# Clinical trial results:
# A Phase 1/2, Open-Label, Dose-Escalation, Safety and Tolerability Study of INCAGN01949 in Subjects With Advanced or Metastatic Solid Tumors

## Summary

| | |
|---|---|
| EudraCT number | 2016-002079-93 |
| Trial protocol | GB |
| Global end of trial date | 26 March 2019 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 10 April 2020 |
| First version publication date | 10 April 2020 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | INCAGN 1949-101 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02923349 |
| WHO universal trial number (UTN) | - |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Incyte Biosciences International Sàrl |
| Sponsor organisation address | 1110 Morges, , Rue Docteur-Yersin , Switzerland, 10 |
| Public contact | call centre, Incyte Corporation, 1 8554633463, RA@INCYTE.COM |
| Scientific contact | call centre, Incyte Corporation, 1 8554633463, RA@INCYTE.COM |

Notes:

### Paediatric regulatory details

| | |
|---|---|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 26 March 2019 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 26 March 2019 |
| Was the trial ended prematurely? | Yes |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the safety, tolerability, and DLTs of INCAGN01949 and to define a MTD or PAD of INCAGN01949 in subjects with metastatic or advanced solid tumors.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles of Good Clinical Practice, according to the International Conference on Harmonisation Guidelines.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 31 October 2016 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Spain: 10 |
| Country: Number of subjects enrolled | United Kingdom: 17 |
| Country: Number of subjects enrolled | United States: 55 |
| Country: Number of subjects enrolled | Switzerland: 5 |
| Worldwide total number of subjects | 87 |
| EEA total number of subjects | 27 |

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 | 28 |

| | |
|---|---|
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

The study was conducted at 4 different sites in US, 1 site in Switzerland, Spain and 2 sites in the United Kingdom

### Pre-assignment

Screening details:

A total of 129 participants were screened for this study, of which 42 participants were screen failures and 87 participants were randomized to treatment.

### Period 1

| | |
|---|---|
| Period 1 title | Overall Trial (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Cohort1 - INCAGN1949 7mg |

Arm description: -

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | INCAGN01949 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

7mg of ICAGN 1949 is dosed as an IV infusion over 30minutes on Day 1 of each cycle

| | |
|---|---|
| **Arm title** | Cohort2 - INCAGN1949 20mg |

Arm description: -

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | INCAGN01949 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

20mg of ICAGN 1949 is dosed as an IV infusion over 30minutes on Day 1 of each cycle

| | |
|---|---|
| **Arm title** | Cohort3 - INCAGN1949 70mg |

Arm description: -

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | INCAGN01949 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

70mg of ICAGN 1949 is dosed as an IV infusion over 30minutes on Day 1 of each cycle

| **Arm title** | Cohort4 - INCAGN1949 200 mg |
|---|---|
| Arm description: - | |
| Arm type | Experimental |
| Investigational medicinal product name | INCAGN01949 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

200mg of ICAGN 1949 is dosed as an IV infusion over 30minutes on Day 1 of each cycle

| **Arm title** | Cohort5 - INCAGN1949 350mg |
|---|---|
| Arm description: - | |
| Arm type | Experimental |
| Investigational medicinal product name | INCAGN01949 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

350mg of ICAGN 1949 is dosed as an IV infusion over 30minutes on Day 1 of each cycle

| **Arm title** | Cohort6 - INCAGN1949 700mg |
|---|---|
| Arm description: - | |
| Arm type | Experimental |
| Investigational medicinal product name | INCAGN01949 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

700mg of ICAGN 1949 is dosed as an IV infusion over 30minutes on Day 1 of each cycle

| **Arm title** | Cohort7 - INCAGN1949 1400mg |
|---|---|
| Arm description: - | |
| Arm type | Experimental |
| Investigational medicinal product name | INCAGN01949 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

1400mg of ICAGN 1949 is dosed as an IV infusion over 30minutes on Day 1 of each cycle

| **Number of subjects in period 1** | Cohort1 - INCAGN1949 7mg | Cohort2 - INCAGN1949 20mg | Cohort3 - INCAGN1949 70mg |
|---|---|---|---|
| Started | 4 | 4 | 22 |
| Completed | 0 | 0 | 5 |
| Not completed | 4 | 4 | 17 |
| Physician decision | - | - | - |
| Death | 1 | - | 2 |
| Unknown | 1 | 2 | 4 |
| Lost to follow-up | - | - | 3 |
| Withdrawal by subject | 2 | 2 | 8 |

| **Number of subjects in period 1** | Cohort4 - INCAGN1949 200 mg | Cohort5 - INCAGN1949 350mg | Cohort6 - INCAGN1949 700mg |
|---|---|---|---|
| Started | 18 | 23 | 12 |
| Completed | 2 | 4 | 5 |
| Not completed | 16 | 19 | 7 |
| Physician decision | 1 | 1 | - |
| Death | 4 | 2 | 3 |
| Unknown | 1 | 3 | - |
| Lost to follow-up | - | 1 | 1 |
| Withdrawal by subject | 10 | 12 | 3 |

| **Number of subjects in period 1** | Cohort7 - INCAGN1949 1400mg |
|---|---|
| Started | 4 |
| Completed | 1 |
| Not completed | 3 |
| Physician decision | 2 |
| Death | - |
| Unknown | 1 |
| Lost to follow-up | - |
| Withdrawal by subject | - |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Cohort1 - INCAGN1949 7mg |
| Reporting group description: - | |
| Reporting group title | Cohort2 - INCAGN1949 20mg |
| Reporting group description: - | |
| Reporting group title | Cohort3 - INCAGN1949 70mg |
| Reporting group description: - | |
| Reporting group title | Cohort4 - INCAGN1949 200 mg |
| Reporting group description: - | |
| Reporting group title | Cohort5 - INCAGN1949 350mg |
| Reporting group description: - | |
| Reporting group title | Cohort6 - INCAGN1949 700mg |
| Reporting group description: - | |
| Reporting group title | Cohort7 - INCAGN1949 1400mg |
| Reporting group description: - | |

| Reporting group values | Cohort1 - INCAGN1949 7mg | Cohort2 - INCAGN1949 20mg | Cohort3 - INCAGN1949 70mg |
|---|---|---|---|
| Number of subjects | 4 | 4 | 22 |
| 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) | 3 | 2 | 14 |
| From 65-84 years | 1 | 2 | 8 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous<br>Units: years | | | |
| geometric mean | 54.3 | 63.8 | 56.8 |
| standard deviation | ± 16.24 | ± 12.63 | ± 14.27 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 2 | 3 | 14 |
| Male | 2 | 1 | 8 |
| Race<br>Units: Subjects | | | |
| White/Caucasian | 4 | 3 | 19 |
| Asian | 0 | 1 | 2 |
| Other | 0 | 0 | 1 |
| Black/African American | 0 | 0 | 0 |
| Ethnicity<br>Units: Subjects | | | |

| | | | |
|---|---|---|---|
| Hispanic or Latino | 0 | 0 | 1 |
| Not Hispanic or Latino | 4 | 4 | 19 |
| Not Reported | 0 | 0 | 1 |
| Other | 0 | 0 | 1 |

| **Reporting group values** | Cohort4 - INCAGN1949 200 mg | Cohort5 - INCAGN1949 350mg | Cohort6 - INCAGN1949 700mg |
|---|---|---|---|
| Number of subjects | 18 | 23 | 12 |
| 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) | 12 | 17 | 8 |
| From 65-84 years | 6 | 6 | 4 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous<br>Units: years | | | |
| geometric mean | 58.9 | 58.1 | 61.3 |
| standard deviation | ± 12.78 | ± 12.44 | ± 9.93 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 12 | 17 | 3 |
| Male | 6 | 6 | 9 |
| Race<br>Units: Subjects | | | |
| White/Caucasian | 17 | 23 | 9 |
| Asian | 0 | 0 | 1 |
| Other | 1 | 0 | 0 |
| Black/African American | 0 | 0 | 2 |
| Ethnicity<br>Units: Subjects | | | |
| Hispanic or Latino | 1 | 0 | 1 |
| Not Hispanic or Latino | 16 | 22 | 11 |
| Not Reported | 1 | 1 | 0 |
| Other | 0 | 0 | 0 |

| **Reporting group values** | Cohort7 - INCAGN1949 1400mg | Total | |
|---|---|---|---|
| Number of subjects | 4 | 87 | |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |

| | | | |
|---|---|---|---|
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 3 | 59 | |
| From 65-84 years | 1 | 28 | |
| 85 years and over | 0 | 0 | |
| Age continuous | | | |
| Units: years | | | |
| geometric mean | 52.8 | | |
| standard deviation | ± 24.50 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 2 | 53 | |
| Male | 2 | 34 | |
| Race | | | |
| Units: Subjects | | | |
| White/Caucasian | 4 | 79 | |
| Asian | 0 | 4 | |
| Other | 0 | 2 | |
| Black/African American | 0 | 2 | |
| Ethnicity | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 1 | 4 | |
| Not Hispanic or Latino | 2 | 78 | |
| Not Reported | 1 | 4 | |
| Other | 0 | 1 | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Cohort1 - INCAGN1949 7mg |
| Reporting group description: - | |
| Reporting group title | Cohort2 - INCAGN1949 20mg |
| Reporting group description: - | |
| Reporting group title | Cohort3 - INCAGN1949 70mg |
| Reporting group description: - | |
| Reporting group title | Cohort4 - INCAGN1949 200 mg |
| Reporting group description: - | |
| Reporting group title | Cohort5 - INCAGN1949 350mg |
| Reporting group description: - | |
| Reporting group title | Cohort6 - INCAGN1949 700mg |
| Reporting group description: - | |
| Reporting group title | Cohort7 - INCAGN1949 1400mg |
| Reporting group description: - | |

### Primary: To evaluate the safety, tolerability, and DLTs of INCAGN01949 and to define a MTD or PAD of INCAGN01949 in subjects with metastatic or advanced solid tumors

| | |
|---|---|
| End point title | To evaluate the safety, tolerability, and DLTs of INCAGN01949 and to define a MTD or PAD of INCAGN01949 in subjects with metastatic or advanced solid tumors[1] |

End point description:

To evaluate the safety, tolerability, and DLTs of INCAGN01949 and to define a MTD or PAD of INCAGN01949 in subjects with metastatic or advanced solid tumors

| | |
|---|---|
| End point type | Primary |

End point timeframe:

From screening through 60 days after end of treatment, up to 11 months

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: There is no hypothesis testing for this endpoint , descriptive analysis is provided.

| End point values | Cohort1 - INCAGN1949 7mg | Cohort2 - INCAGN1949 20mg | Cohort3 - INCAGN1949 70mg | Cohort4 - INCAGN1949 200 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4 | 4 | 22 | 18 |
| Units: participants | 4 | 4 | 21 | 17 |

| End point values | Cohort5 - INCAGN1949 350mg | Cohort6 - INCAGN1949 700mg | Cohort7 - INCAGN1949 1400mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 23 | 12 | 4 | |
| Units: participants | 22 | 11 | 4 | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: To evaluate the preliminary efficacy of INCAGN01949 by assessing the objective response rate per RECIST v1.1 and mRECIST v1.1.

| End point title | To evaluate the preliminary efficacy of INCAGN01949 by assessing the objective response rate per RECIST v1.1 and mRECIST v1.1. |
|---|---|

End point description:

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

End point timeframe:

Baseline and every 8 weeks, up to 11 months

| End point values | Cohort1 - INCAGN1949 7mg | Cohort2 - INCAGN1949 20mg | Cohort3 - INCAGN1949 70mg | Cohort4 - INCAGN1949 200 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4 | 4 | 22 | 18 |
| Units: participants | 0 | 0 | 0 | 0 |

| End point values | Cohort5 - INCAGN1949 350mg | Cohort6 - INCAGN1949 700mg | Cohort7 - INCAGN1949 1400mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 23 | 12 | 4 | |
| Units: participants | 0 | 1 | 0 | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: To evaluate the preliminary efficacy of INCAGN01949 by assessing the duration of response per RECIST v1.1 and mRECIST v1.1.

| End point title | To evaluate the preliminary efficacy of INCAGN01949 by assessing the duration of response per RECIST v1.1 and mRECIST v1.1. |
|---|---|

End point description:

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

End point timeframe:

Baseline and every 8 weeks , up to 11 months

| **End point values** | Cohort1 - INCAGN1949 7mg | Cohort2 - INCAGN1949 20mg | Cohort3 - INCAGN1949 70mg | Cohort4 - INCAGN1949 200 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0[2] | 0[3] | 0[4] | 0[5] |
| Units: days | | | | |
| median (full range (min-max)) | ( to ) | ( to ) | ( to ) | ( to ) |

Notes:

[2] - There were no responders in this group

[3] - There were no responders in this group

[4] - There were no responders in this group

[5] - There were no responders in this group

| **End point values** | Cohort5 - INCAGN1949 350mg | Cohort6 - INCAGN1949 700mg | Cohort7 - INCAGN1949 1400mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0[6] | 1 | 0[7] | |
| Units: days | | | | |
| median (full range (min-max)) | ( to ) | 192 (192 to 192) | ( to ) | |

Notes:

[6] - There were no responders in this group

[7] - There were no responders in this group

### Statistical analyses

No statistical analyses for this end point

## Secondary: To evaluate the preliminary efficacy of INCAGN01949 by assessing the progression free survival per RECIST v1.1 and mRECIST v1.1.

| End point title | To evaluate the preliminary efficacy of INCAGN01949 by assessing the progression free survival per RECIST v1.1 and mRECIST v1.1. |
|---|---|

End point description:

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

End point timeframe:

Baseline and every 8 weeks , up to 11 months

| End point values | Cohort1 - INCAGN1949 7mg | Cohort2 - INCAGN1949 20mg | Cohort3 - INCAGN1949 70mg | Cohort4 - INCAGN1949 200 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4 | 4 | 22 | 18 |
| Units: days | | | | |
| median (full range (min-max)) | 57 (55 to 59) | 47.5 (29 to 112) | 54 (23 to 216) | 56 (26 to 281) |

| End point values | Cohort5 - INCAGN1949 350mg | Cohort6 - INCAGN1949 700mg | Cohort7 - INCAGN1949 1400mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 23 | 12 | 4 | |
| Units: days | | | | |
| median (full range (min-max)) | 52 (1 to 166) | 125 (21 to 298) | 46.5 (42 to 53) | |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: To evaluate the preliminary efficacy of INCAGN01949 by assessing the duration of disease control per RECIST v1.1 and mRECIST v1.1.**

| End point title | To evaluate the preliminary efficacy of INCAGN01949 by assessing the duration of disease control per RECIST v1.1 and mRECIST v1.1. |
|---|---|

End point description:

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

End point timeframe:

Baseline and every 8 weeks , up to 11 months

| End point values | Cohort1 - INCAGN1949 7mg | Cohort2 - INCAGN1949 20mg | Cohort3 - INCAGN1949 70mg | Cohort4 - INCAGN1949 200 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1 | 1 | 8 | 7 |
| Units: days | | | | |
| median (full range (min-max)) | 0 (0 to 0) | 57 (57 to 57) | 64 (1 to 160) | 57 (1 to 225) |

| End point values | Cohort5 - INCAGN1949 | Cohort6 - INCAGN1949 | Cohort7 - INCAGN1949 | |
|---|---|---|---|---|

| | 350mg | 700mg | 1400mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 3 | 7 | 0[8] | |
| Units: days | | | | |
| median (full range (min-max)) | 0 (0 to 0) | 120 (1 to 249) | ( to ) | |

Notes:

[8] - All subjects had a response of progressive disease

### Statistical analyses

No statistical analyses for this end point

## Secondary: To evaluate the Tmax of INCAGN01949 in subjects with advanced or metastatic solid tumors

| End point title | To evaluate the Tmax of INCAGN01949 in subjects with advanced or metastatic solid tumors |
|---|---|

End point description:

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

End point timeframe:

cycle 1

| End point values | Cohort1 - INCAGN1949 7mg | Cohort2 - INCAGN1949 20mg | Cohort3 - INCAGN1949 70mg | Cohort4 - INCAGN1949 200 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4 | 4 | 21 | 17 |
| Units: hr | | | | |
| median (full range (min-max)) | 0.64 (0.6 to 4.4) | 2.53 (0.55 to 4.5) | 4.3 (0.50 to 25.2) | 0.63 (0.5 to 4.5) |

| End point values | Cohort5 - INCAGN1949 350mg | Cohort6 - INCAGN1949 700mg | Cohort7 - INCAGN1949 1400mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 21 | 7 | 4 | |
| Units: hr | | | | |
| median (full range (min-max)) | 0.6 (0.0 to 194) | 0.7 (0.53 to 4.2) | 0.73 (0.0 to 2.43) | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: To evaluate the Cmin of INCAGN01949 in subjects with advanced or

**metastatic solid tumors. Cmin is the minimum observed concentration of INCAGN1949**

| End point title | To evaluate the Cmin of INCAGN01949 in subjects with advanced or metastatic solid tumors. Cmin is the minimum observed concentration of INCAGN1949 |
|---|---|

End point description:

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

End point timeframe:

cycle 1

| **End point values** | Cohort1 - INCAGN1949 7mg | Cohort2 - INCAGN1949 20mg | Cohort3 - INCAGN1949 70mg | Cohort4 - INCAGN1949 200 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4 | 4 | 20 | 17 |
| Units: ng/ml | | | | |
| arithmetic mean (standard deviation) | 303 (± 202) | 1890 (± 1570) | 3620 (± 1550) | 8880 (± 4510) |

| **End point values** | Cohort5 - INCAGN1949 350mg | Cohort6 - INCAGN1949 700mg | Cohort7 - INCAGN1949 1400mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 18 | 7 | 3 | |
| Units: ng/ml | | | | |
| arithmetic mean (standard deviation) | 17000 (± 8040) | 41000 (± 13000) | 117000 (± 19300) | |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: To evaluate the Cmax of INCAGN01949 in subjects with advanced or metastatic solid tumors.**

| End point title | To evaluate the Cmax of INCAGN01949 in subjects with advanced or metastatic solid tumors. |
|---|---|

End point description:

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

End point timeframe:

cycle 1

| End point values | Cohort1 - INCAGN1949 7mg | Cohort2 - INCAGN1949 20mg | Cohort3 - INCAGN1949 70mg | Cohort4 - INCAGN1949 200 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4 | 4 | 21 | 17 |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | 1630 (± 735) | 5820 (± 324) | 22300 (± 32800) | 39200 (± 10300) |

| End point values | Cohort5 - INCAGN1949 350mg | Cohort6 - INCAGN1949 700mg | Cohort7 - INCAGN1949 1400mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 21 | 7 | 4 | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | 84900 (± 76700) | 207000 (± 45500) | 347000 (± 130000) | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: To evaluate the AUC0-t of INCAGN01949 in subjects with advanced or metastatic solid tumors

| End point title | To evaluate the AUC0-t of INCAGN01949 in subjects with advanced or metastatic solid tumors |
|---|---|

End point description:

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

End point timeframe:

cycle 1

| End point values | Cohort1 - INCAGN1949 7mg | Cohort2 - INCAGN1949 20mg | Cohort3 - INCAGN1949 70mg | Cohort4 - INCAGN1949 200 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4 | 4 | 21 | 17 |
| Units: ug*hr/mL | | | | |
| arithmetic mean (standard deviation) | 185 (± 81.7) | 904 (± 197) | 2370 (± 841) | 5400 (± 1820) |

| End point values | Cohort5 - INCAGN1949 350mg | Cohort6 - INCAGN1949 700mg | Cohort7 - INCAGN1949 1400mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 21 | 7 | 4 | |

| | | | | |
|---|---|---|---|---|
| Units: ug*hr/mL | | | | |
| arithmetic mean (standard deviation) | 10000 (± 5600) | 28300 (± 7720) | 61600 (± 9130) | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events:<br>From screening through 60 days after end of treatment, up to 11 months | |
| Adverse event reporting additional description:<br>AE additional description | |
| Assessment type | Systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 19 |

| Reporting groups | |
|---|---|
| Reporting group title | PART 1 Dose 1 (7 mg) |
| Reporting group description:<br>PART 1 Dose 1 (7 mg) | |
| Reporting group title | PART 1 Dose 2 (20 mg) |
| Reporting group description:<br>PART 1 Dose 2 (20 mg) | |
| Reporting group title | PART 1 Dose 3 (70 mg) |
| Reporting group description:<br>PART 1 Dose 3 (70 mg) | |
| Reporting group title | PART 1 Dose 4 (200 mg) |
| Reporting group description:<br>PART 1 Dose 4 (200 mg) | |
| Reporting group title | PART 1 Dose 5 (350 mg) |
| Reporting group description:<br>PART 1 Dose 5 (350 mg) | |
| Reporting group title | PART 1 Dose 6 (700 mg) |
| Reporting group description:<br>PART 1 Dose 6 (700 mg) | |
| Reporting group title | PART 1 Dose 7 (1400 mg) |
| Reporting group description:<br>PART 1 Dose 7 (1400 mg) | |

| Serious adverse events | PART 1 Dose 1 (7 mg) | PART 1 Dose 2 (20 mg) | PART 1 Dose 3 (70 mg) |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 4 (25.00%) | 8 / 22 (36.36%) |
| number of deaths (all causes) | 1 | 0 | 2 |
| number of deaths resulting from adverse events | 1 | 0 | 1 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Cancer pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 22 (4.55%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malignant neoplasm progression | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 1 / 22 (4.55%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Tumour pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 22 (4.55%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Embolism | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 22 (4.55%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oedema | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 22 (4.55%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| Pyrexia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Spinal fracture | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Ventricular tachycardia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Ataxia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cauda equina syndrome | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal cord compression | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 22 (4.55%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 22 (4.55%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ascites | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal obstruction | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 22 (4.55%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nausea | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 22 (4.55%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 22 (4.55%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Jaundice | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Jaundice cholestatic | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hydronephrosis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary incontinence | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| Back pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 22 (4.55%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower respiratory tract infection bacterial | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myelitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia streptococcal | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| **Serious adverse events** | PART 1 Dose 4 (200 mg) | PART 1 Dose 5 (350 mg) | PART 1 Dose 6 (700 mg) |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 9 / 18 (50.00%) | 9 / 23 (39.13%) | 5 / 12 (41.67%) |

| | | | |
|---|---|---|---|
| number of deaths (all causes) | 4 | 2 | 3 |
| number of deaths resulting from adverse events | 1 | 2 | 3 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Cancer pain | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malignant neoplasm progression | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 2 / 23 (8.70%) | 3 / 12 (25.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 3 |
| Tumour pain | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Embolism | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 23 (4.35%) | 1 / 12 (8.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oedema | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 1 / 12 (8.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 23 (4.35%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 23 (4.35%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Spinal fracture | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Ventricular tachycardia | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Ataxia | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 23 (4.35%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cauda equina syndrome | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 1 / 12 (8.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal cord compression | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 23 (4.35%) | 2 / 12 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 1 / 12 (8.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ascites | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colitis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 23 (4.35%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 23 (4.35%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal obstruction | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nausea | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Small intestinal obstruction | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 18 (11.11%) | 2 / 23 (8.70%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 23 (4.35%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Jaundice | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Jaundice cholestatic | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 23 (4.35%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 23 (4.35%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hydronephrosis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 23 (4.35%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary incontinence | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 23 (4.35%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract pain | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 1 / 12 (8.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue | | | |

| | | | |
|---|---|---|---|
| disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 23 (4.35%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Back pain | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 23 (4.35%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower respiratory tract infection bacterial | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myelitis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 23 (4.35%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia streptococcal | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 23 (4.35%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| **Serious adverse events** | PART 1 Dose 7 (1400 mg) | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Cancer pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Malignant neoplasm progression | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tumour pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Embolism | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| General physical health deterioration | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Oedema | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Investigations | | | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Spinal fracture | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Ventricular tachycardia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Ataxia | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 0 / 4 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cauda equina syndrome | | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Spinal cord compression | | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastrointestinal disorders | | | | |
| Abdominal pain | | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Abdominal pain upper | | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ascites | | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Colitis | | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Diarrhoea | | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Intestinal obstruction | | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 0 / 4 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Nausea | | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Small intestinal obstruction | | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Vomiting | | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hepatobiliary disorders | | | | |
| Jaundice | | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Jaundice cholestatic | | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Renal and urinary disorders | | | | |
| Acute kidney injury | | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hydronephrosis | | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Urinary incontinence | | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 0 / 4 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Urinary tract pain | | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Musculoskeletal and connective tissue disorders | | | | |
| Arthralgia | | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Back pain | | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Infections and infestations | | | | |
| Appendicitis | | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lower respiratory tract infection | | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lower respiratory tract infection bacterial | | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Myelitis | | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |

| | | | |
|---|---|---|---|
| Pneumonia streptococcal | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 5 %

| **Non-serious adverse events** | PART 1 Dose 1 (7 mg) | PART 1 Dose 2 (20 mg) | PART 1 Dose 3 (70 mg) |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 4 / 4 (100.00%) | 4 / 4 (100.00%) | 21 / 22 (95.45%) |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypertension | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Thrombophlebitis superficial | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 2 / 22 (9.09%) |
| occurrences (all) | 0 | 0 | 2 |
| Chills | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 1 / 22 (4.55%) |
| occurrences (all) | 0 | 1 | 3 |
| Early satiety | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fatigue | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 4 (50.00%) | 2 / 4 (50.00%) | 6 / 22 (27.27%) |
| occurrences (all) | 2 | 2 | 8 |
| Gait disturbance | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 1 / 22 (4.55%) |
| occurrences (all) | 0 | 1 | 1 |
| Nodule | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 22 (4.55%) |
| occurrences (all) | 0 | 0 | 1 |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 22 (4.55%) |
| occurrences (all) | 0 | 0 | 1 |
| Peripheral swelling | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 2 / 22 (9.09%) |
| occurrences (all) | 0 | 0 | 2 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 4 (50.00%) | 1 / 22 (4.55%) |
| occurrences (all) | 0 | 4 | 1 |
| Immune system disorders | | | |
| Seasonal allergy | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Reproductive system and breast disorders | | | |
| Vaginal haemorrhage | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 4 / 22 (18.18%) |
| occurrences (all) | 0 | 1 | 5 |
| Dyspnoea | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 4 (25.00%) | 2 / 4 (50.00%) | 2 / 22 (9.09%) |
| occurrences (all) | 1 | 2 | 2 |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 22 (4.55%) |
| occurrences (all) | 0 | 0 | 1 |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haemothorax | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasal congestion | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Productive cough | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinitis allergic | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Upper-airway cough syndrome | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 22 (4.55%) |
| occurrences (all) | 0 | 0 | 1 |
| Wheezing | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 1 / 22 (4.55%) |
| occurrences (all) | 0 | 1 | 1 |
| Hallucination | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Investigations | | | |
| Amylase increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood lactate dehydrogenase increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood urea increased | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| C-reactive protein increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Electrocardiogram QT prolonged | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lipase increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lymph node palpable | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 2 / 22 (9.09%) |
| occurrences (all) | 0 | 0 | 2 |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Weight decreased | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | 1 / 4 (25.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Weight increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 22 (4.55%) |
| occurrences (all) | 0 | 0 | 1 |
| Joint injury | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Meniscus injury | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rib fracture | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Spinal fracture | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Tooth fracture | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Sinus bradycardia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Ventricular tachycardia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nervous system disorders | | | |
| Ataxia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 22 (4.55%) |
| occurrences (all) | 0 | 0 | 1 |
| Dysgeusia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 1 / 22 (4.55%) |
| occurrences (all) | 1 | 0 | 1 |
| Hypoaesthesia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 2 / 22 (9.09%) |
| occurrences (all) | 0 | 0 | 2 |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 22 (4.55%) |
| occurrences (all) | 0 | 0 | 1 |
| Spinal cord compression | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Tremor | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood and lymphatic system disorders | | | |

| | | | |
|---|---|---|---|
| Anaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 4 / 22 (18.18%) |
| occurrences (all) | 0 | 0 | 5 |
| Ear and labyrinth disorders | | | |
| Tinnitus | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 1 / 22 (4.55%) |
| occurrences (all) | 0 | 1 | 1 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Ascites | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Constipation | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 4 (25.00%) | 4 / 22 (18.18%) |
| occurrences (all) | 1 | 1 | 4 |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 3 / 22 (13.64%) |
| occurrences (all) | 2 | 0 | 3 |
| Dry mouth | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Epigastric discomfort | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 22 (4.55%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 2 / 22 (9.09%) |
| occurrences (all) | 0 | 0 | 2 |
| Nausea | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 3 / 22 (13.64%) |
| occurrences (all) | 0 | 1 | 5 |
| Vomiting | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 5 / 22 (22.73%) |
| occurrences (all) | 1 | 0 | 5 |
| Hepatobiliary disorders | | | |
| Cholangitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Erythema | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 1 / 22 (4.55%) |
| occurrences (all) | 1 | 0 | 1 |
| Hyperhidrosis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 22 (4.55%) |
| occurrences (all) | 0 | 0 | 1 |
| Night sweats | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 2 / 22 (9.09%) |
| occurrences (all) | 0 | 0 | 2 |
| Pruritus | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 2 / 22 (9.09%) |
| occurrences (all) | 0 | 0 | 2 |
| Pruritus generalised | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 2 / 22 (9.09%) |
| occurrences (all) | 0 | 0 | 2 |
| Rash maculo-papular | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tumour pruritus | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal and urinary disorders | | | |
| Haematuria | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 22 (4.55%) |
| occurrences (all) | 0 | 0 | 1 |
| Haemorrhage urinary tract | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nocturia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary incontinence | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary retention | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary tract obstruction | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Endocrine disorders | | | |
| Hypothyroidism | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 3 / 4 (75.00%) | 3 / 22 (13.64%) |
| occurrences (all) | 0 | 4 | 3 |
| Back pain | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 3 / 22 (13.64%) |
| occurrences (all) | 1 | 0 | 3 |
| Bone pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 22 (4.55%) |
| occurrences (all) | 0 | 0 | 1 |
| Fistula | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Flank pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Groin pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 1 / 22 (4.55%) |
| occurrences (all) | 1 | 0 | 1 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 2 / 4 (50.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 22 (4.55%) |
| occurrences (all) | 0 | 0 | 1 |
| Infections and infestations | | | |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infectious pleural effusion | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Pneumonia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 22 (4.55%) |
| occurrences (all) | 0 | 0 | 1 |
| Rash pustular | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 2 / 22 (9.09%) |
| occurrences (all) | 0 | 0 | 2 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 1 / 22 (4.55%) |
| occurrences (all) | 0 | 1 | 1 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wound infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 3 / 4 (75.00%) | 6 / 22 (27.27%) |
| occurrences (all) | 1 | 3 | 6 |
| Dehydration | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 1 / 22 (4.55%) |
| occurrences (all) | 0 | 2 | 2 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| **Non-serious adverse events** | PART 1 Dose 4 (200 mg) | PART 1 Dose 5 (350 mg) | PART 1 Dose 6 (700 mg) |
|---|---|---|---|

| | | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events<br>subjects affected / exposed | 17 / 18 (94.44%) | 22 / 23 (95.65%) | 10 / 12 (83.33%) |
| Vascular disorders | | | |
| Deep vein thrombosis<br>subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypertension<br>subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Thrombophlebitis superficial<br>subjects affected / exposed | 1 / 18 (5.56%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Asthenia<br>subjects affected / exposed | 1 / 18 (5.56%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Chills<br>subjects affected / exposed | 0 / 18 (0.00%) | 2 / 23 (8.70%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Early satiety<br>subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fatigue<br>subjects affected / exposed | 7 / 18 (38.89%) | 8 / 23 (34.78%) | 4 / 12 (33.33%) |
| occurrences (all) | 7 | 8 | 4 |
| Gait disturbance<br>subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Influenza like illness<br>subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nodule<br>subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Non-cardiac chest pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 23 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 1 | 0 | 1 |
| Oedema peripheral | | | |
| subjects affected / exposed | 3 / 18 (16.67%) | 0 / 23 (0.00%) | 2 / 12 (16.67%) |
| occurrences (all) | 3 | 0 | 2 |
| Peripheral swelling | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 2 / 23 (8.70%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 2 | 1 |
| Immune system disorders | | | |
| Seasonal allergy | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 2 / 23 (8.70%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 2 | 1 |
| Reproductive system and breast disorders | | | |
| Vaginal haemorrhage | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 5 / 18 (27.78%) | 1 / 23 (4.35%) | 1 / 12 (8.33%) |
| occurrences (all) | 7 | 1 | 1 |
| Dyspnoea | | | |
| subjects affected / exposed | 3 / 18 (16.67%) | 3 / 23 (13.04%) | 2 / 12 (16.67%) |
| occurrences (all) | 3 | 3 | 2 |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 23 (0.00%) | 2 / 12 (16.67%) |
| occurrences (all) | 1 | 0 | 2 |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Haemothorax | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hypoxia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Nasal congestion | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 23 (4.35%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 2 / 23 (8.70%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Productive cough | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Rhinitis allergic | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Upper-airway cough syndrome | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Wheezing | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 23 (4.35%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hallucination | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Investigations | | | |
| Amylase increased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 18 (11.11%) | 0 / 23 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 2 | 0 | 3 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 23 (4.35%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 1 | 1 |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 2 / 12 (16.67%) |
| occurrences (all) | 0 | 0 | 2 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 2 / 12 (16.67%) |
| occurrences (all) | 0 | 0 | 2 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 2 / 23 (8.70%) | 1 / 12 (8.33%) |
| occurrences (all) | 1 | 2 | 1 |
| Blood lactate dehydrogenase increased | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood urea increased | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| C-reactive protein increased | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lipase increased | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 23 (4.35%) | 1 / 12 (8.33%) |
| occurrences (all) | 1 | 1 | 2 |
| Lymph node palpable | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lymphocyte count decreased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 23 (4.35%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Weight decreased | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 2 / 23 (8.70%) | 0 / 12 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Weight increased | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 23 (4.35%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Joint injury | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Meniscus injury | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rib fracture | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Spinal fracture | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tooth fracture | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Cardiac disorders | | | |
| Sinus bradycardia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ventricular tachycardia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nervous system disorders | | | |
| Ataxia | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dizziness | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 23 (4.35%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Dysgeusia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypoaesthesia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 23 (4.35%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Spinal cord compression | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tremor | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 1 / 23 (4.35%) | 2 / 12 (16.67%) |
| occurrences (all) | 2 | 1 | 2 |
| Ear and labyrinth disorders | | | |
| Tinnitus | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal distension | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Abdominal pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 18 (16.67%) | 4 / 23 (17.39%) | 0 / 12 (0.00%) |
| occurrences (all) | 3 | 4 | 0 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ascites | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 23 (4.35%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Constipation | | | |
| subjects affected / exposed | 6 / 18 (33.33%) | 4 / 23 (17.39%) | 1 / 12 (8.33%) |
| occurrences (all) | 6 | 4 | 1 |
| Diarrhoea | | | |
| subjects affected / exposed | 4 / 18 (22.22%) | 3 / 23 (13.04%) | 1 / 12 (8.33%) |
| occurrences (all) | 7 | 3 | 1 |
| Dry mouth | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysphagia | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Epigastric discomfort | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 3 / 18 (16.67%) | 6 / 23 (26.09%) | 0 / 12 (0.00%) |
| occurrences (all) | 3 | 7 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 3 / 18 (16.67%) | 4 / 23 (17.39%) | 0 / 12 (0.00%) |
| occurrences (all) | 3 | 6 | 0 |
| Hepatobiliary disorders | | | |

| | | | |
|---|---|---|---|
| Cholangitis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Erythema | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperhidrosis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Night sweats | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pruritus | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 2 / 23 (8.70%) | 0 / 12 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Pruritus generalised | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Rash | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 1 / 23 (4.35%) | 0 / 12 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Rash maculo-papular | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Tumour pruritus | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Renal and urinary disorders | | | |
| Haematuria | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 23 (4.35%) | 1 / 12 (8.33%) |
| occurrences (all) | 1 | 1 | 1 |
| Haemorrhage urinary tract | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nocturia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary incontinence | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 23 (4.35%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Urinary retention | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Urinary tract obstruction | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Endocrine disorders | | | |
| Hypothyroidism | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 1 / 23 (4.35%) | 0 / 12 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 23 (4.35%) | 1 / 12 (8.33%) |
| occurrences (all) | 1 | 1 | 1 |
| Back pain | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 5 / 23 (21.74%) | 1 / 12 (8.33%) |
| occurrences (all) | 3 | 5 | 1 |
| Bone pain | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Fistula | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Flank pain | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Groin pain | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Musculoskeletal chest pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Myalgia | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 23 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 1 | 0 | 2 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Infections and infestations | | | |
| Cellulitis | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Infectious pleural effusion | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rash pustular | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin infection | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Wound infection | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 4 / 18 (22.22%) | 7 / 23 (30.43%) | 3 / 12 (25.00%) |
| occurrences (all) | 4 | 8 | 4 |
| Dehydration | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 23 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 23 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 1 | 0 | 2 |
| Hypokalaemia | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 23 (4.35%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |

| **Non-serious adverse events** | PART 1 Dose 7 (1400 mg) | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 4 / 4 (100.00%) | | |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Thrombophlebitis superficial | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| General disorders and administration | | | |

| | | | |
|---|---|---|---|
| site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Chills | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Early satiety | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Fatigue | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | | |
| occurrences (all) | 2 | | |
| Gait disturbance | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nodule | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Oedema peripheral | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Peripheral swelling | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Immune system disorders | | | |

| | | | |
|---|---|---|---|
| Seasonal allergy | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Reproductive system and breast disorders | | | |
| Vaginal haemorrhage | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | | |
| occurrences (all) | 2 | | |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | | |
| occurrences (all) | 3 | | |
| Epistaxis | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Haemothorax | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nasal congestion | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pleural effusion | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Productive cough | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rhinitis allergic | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Upper-airway cough syndrome | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Wheezing | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hallucination | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Investigations | | | |
| Amylase increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blood creatinine increased | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 0 / 4 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Blood lactate dehydrogenase increased | | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Blood urea increased | | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| C-reactive protein increased | | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Electrocardiogram QT prolonged | | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Lipase increased | | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Lymph node palpable | | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | | |
| occurrences (all) | 1 | | | |
| Lymphocyte count decreased | | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | | |
| occurrences (all) | 1 | | | |
| Platelet count decreased | | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Weight decreased | | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Weight increased | | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | | |
| occurrences (all) | 1 | | | |
| Injury, poisoning and procedural complications | | | | |

| | | | |
|---|---|---|---|
| Fall | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Joint injury | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Meniscus injury | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rib fracture | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Spinal fracture | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Tooth fracture | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Cardiac disorders | | | |
| Sinus bradycardia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Ventricular tachycardia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nervous system disorders | | | |
| Ataxia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dizziness | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dysgeusia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypoaesthesia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Spinal cord compression | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Tremor | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | | |
| occurrences (all) | 3 | | |
| Ear and labyrinth disorders | | | |
| Tinnitus | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 2 | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Ascites | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Constipation | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Diarrhoea | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dry mouth | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dyspepsia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Epigastric discomfort | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nausea | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hepatobiliary disorders | | | |
| Cholangitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Erythema | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hyperhidrosis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Night sweats | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pruritus | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pruritus generalised | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rash | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Rash maculo-papular | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Tumour pruritus | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Renal and urinary disorders | | | |
| Haematuria | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Haemorrhage urinary tract | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Nocturia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Urinary incontinence | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Urinary retention | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Urinary tract obstruction | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|---|---|---|---|
| Endocrine disorders | | | |
| Hypothyroidism | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Bone pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Fistula | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Flank pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Groin pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Myalgia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Infections and infestations | | | |

| | | | |
|---|---|---|---|
| Cellulitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Infectious pleural effusion | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rash pustular | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Skin infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | | |
| occurrences (all) | 1 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Wound infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | | |
| occurrences (all) | 0 | | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported