                                | 11 / 14 (78.57%)        | 9 / 14 (64.29%)         |  |
| Vascular disorders<br>Hot flush<br>subjects affected / exposed<br>occurrences (all)                                    | 0 / 14 (0.00%)<br>0     | 1 / 14 (7.14%)<br>1     |  |
| Surgical and medical procedures<br>Tooth extraction<br>subjects affected / exposed<br>occurrences (all)                | 1 / 14 (7.14%)<br>1     | 0 / 14 (0.00%)<br>0     |  |
| General disorders and administration<br>site conditions<br>Fatigue<br>subjects affected / exposed<br>occurrences (all) | 1 / 14 (7.14%)<br>1     | 2 / 14 (14.29%)<br>3    |  |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)  | 2 / 14 (14.29%)<br>2    | 0 / 14 (0.00%)<br>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<br>occurrences (all)   | 0 / 14 (0.00%)<br>0 | 1 / 14 (7.14%)<br>1 |  |
| Sputum discoloured<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 14 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0 |  |
| Psychiatric disorders<br>Insomnia<br>subjects affected / exposed<br>occurrences (all)                      | 1 / 14 (7.14%)<br>1 | 0 / 14 (0.00%)<br>0 |  |
| Investigations<br>Blood alkaline phosphatase increased<br>subjects affected / exposed<br>occurrences (all) | 1 / 14 (7.14%)<br>1 | 0 / 14 (0.00%)<br>0 |  |
| Blood glucose decreased<br>subjects affected / exposed<br>occurrences (all)                                | 1 / 14 (7.14%)<br>1 | 0 / 14 (0.00%)<br>0 |  |
| Blood uric acid increased<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 14 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0 |  |
| Body temperature increased<br>subjects affected / exposed<br>occurrences (all)                             | 0 / 14 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0 |  |
| Hepatic enzyme increased<br>subjects affected / exposed<br>occurrences (all)                               | 1 / 14 (7.14%)<br>1 | 0 / 14 (0.00%)<br>0 |  |
| Lymphocyte count decreased<br>subjects affected / exposed<br>occurrences (all)                             | 0 / 14 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0 |  |
| Neutrophil count increased<br>subjects affected / exposed<br>occurrences (all)                             | 0 / 14 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0 |  |
| Platelet count increased<br>subjects affected / exposed<br>occurrences (all)                               | 0 / 14 (0.00%)<br>0 | 0 / 14 (0.00%)<br>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<br>occurrences (all)  | 0 / 14 (0.00%)<br>0 | 1 / 14 (7.14%)<br>1  |  |
| Retrograde amnesia<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 14 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0  |  |
| Blood and lymphatic system disorders<br>Anaemia<br>subjects affected / exposed<br>occurrences (all) | 0 / 14 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0  |  |
| Eye disorders<br>Blepharospasm<br>subjects affected / exposed<br>occurrences (all)                  | 1 / 14 (7.14%)<br>1 | 0 / 14 (0.00%)<br>0  |  |
| Eye pruritus<br>subjects affected / exposed<br>occurrences (all)                                    | 0 / 14 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0  |  |
| Gastrointestinal disorders<br>Diarrhoea<br>subjects affected / exposed<br>occurrences (all)         | 1 / 14 (7.14%)<br>1 | 1 / 14 (7.14%)<br>1  |  |
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)                                  | 1 / 14 (7.14%)<br>3 | 1 / 14 (7.14%)<br>2  |  |
| Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all)                            | 1 / 14 (7.14%)<br>1 | 2 / 14 (14.29%)<br>2 |  |
| Nausea<br>subjects affected / exposed<br>occurrences (all)  | 0 / 14 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0  |  |
| Dyspepsia<br>subjects affected / exposed<br>occurrences (all)                                       | 0 / 14 (0.00%)<br>0 | 1 / 14 (7.14%)<br>1  |  |
| Constipation<br>subjects affected / exposed<br>occurrences (all)                                    | 0 / 14 (0.00%)<br>0 | 0 / 14 (0.00%)<br>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

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported