



## Clinical trial results:

### Phase 1/2 Open-Label Study of the Safety, Pharmacokinetics, and Preliminary Activity of ASTX295 in Subjects with Wild-Type TP53 Advanced Solid Tumors

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2021-005033-16 |
| Trial protocol           | DE FR ES IT    |
| Global end of trial date | 15 August 2024 |

#### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 05 June 2025 |
| First version publication date | 05 June 2025 |

#### Trial information

##### Trial identification

|                       |            |
|-----------------------|------------|
| Sponsor protocol code | ASTX295-01 |
|-----------------------|------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03975387 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |                                                                                                    |
|------------------------------|----------------------------------------------------------------------------------------------------|
| Sponsor organisation name    | Taiho Oncology, Inc.                                                                               |
| Sponsor organisation address | 101 Carnegie Center, Suite 101, Princeton, NJ, United States, 08540                                |
| Public contact               | Senior Study Manager, Taiho Oncology, Inc., , 1 844-878-2446, medicalinformation@taihooncology.com |
| Scientific contact           | Senior Study Manager, Taiho Oncology, Inc., +1 844-878-2446, medicalinformation@taihooncology.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                       | 15 August 2024 |
| Is this the analysis of the primary completion data? | No             |

|                                  |                |
|----------------------------------|----------------|
| Global end of trial reached?     | Yes            |
| Global end of trial date         | 15 August 2024 |
| Was the trial ended prematurely? | Yes            |

Notes:

## General information about the trial

Main objective of the trial:

The main objective of this study was to assess safety and tolerability of ASTX295 including determination of maximum tolerated dose (MTD), and/or recommended dose for expansion (RDE) in Phase 1a (dose escalation) part of the study, and to determine the recommended Phase 2 dose (RP2D) and regimen of ASTX295 in Phase 1b (dose expansion) part of the study.

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form (ICF).

Background therapy: -

Evidence for comparator: -

|                                                           |              |
|-----------------------------------------------------------|--------------|
| Actual start date of recruitment                          | 05 July 2019 |
| Long term follow-up planned                               | No           |
| Independent data monitoring committee (IDMC) involvement? | Yes          |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | United States: 106 |
| Worldwide total number of subjects   | 106                |
| EEA total number of subjects         | 0                  |

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)                      | 67 |
| From 65 to 84 years                       | 38 |
| 85 years and over                         | 1  |

## Subject disposition

### Recruitment

Recruitment details:

Subjects were enrolled at 11 sites in the United States from 05 July 2019 to 15 August 2024.

### Pre-assignment

Screening details:

A total of 106 subjects with wild-type TP53 advanced solid tumors were enrolled to receive ASTX295 in Phase 1 which consisted of 2 parts: Phase 1a (dose escalation) and Phase 1b (dose expansion). Phase 2 part of the study was terminated by the sponsor's strategic decision.

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Overall Study (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Non-randomised - controlled    |
| Blinding used                | Not blinded                    |

### Arms

|                              |                                     |
|------------------------------|-------------------------------------|
| Are arms mutually exclusive? | Yes                                 |
| <b>Arm title</b>             | Dose Escalation: Phase 1a: Cohort 1 |

Arm description:

Subjects received ASTX295 at starting dose of 15 milligrams (mg), orally, administered once daily (QD) in each 28-day cycle under fasted condition, up to a maximum of 1.8 months.

|                                        |              |
|----------------------------------------|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | ASTX295      |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

ASTX295 at an oral dose of 15 mg, administered QD in each 28-day cycle up to a maximum of 1.8 months.

|                  |                                     |
|------------------|-------------------------------------|
| <b>Arm title</b> | Dose Escalation: Phase 1a: Cohort 2 |
|------------------|-------------------------------------|

Arm description:

Subjects received ASTX295 at an oral dose of 45 mg, administered QD in each 28-day cycle under fasted condition, up to a maximum of 17.4 months.

|                                        |              |
|----------------------------------------|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | ASTX295      |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

ASTX295 at an oral dose of 45 mg, administered QD in each 28-day cycle up to a maximum of 17.4 months.

|                  |                                     |
|------------------|-------------------------------------|
| <b>Arm title</b> | Dose Escalation: Phase 1a: Cohort 3 |
|------------------|-------------------------------------|

Arm description:

Subjects received ASTX295 at an oral dose of 120 mg, administered QD in each 28-day cycle under fasted condition, up to a maximum of 1.8 months.

|          |              |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

|                                                                                                                                                                       |                                     |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|
| Investigational medicinal product name                                                                                                                                | ASTX295                             |
| Investigational medicinal product code                                                                                                                                |                                     |
| Other name                                                                                                                                                            |                                     |
| Pharmaceutical forms                                                                                                                                                  | Tablet                              |
| Routes of administration                                                                                                                                              | Oral use                            |
| Dosage and administration details:<br>ASTX295 at an oral dose of 120 mg, administered QD in each 28-day cycle up to a maximum of 1.8 months.                          |                                     |
| <b>Arm title</b>                                                                                                                                                      | Dose Escalation: Phase 1a: Cohort 4 |
| Arm description:<br>Subjects received ASTX295 at an oral dose of 240 mg, administered QD in each 28-day cycle under fasted condition, up to a maximum of 6.4 months.  |                                     |
| Arm type                                                                                                                                                              | Experimental                        |
| Investigational medicinal product name                                                                                                                                | ASTX295                             |
| Investigational medicinal product code                                                                                                                                |                                     |
| Other name                                                                                                                                                            |                                     |
| Pharmaceutical forms                                                                                                                                                  | Tablet                              |
| Routes of administration                                                                                                                                              | Oral use                            |
| Dosage and administration details:<br>ASTX295 at an oral dose of 240 mg, administered QD in each 28-day cycle up to a maximum of 6.4 months.                          |                                     |
| <b>Arm title</b>                                                                                                                                                      | Dose Escalation: Phase 1a: Cohort 5 |
| Arm description:<br>Subjects received ASTX295 at an oral dose of 420 mg, administered QD in each 28-day cycle under fasted condition, up to a maximum of 14.7 months. |                                     |
| Arm type                                                                                                                                                              | Experimental                        |
| Investigational medicinal product name                                                                                                                                | ASTX295                             |
| Investigational medicinal product code                                                                                                                                |                                     |
| Other name                                                                                                                                                            |                                     |
| Pharmaceutical forms                                                                                                                                                  | Tablet                              |
| Routes of administration                                                                                                                                              | Oral use                            |
| Dosage and administration details:<br>ASTX295 at an oral dose of 240 mg, administered QD in each 28-day cycle up to a maximum of 14.7 months.                         |                                     |
| <b>Arm title</b>                                                                                                                                                      | Dose Escalation: Phase 1a: Cohort 6 |
| Arm description:<br>Subjects received ASTX295 at an oral dose of 520 mg, administered QD in each 28-day cycle under fasted condition, up to a maximum of 42.4 months. |                                     |
| Arm type                                                                                                                                                              | Experimental                        |
| Investigational medicinal product name                                                                                                                                | ASTX295                             |
| Investigational medicinal product code                                                                                                                                |                                     |
| Other name                                                                                                                                                            |                                     |
| Pharmaceutical forms                                                                                                                                                  | Tablet                              |
| Routes of administration                                                                                                                                              | Oral use                            |
| Dosage and administration details:<br>ASTX295 at an oral dose of 520 mg, administered QD in each 28-day cycle up to a maximum of 42.4 months.                         |                                     |
| <b>Arm title</b>                                                                                                                                                      | Dose Escalation: Phase 1a: Cohort 7 |
| Arm description:<br>Subjects received ASTX295 at an oral dose of 415 mg, administered QD in each 28-day cycle under fed state, up to a maximum of 22.5 months.        |                                     |
| Arm type                                                                                                                                                              | Experimental                        |

|                                                                                                                                                                                             |                                      |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------|
| Investigational medicinal product name                                                                                                                                                      | ASTX295                              |
| Investigational medicinal product code                                                                                                                                                      |                                      |
| Other name                                                                                                                                                                                  |                                      |
| Pharmaceutical forms                                                                                                                                                                        | Tablet                               |
| Routes of administration                                                                                                                                                                    | Oral use                             |
| Dosage and administration details:<br>ASTX295 at an oral dose of 415 mg, administered QD in each 28-day cycle up to a maximum of 22.5 months.                                               |                                      |
| <b>Arm title</b>                                                                                                                                                                            | Dose Escalation: Phase 1a: Cohort 8  |
| Arm description:<br>Subjects received ASTX295 at an oral dose of 200 mg, administered twice daily (BID) in each 28-day cycle under fasted condition, up to a maximum of 17.4 months.        |                                      |
| Arm type                                                                                                                                                                                    | Experimental                         |
| Investigational medicinal product name                                                                                                                                                      | ASTX295                              |
| Investigational medicinal product code                                                                                                                                                      |                                      |
| Other name                                                                                                                                                                                  |                                      |
| Pharmaceutical forms                                                                                                                                                                        | Tablet                               |
| Routes of administration                                                                                                                                                                    | Oral use                             |
| Dosage and administration details:<br>ASTX295 at an oral dose of 200 mg, administered BID in each 28-day cycle up to a maximum of 17.4 months.                                              |                                      |
| <b>Arm title</b>                                                                                                                                                                            | Dose Escalation: Phase 1a: Cohort 9  |
| Arm description:<br>Subjects received ASTX295 at an oral dose of 320 mg, administered BID in each 28-day cycle under fasted condition, up to a maximum of 27.5 months.                      |                                      |
| Arm type                                                                                                                                                                                    | Experimental                         |
| Investigational medicinal product name                                                                                                                                                      | ASTX295                              |
| Investigational medicinal product code                                                                                                                                                      |                                      |
| Other name                                                                                                                                                                                  |                                      |
| Pharmaceutical forms                                                                                                                                                                        | Tablet                               |
| Routes of administration                                                                                                                                                                    | Oral use                             |
| Dosage and administration details:<br>ASTX295 at an oral dose of 320 mg, administered BID in each 28-day cycle up to a maximum of 27.5 months.                                              |                                      |
| <b>Arm title</b>                                                                                                                                                                            | Dose Escalation: Phase 1a: Cohort 10 |
| Arm description:<br>Subjects received ASTX295 at an oral dose of 520 mg (5 days on, 2 days off), administered QD in each 28-day cycle, with or without food, up to a maximum of 12 months.  |                                      |
| Arm type                                                                                                                                                                                    | Experimental                         |
| Investigational medicinal product name                                                                                                                                                      | ASTX295                              |
| Investigational medicinal product code                                                                                                                                                      |                                      |
| Other name                                                                                                                                                                                  |                                      |
| Pharmaceutical forms                                                                                                                                                                        | Tablet                               |
| Routes of administration                                                                                                                                                                    | Oral use                             |
| Dosage and administration details:<br>ASTX295 at an oral dose of 520 mg, administered QD, in each 28-day cycle up to a maximum of 12 months.                                                |                                      |
| <b>Arm title</b>                                                                                                                                                                            | Dose Escalation: Phase 1a: Cohort 11 |
| Arm description:<br>Subjects received ASTX295 at an oral dose of 520 mg (3 days on, 4 days off), administered QD in each 28-day cycle, with or without food, up to a maximum of 1.8 months. |                                      |
| Arm type                                                                                                                                                                                    | Experimental                         |

|                                                                                                                                                                                               |                                      |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------|
| Investigational medicinal product name                                                                                                                                                        | ASTX295                              |
| Investigational medicinal product code                                                                                                                                                        |                                      |
| Other name                                                                                                                                                                                    |                                      |
| Pharmaceutical forms                                                                                                                                                                          | Tablet                               |
| Routes of administration                                                                                                                                                                      | Oral use                             |
| Dosage and administration details:<br>ASTX295 at an oral dose of 520 mg, administered QD in each 28-day cycle up to a maximum of 1.8 months.                                                  |                                      |
| <b>Arm title</b>                                                                                                                                                                              | Dose Escalation: Phase 1a: Cohort 12 |
| Arm description:<br>Subjects received ASTX295 at an oral dose of 660 mg, administered QD, twice a week, in each 28-day cycle, with or without food, up to a maximum of 11.7 months.           |                                      |
| Arm type                                                                                                                                                                                      | Experimental                         |
| Investigational medicinal product name                                                                                                                                                        | ASTX295                              |
| Investigational medicinal product code                                                                                                                                                        |                                      |
| Other name                                                                                                                                                                                    |                                      |
| Pharmaceutical forms                                                                                                                                                                          | Tablet                               |
| Routes of administration                                                                                                                                                                      | Oral use                             |
| Dosage and administration details:<br>ASTX295 at an oral dose of 660 mg, administered QD, twice a week, in each 28-day cycle up to a maximum of 11.7 months.                                  |                                      |
| <b>Arm title</b>                                                                                                                                                                              | Dose Escalation: Phase 1a: Cohort 13 |
| Arm description:<br>Subjects received ASTX295 at an oral dose of 660 mg (3 days on, 4 days off), administered QD, in each 28-day cycle, with or without food, up to a maximum of 18.5 months. |                                      |
| Arm type                                                                                                                                                                                      | Experimental                         |
| Investigational medicinal product name                                                                                                                                                        | ASTX295                              |
| Investigational medicinal product code                                                                                                                                                        |                                      |
| Other name                                                                                                                                                                                    |                                      |
| Pharmaceutical forms                                                                                                                                                                          | Tablet                               |
| Routes of administration                                                                                                                                                                      | Oral use                             |
| Dosage and administration details:<br>ASTX295 at an oral dose of 660 mg, administered QD in each 28-day cycle up to a maximum of 18.5 months.                                                 |                                      |
| <b>Arm title</b>                                                                                                                                                                              | Dose Escalation: Phase 1a: Cohort 14 |
| Arm description:<br>Subjects received ASTX295 at an oral dose of 800 mg, administered QD, twice a week, in each 28-day cycle, with or without food, up to a maximum of 6 months.              |                                      |
| Arm type                                                                                                                                                                                      | Experimental                         |
| Investigational medicinal product name                                                                                                                                                        | ASTX295                              |
| Investigational medicinal product code                                                                                                                                                        |                                      |
| Other name                                                                                                                                                                                    |                                      |
| Pharmaceutical forms                                                                                                                                                                          | Tablet                               |
| Routes of administration                                                                                                                                                                      | Oral use                             |
| Dosage and administration details:<br>ASTX295 at an oral dose of 800 mg, administered QD, twice a week, in each 28-day cycle up to a maximum of 6 months.                                     |                                      |
| <b>Arm title</b>                                                                                                                                                                              | Dose Expansion: Phase 1b: Cohort 1   |
| Arm description:<br>Subjects received ASTX295 at an oral dose of 400 mg, administered daily, in each 28-day cycle, with or without food, up to a maximum of 14.7 months.                      |                                      |
| Arm type                                                                                                                                                                                      | Experimental                         |

|                                        |          |
|----------------------------------------|----------|
| Investigational medicinal product name | ASTX295  |
| Investigational medicinal product code |          |
| Other name                             |          |
| Pharmaceutical forms                   | Tablet   |
| Routes of administration               | Oral use |

Dosage and administration details:

ASTX295 at an oral dose of 400 mg, administered daily, in each 28-day cycle up to a maximum of 14.7 months.

|                  |                                    |
|------------------|------------------------------------|
| <b>Arm title</b> | Dose Expansion: Phase 1b: Cohort 2 |
|------------------|------------------------------------|

Arm description:

Subjects received ASTX295 at an oral dose of 660 mg, administered QD, twice a week, in each 28-day cycle, with or without food, up to a maximum of 14.2 months.

|                                        |              |
|----------------------------------------|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | ASTX295      |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

ASTX295 at an oral dose of 660 mg, administered QD, twice a week, in each 28-day cycle up to a maximum of 14.2 months.

| <b>Number of subjects in period 1</b> | Dose Escalation:<br>Phase 1a: Cohort 1 | Dose Escalation:<br>Phase 1a: Cohort 2 | Dose Escalation:<br>Phase 1a: Cohort 3 |
|---------------------------------------|----------------------------------------|----------------------------------------|----------------------------------------|
| Started                               | 1                                      | 3                                      | 4                                      |
| Completed                             | 0                                      | 0                                      | 0                                      |
| Not completed                         | 1                                      | 3                                      | 4                                      |
| Death                                 | 1                                      | -                                      | 2                                      |
| Complete Consent Withdrawal           | -                                      | 1                                      | 2                                      |
| Study Terminated by Sponsor           | -                                      | 1                                      | -                                      |
| Lost to follow-up                     | -                                      | 1                                      | -                                      |

| <b>Number of subjects in period 1</b> | Dose Escalation:<br>Phase 1a: Cohort 4 | Dose Escalation:<br>Phase 1a: Cohort 5 | Dose Escalation:<br>Phase 1a: Cohort 6 |
|---------------------------------------|----------------------------------------|----------------------------------------|----------------------------------------|
| Started                               | 4                                      | 9                                      | 8                                      |
| Completed                             | 0                                      | 0                                      | 0                                      |
| Not completed                         | 4                                      | 9                                      | 8                                      |
| Death                                 | 2                                      | 4                                      | 6                                      |
| Complete Consent Withdrawal           | -                                      | 1                                      | 1                                      |
| Study Terminated by Sponsor           | 1                                      | 2                                      | 1                                      |
| Lost to follow-up                     | 1                                      | 2                                      | -                                      |

| <b>Number of subjects in period 1</b> | Dose Escalation:<br>Phase 1a: Cohort 7 | Dose Escalation:<br>Phase 1a: Cohort 8 | Dose Escalation:<br>Phase 1a: Cohort 9 |
|---------------------------------------|----------------------------------------|----------------------------------------|----------------------------------------|
| Started                               | 5                                      | 6                                      | 7                                      |
| Completed                             | 0                                      | 0                                      | 0                                      |
| Not completed                         | 5                                      | 6                                      | 7                                      |

|                             |   |   |   |
|-----------------------------|---|---|---|
| Death                       | 3 | 4 | 3 |
| Complete Consent Withdrawal | 1 | 1 | 2 |
| Study Terminated by Sponsor | 1 | 1 | 2 |
| Lost to follow-up           | - | - | - |

| <b>Number of subjects in period 1</b> | Dose Escalation:<br>Phase 1a: Cohort 10 | Dose Escalation:<br>Phase 1a: Cohort 11 | Dose Escalation:<br>Phase 1a: Cohort 12 |
|---------------------------------------|-----------------------------------------|-----------------------------------------|-----------------------------------------|
| Started                               | 8                                       | 4                                       | 9                                       |
| Completed                             | 0                                       | 0                                       | 0                                       |
| Not completed                         | 8                                       | 4                                       | 9                                       |
| Death                                 | 6                                       | 4                                       | 6                                       |
| Complete Consent Withdrawal           | -                                       | -                                       | -                                       |
| Study Terminated by Sponsor           | 2                                       | -                                       | 2                                       |
| Lost to follow-up                     | -                                       | -                                       | 1                                       |

| <b>Number of subjects in period 1</b> | Dose Escalation:<br>Phase 1a: Cohort 13 | Dose Escalation:<br>Phase 1a: Cohort 14 | Dose Expansion:<br>Phase 1b: Cohort 1 |
|---------------------------------------|-----------------------------------------|-----------------------------------------|---------------------------------------|
| Started                               | 8                                       | 6                                       | 12                                    |
| Completed                             | 0                                       | 0                                       | 0                                     |
| Not completed                         | 8                                       | 6                                       | 12                                    |
| Death                                 | 5                                       | 5                                       | 4                                     |
| Complete Consent Withdrawal           | -                                       | 1                                       | -                                     |
| Study Terminated by Sponsor           | 2                                       | -                                       | 7                                     |
| Lost to follow-up                     | 1                                       | -                                       | 1                                     |

| <b>Number of subjects in period 1</b> | Dose Expansion:<br>Phase 1b: Cohort 2 |
|---------------------------------------|---------------------------------------|
| Started                               | 12                                    |
| Completed                             | 0                                     |
| Not completed                         | 12                                    |
| Death                                 | 3                                     |
| Complete Consent Withdrawal           | 1                                     |
| Study Terminated by Sponsor           | 7                                     |
| Lost to follow-up                     | 1                                     |

## Baseline characteristics

### Reporting groups

|                                                                                                                                                                                                                    |                                      |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------|
| Reporting group title                                                                                                                                                                                              | Dose Escalation: Phase 1a: Cohort 1  |
| Reporting group description:<br>Subjects received ASTX295 at starting dose of 15 milligrams (mg), orally, administered once daily (QD) in each 28-day cycle under fasted condition, up to a maximum of 1.8 months. |                                      |
| Reporting group title                                                                                                                                                                                              | Dose Escalation: Phase 1a: Cohort 2  |
| Reporting group description:<br>Subjects received ASTX295 at an oral dose of 45 mg, administered QD in each 28-day cycle under fasted condition, up to a maximum of 17.4 months.                                   |                                      |
| Reporting group title                                                                                                                                                                                              | Dose Escalation: Phase 1a: Cohort 3  |
| Reporting group description:<br>Subjects received ASTX295 at an oral dose of 120 mg, administered QD in each 28-day cycle under fasted condition, up to a maximum of 1.8 months.                                   |                                      |
| Reporting group title                                                                                                                                                                                              | Dose Escalation: Phase 1a: Cohort 4  |
| Reporting group description:<br>Subjects received ASTX295 at an oral dose of 240 mg, administered QD in each 28-day cycle under fasted condition, up to a maximum of 6.4 months.                                   |                                      |
| Reporting group title                                                                                                                                                                                              | Dose Escalation: Phase 1a: Cohort 5  |
| Reporting group description:<br>Subjects received ASTX295 at an oral dose of 420 mg, administered QD in each 28-day cycle under fasted condition, up to a maximum of 14.7 months.                                  |                                      |
| Reporting group title                                                                                                                                                                                              | Dose Escalation: Phase 1a: Cohort 6  |
| Reporting group description:<br>Subjects received ASTX295 at an oral dose of 520 mg, administered QD in each 28-day cycle under fasted condition, up to a maximum of 42.4 months.                                  |                                      |
| Reporting group title                                                                                                                                                                                              | Dose Escalation: Phase 1a: Cohort 7  |
| Reporting group description:<br>Subjects received ASTX295 at an oral dose of 415 mg, administered QD in each 28-day cycle under fed state, up to a maximum of 22.5 months.                                         |                                      |
| Reporting group title                                                                                                                                                                                              | Dose Escalation: Phase 1a: Cohort 8  |
| Reporting group description:<br>Subjects received ASTX295 at an oral dose of 200 mg, administered twice daily (BID) in each 28-day cycle under fasted condition, up to a maximum of 17.4 months.                   |                                      |
| Reporting group title                                                                                                                                                                                              | Dose Escalation: Phase 1a: Cohort 9  |
| Reporting group description:<br>Subjects received ASTX295 at an oral dose of 320 mg, administered BID in each 28-day cycle under fasted condition, up to a maximum of 27.5 months.                                 |                                      |
| Reporting group title                                                                                                                                                                                              | Dose Escalation: Phase 1a: Cohort 10 |
| Reporting group description:<br>Subjects received ASTX295 at an oral dose of 520 mg (5 days on, 2 days off), administered QD in each 28-day cycle, with or without food, up to a maximum of 12 months.             |                                      |
| Reporting group title                                                                                                                                                                                              | Dose Escalation: Phase 1a: Cohort 11 |
| Reporting group description:<br>Subjects received ASTX295 at an oral dose of 520 mg (3 days on, 4 days off), administered QD in each 28-day cycle, with or without food, up to a maximum of 1.8 months.            |                                      |
| Reporting group title                                                                                                                                                                                              | Dose Escalation: Phase 1a: Cohort 12 |
| Reporting group description:<br>Subjects received ASTX295 at an oral dose of 660 mg, administered QD, twice a week, in each 28-day cycle, with or without food, up to a maximum of 11.7 months.                    |                                      |
| Reporting group title                                                                                                                                                                                              | Dose Escalation: Phase 1a: Cohort 13 |
| Reporting group description:<br>Subjects received ASTX295 at an oral dose of 660 mg (3 days on, 4 days off), administered QD, in each 28-day cycle, with or without food, up to a maximum of 18.5 months.          |                                      |

|                                                                                                                                                                                                 |                                      |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------|
| Reporting group title                                                                                                                                                                           | Dose Escalation: Phase 1a: Cohort 14 |
| Reporting group description:<br>Subjects received ASTX295 at an oral dose of 800 mg, administered QD, twice a week, in each 28-day cycle, with or without food, up to a maximum of 6 months.    |                                      |
| Reporting group title                                                                                                                                                                           | Dose Expansion: Phase 1b: Cohort 1   |
| Reporting group description:<br>Subjects received ASTX295 at an oral dose of 400 mg, administered daily, in each 28-day cycle, with or without food, up to a maximum of 14.7 months.            |                                      |
| Reporting group title                                                                                                                                                                           | Dose Expansion: Phase 1b: Cohort 2   |
| Reporting group description:<br>Subjects received ASTX295 at an oral dose of 660 mg, administered QD, twice a week, in each 28-day cycle, with or without food, up to a maximum of 14.2 months. |                                      |

| Reporting group values                                                                                                                                                                                                                                    | Dose Escalation:<br>Phase 1a: Cohort 1 | Dose Escalation:<br>Phase 1a: Cohort 2 | Dose Escalation:<br>Phase 1a: Cohort 3 |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------|----------------------------------------|----------------------------------------|
| Number of subjects                                                                                                                                                                                                                                        | 1                                      | 3                                      | 4                                      |
| Age categorical<br>Units: Subjects                                                                                                                                                                                                                        |                                        |                                        |                                        |
| In utero<br>Preterm newborn infants (gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years)<br>Adolescents (12-17 years)<br>Adults (18-64 years)<br>From 65-84 years<br>85 years and over |                                        |                                        |                                        |
| Age continuous                                                                                                                                                                                                                                            |                                        |                                        |                                        |
| Here, for Dose Escalation: Phase 1a: Cohort 1, "99999" represents that data for standard deviation could not be collected as only 1 subject was present in the cohort.                                                                                    |                                        |                                        |                                        |
| Units: years                                                                                                                                                                                                                                              |                                        |                                        |                                        |
| arithmetic mean<br>standard deviation                                                                                                                                                                                                                     | 41.0<br>± 99999                        | 60.3<br>± 2.31                         | 55.3<br>± 10.78                        |
| Gender categorical<br>Units: Subjects                                                                                                                                                                                                                     |                                        |                                        |                                        |
| Female<br>Male                                                                                                                                                                                                                                            | 0<br>1                                 | 1<br>2                                 | 1<br>3                                 |
| Race<br>Units: Subjects                                                                                                                                                                                                                                   |                                        |                                        |                                        |
| Asian<br>American Indian or Alaska Native<br>Black or African American<br>Native Hawaiian<br>White<br>Other<br>Not Reported<br>Unknown                                                                                                                    | 0<br>0<br>0<br>0<br>1<br>0<br>0<br>0   | 0<br>0<br>0<br>0<br>3<br>0<br>0<br>0   | 1<br>0<br>0<br>0<br>2<br>0<br>1<br>0   |
| Ethnicity<br>Units: Subjects                                                                                                                                                                                                                              |                                        |                                        |                                        |
| Hispanic or Latino                                                                                                                                                                                                                                        | 1                                      | 0                                      | 1                                      |

|                        |   |   |   |
|------------------------|---|---|---|
| Not Hispanic or Latino | 0 | 3 | 3 |
| Not Reported           | 0 | 0 | 0 |
| Unknown                | 0 | 0 | 0 |

| Reporting group values                                                                                                                                                 | Dose Escalation:<br>Phase 1a: Cohort 4 | Dose Escalation:<br>Phase 1a: Cohort 5 | Dose Escalation:<br>Phase 1a: Cohort 6 |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------|----------------------------------------|----------------------------------------|
| Number of subjects                                                                                                                                                     | 4                                      | 9                                      | 8                                      |
| Age categorical<br>Units: Subjects                                                                                                                                     |                                        |                                        |                                        |
| In utero                                                                                                                                                               |                                        |                                        |                                        |
| Preterm newborn infants<br>(gestational age < 37 wks)                                                                                                                  |                                        |                                        |                                        |
| Newborns (0-27 days)                                                                                                                                                   |                                        |                                        |                                        |
| Infants and toddlers (28 days-23 months)                                                                                                                               |                                        |                                        |                                        |
| Children (2-11 years)                                                                                                                                                  |                                        |                                        |                                        |
| Adolescents (12-17 years)                                                                                                                                              |                                        |                                        |                                        |
| Adults (18-64 years)                                                                                                                                                   |                                        |                                        |                                        |
| From 65-84 years                                                                                                                                                       |                                        |                                        |                                        |
| 85 years and over                                                                                                                                                      |                                        |                                        |                                        |
| Age continuous                                                                                                                                                         |                                        |                                        |                                        |
| Here, for Dose Escalation: Phase 1a: Cohort 1, "99999" represents that data for standard deviation could not be collected as only 1 subject was present in the cohort. |                                        |                                        |                                        |
| Units: years                                                                                                                                                           |                                        |                                        |                                        |
| arithmetic mean                                                                                                                                                        | 63.8                                   | 65.6                                   | 61.0                                   |
| standard deviation                                                                                                                                                     | ± 7.04                                 | ± 6.67                                 | ± 8.30                                 |
| Gender categorical<br>Units: Subjects                                                                                                                                  |                                        |                                        |                                        |
| Female                                                                                                                                                                 | 2                                      | 3                                      | 2                                      |
| Male                                                                                                                                                                   | 2                                      | 6                                      | 6                                      |
| Race<br>Units: Subjects                                                                                                                                                |                                        |                                        |                                        |
| Asian                                                                                                                                                                  | 0                                      | 0                                      | 0                                      |
| American Indian or Alaska Native                                                                                                                                       | 0                                      | 0                                      | 0                                      |
| Black or African American                                                                                                                                              | 1                                      | 0                                      | 1                                      |
| Native Hawaiian                                                                                                                                                        | 0                                      | 0                                      | 0                                      |
| White                                                                                                                                                                  | 2                                      | 9                                      | 7                                      |
| Other                                                                                                                                                                  | 0                                      | 0                                      | 0                                      |
| Not Reported                                                                                                                                                           | 1                                      | 0                                      | 0                                      |
| Unknown                                                                                                                                                                | 0                                      | 0                                      | 0                                      |
| Ethnicity<br>Units: Subjects                                                                                                                                           |                                        |                                        |                                        |
| Hispanic or Latino                                                                                                                                                     | 1                                      | 1                                      | 2                                      |
| Not Hispanic or Latino                                                                                                                                                 | 3                                      | 8                                      | 5                                      |
| Not Reported                                                                                                                                                           | 0                                      | 0                                      | 0                                      |
| Unknown                                                                                                                                                                | 0                                      | 0                                      | 1                                      |

| Reporting group values             | Dose Escalation:<br>Phase 1a: Cohort 7 | Dose Escalation:<br>Phase 1a: Cohort 8 | Dose Escalation:<br>Phase 1a: Cohort 9 |
|------------------------------------|----------------------------------------|----------------------------------------|----------------------------------------|
| Number of subjects                 | 5                                      | 6                                      | 7                                      |
| Age categorical<br>Units: Subjects |                                        |                                        |                                        |
| In utero                           |                                        |                                        |                                        |

|                                                                                                                                                                                                                                                  |         |         |         |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|---------|---------|
| Preterm newborn infants<br>(gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years)<br>Adolescents (12-17 years)<br>Adults (18-64 years)<br>From 65-84 years<br>85 years and over |         |         |         |
| Age continuous                                                                                                                                                                                                                                   |         |         |         |
| Here, for Dose Escalation: Phase 1a: Cohort 1, "99999" represents that data for standard deviation could not be collected as only 1 subject was present in the cohort.                                                                           |         |         |         |
| Units: years                                                                                                                                                                                                                                     |         |         |         |
| arithmetic mean                                                                                                                                                                                                                                  | 62.0    | 57.2    | 57.9    |
| standard deviation                                                                                                                                                                                                                               | ± 12.90 | ± 14.47 | ± 15.48 |
| Gender categorical                                                                                                                                                                                                                               |         |         |         |
| Units: Subjects                                                                                                                                                                                                                                  |         |         |         |
| Female                                                                                                                                                                                                                                           | 4       | 3       | 3       |
| Male                                                                                                                                                                                                                                             | 1       | 3       | 4       |
| Race                                                                                                                                                                                                                                             |         |         |         |
| Units: Subjects                                                                                                                                                                                                                                  |         |         |         |
| Asian                                                                                                                                                                                                                                            | 1       | 0       | 0       |
| American Indian or Alaska Native                                                                                                                                                                                                                 | 0       | 0       | 1       |
| Black or African American                                                                                                                                                                                                                        | 0       | 1       | 0       |
| Native Hawaiian                                                                                                                                                                                                                                  | 0       | 0       | 0       |
| White                                                                                                                                                                                                                                            | 4       | 4       | 6       |
| Other                                                                                                                                                                                                                                            | 0       | 0       | 0       |
| Not Reported                                                                                                                                                                                                                                     | 0       | 1       | 0       |
| Unknown                                                                                                                                                                                                                                          | 0       | 0       | 0       |
| Ethnicity                                                                                                                                                                                                                                        |         |         |         |
| Units: Subjects                                                                                                                                                                                                                                  |         |         |         |
| Hispanic or Latino                                                                                                                                                                                                                               | 1       | 1       | 1       |
| Not Hispanic or Latino                                                                                                                                                                                                                           | 3       | 4       | 6       |
| Not Reported                                                                                                                                                                                                                                     | 1       | 1       | 0       |
| Unknown                                                                                                                                                                                                                                          | 0       | 0       | 0       |

| <b>Reporting group values</b>                         | Dose Escalation:<br>Phase 1a: Cohort 10 | Dose Escalation:<br>Phase 1a: Cohort 11 | Dose Escalation:<br>Phase 1a: Cohort 12 |
|-------------------------------------------------------|-----------------------------------------|-----------------------------------------|-----------------------------------------|
| Number of subjects                                    | 8                                       | 4                                       | 9                                       |
| Age categorical                                       |                                         |                                         |                                         |
| Units: Subjects                                       |                                         |                                         |                                         |
| In utero                                              |                                         |                                         |                                         |
| Preterm newborn infants<br>(gestational age < 37 wks) |                                         |                                         |                                         |
| Newborns (0-27 days)                                  |                                         |                                         |                                         |
| Infants and toddlers (28 days-23 months)              |                                         |                                         |                                         |
| Children (2-11 years)                                 |                                         |                                         |                                         |
| Adolescents (12-17 years)                             |                                         |                                         |                                         |
| Adults (18-64 years)                                  |                                         |                                         |                                         |
| From 65-84 years                                      |                                         |                                         |                                         |
| 85 years and over                                     |                                         |                                         |                                         |

|                                                                                                                                                                        |         |        |         |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|--------|---------|
| Age continuous                                                                                                                                                         |         |        |         |
| Here, for Dose Escalation: Phase 1a: Cohort 1, "99999" represents that data for standard deviation could not be collected as only 1 subject was present in the cohort. |         |        |         |
| Units: years                                                                                                                                                           |         |        |         |
| arithmetic mean                                                                                                                                                        | 57.6    | 60.8   | 52.1    |
| standard deviation                                                                                                                                                     | ± 11.55 | ± 4.35 | ± 16.84 |
| Gender categorical                                                                                                                                                     |         |        |         |
| Units: Subjects                                                                                                                                                        |         |        |         |
| Female                                                                                                                                                                 | 4       | 2      | 4       |
| Male                                                                                                                                                                   | 4       | 2      | 5       |
| Race                                                                                                                                                                   |         |        |         |
| Units: Subjects                                                                                                                                                        |         |        |         |
| Asian                                                                                                                                                                  | 0       | 0      | 0       |
| American Indian or Alaska Native                                                                                                                                       | 0       | 0      | 0       |
| Black or African American                                                                                                                                              | 2       | 1      | 1       |
| Native Hawaiian                                                                                                                                                        | 0       | 0      | 0       |
| White                                                                                                                                                                  | 5       | 3      | 6       |
| Other                                                                                                                                                                  | 0       | 0      | 2       |
| Not Reported                                                                                                                                                           | 0       | 0      | 0       |
| Unknown                                                                                                                                                                | 1       | 0      | 0       |
| Ethnicity                                                                                                                                                              |         |        |         |
| Units: Subjects                                                                                                                                                        |         |        |         |
| Hispanic or Latino                                                                                                                                                     | 0       | 1      | 3       |
| Not Hispanic or Latino                                                                                                                                                 | 7       | 3      | 6       |
| Not Reported                                                                                                                                                           | 0       | 0      | 0       |
| Unknown                                                                                                                                                                | 1       | 0      | 0       |

| Reporting group values                                                                                                                                                 | Dose Escalation:<br>Phase 1a: Cohort 13 | Dose Escalation:<br>Phase 1a: Cohort 14 | Dose Expansion:<br>Phase 1b: Cohort 1 |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------|-----------------------------------------|---------------------------------------|
| Number of subjects                                                                                                                                                     | 8                                       | 6                                       | 12                                    |
| Age categorical                                                                                                                                                        |                                         |                                         |                                       |
| Units: Subjects                                                                                                                                                        |                                         |                                         |                                       |
| In utero                                                                                                                                                               |                                         |                                         |                                       |
| Preterm newborn infants<br>(gestational age < 37 wks)                                                                                                                  |                                         |                                         |                                       |
| Newborns (0-27 days)                                                                                                                                                   |                                         |                                         |                                       |
| Infants and toddlers (28 days-23<br>months)                                                                                                                            |                                         |                                         |                                       |
| Children (2-11 years)                                                                                                                                                  |                                         |                                         |                                       |
| Adolescents (12-17 years)                                                                                                                                              |                                         |                                         |                                       |
| Adults (18-64 years)                                                                                                                                                   |                                         |                                         |                                       |
| From 65-84 years                                                                                                                                                       |                                         |                                         |                                       |
| 85 years and over                                                                                                                                                      |                                         |                                         |                                       |
| Age continuous                                                                                                                                                         |                                         |                                         |                                       |
| Here, for Dose Escalation: Phase 1a: Cohort 1, "99999" represents that data for standard deviation could not be collected as only 1 subject was present in the cohort. |                                         |                                         |                                       |
| Units: years                                                                                                                                                           |                                         |                                         |                                       |
| arithmetic mean                                                                                                                                                        | 67.6                                    | 60.3                                    | 61.0                                  |
| standard deviation                                                                                                                                                     | ± 12.70                                 | ± 11.09                                 | ± 12.25                               |
| Gender categorical                                                                                                                                                     |                                         |                                         |                                       |
| Units: Subjects                                                                                                                                                        |                                         |                                         |                                       |
| Female                                                                                                                                                                 | 5                                       | 3                                       | 8                                     |
| Male                                                                                                                                                                   | 3                                       | 3                                       | 4                                     |

|                                  |   |   |    |
|----------------------------------|---|---|----|
| Race                             |   |   |    |
| Units: Subjects                  |   |   |    |
| Asian                            | 0 | 0 | 0  |
| American Indian or Alaska Native | 0 | 0 | 0  |
| Black or African American        | 1 | 1 | 0  |
| Native Hawaiian                  | 0 | 0 | 0  |
| White                            | 7 | 5 | 12 |
| Other                            | 0 | 0 | 0  |
| Not Reported                     | 0 | 0 | 0  |
| Unknown                          | 0 | 0 | 0  |
| Ethnicity                        |   |   |    |
| Units: Subjects                  |   |   |    |
| Hispanic or Latino               | 0 | 1 | 0  |
| Not Hispanic or Latino           | 8 | 4 | 12 |
| Not Reported                     | 0 | 1 | 0  |
| Unknown                          | 0 | 0 | 0  |

| Reporting group values                                                                                                                                                 | Dose Expansion:<br>Phase 1b: Cohort 2 | Total |  |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------|-------|--|
| Number of subjects                                                                                                                                                     | 12                                    | 106   |  |
| Age categorical                                                                                                                                                        |                                       |       |  |
| Units: Subjects                                                                                                                                                        |                                       |       |  |
| In utero                                                                                                                                                               |                                       | 0     |  |
| Preterm newborn infants<br>(gestational age < 37 wks)                                                                                                                  |                                       | 0     |  |
| Newborns (0-27 days)                                                                                                                                                   |                                       | 0     |  |
| Infants and toddlers (28 days-23<br>months)                                                                                                                            |                                       | 0     |  |
| Children (2-11 years)                                                                                                                                                  |                                       | 0     |  |
| Adolescents (12-17 years)                                                                                                                                              |                                       | 0     |  |
| Adults (18-64 years)                                                                                                                                                   |                                       | 0     |  |
| From 65-84 years                                                                                                                                                       |                                       | 0     |  |
| 85 years and over                                                                                                                                                      |                                       | 0     |  |
| Age continuous                                                                                                                                                         |                                       |       |  |
| Here, for Dose Escalation: Phase 1a: Cohort 1, "99999" represents that data for standard deviation could not be collected as only 1 subject was present in the cohort. |                                       |       |  |
| Units: years                                                                                                                                                           |                                       |       |  |
| arithmetic mean                                                                                                                                                        | 58.4                                  |       |  |
| standard deviation                                                                                                                                                     | ± 16.82                               | -     |  |
| Gender categorical                                                                                                                                                     |                                       |       |  |
| Units: Subjects                                                                                                                                                        |                                       |       |  |
| Female                                                                                                                                                                 | 9                                     | 54    |  |
| Male                                                                                                                                                                   | 3                                     | 52    |  |
| Race                                                                                                                                                                   |                                       |       |  |
| Units: Subjects                                                                                                                                                        |                                       |       |  |
| Asian                                                                                                                                                                  | 2                                     | 4     |  |
| American Indian or Alaska Native                                                                                                                                       | 0                                     | 1     |  |
| Black or African American                                                                                                                                              | 0                                     | 9     |  |
| Native Hawaiian                                                                                                                                                        | 0                                     | 0     |  |
| White                                                                                                                                                                  | 9                                     | 85    |  |
| Other                                                                                                                                                                  | 0                                     | 2     |  |
| Not Reported                                                                                                                                                           | 1                                     | 4     |  |
| Unknown                                                                                                                                                                | 0                                     | 1     |  |

|                        |   |    |  |
|------------------------|---|----|--|
| Ethnicity              |   |    |  |
| Units: Subjects        |   |    |  |
| Hispanic or Latino     | 2 | 16 |  |
| Not Hispanic or Latino | 9 | 84 |  |
| Not Reported           | 1 | 4  |  |
| Unknown                | 0 | 2  |  |

## End points

### End points reporting groups

|                                                                                                                                                                                                                    |                                      |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------|
| Reporting group title                                                                                                                                                                                              | Dose Escalation: Phase 1a: Cohort 1  |
| Reporting group description:<br>Subjects received ASTX295 at starting dose of 15 milligrams (mg), orally, administered once daily (QD) in each 28-day cycle under fasted condition, up to a maximum of 1.8 months. |                                      |
| Reporting group title                                                                                                                                                                                              | Dose Escalation: Phase 1a: Cohort 2  |
| Reporting group description:<br>Subjects received ASTX295 at an oral dose of 45 mg, administered QD in each 28-day cycle under fasted condition, up to a maximum of 17.4 months.                                   |                                      |
| Reporting group title                                                                                                                                                                                              | Dose Escalation: Phase 1a: Cohort 3  |
| Reporting group description:<br>Subjects received ASTX295 at an oral dose of 120 mg, administered QD in each 28-day cycle under fasted condition, up to a maximum of 1.8 months.                                   |                                      |
| Reporting group title                                                                                                                                                                                              | Dose Escalation: Phase 1a: Cohort 4  |
| Reporting group description:<br>Subjects received ASTX295 at an oral dose of 240 mg, administered QD in each 28-day cycle under fasted condition, up to a maximum of 6.4 months.                                   |                                      |
| Reporting group title                                                                                                                                                                                              | Dose Escalation: Phase 1a: Cohort 5  |
| Reporting group description:<br>Subjects received ASTX295 at an oral dose of 420 mg, administered QD in each 28-day cycle under fasted condition, up to a maximum of 14.7 months.                                  |                                      |
| Reporting group title                                                                                                                                                                                              | Dose Escalation: Phase 1a: Cohort 6  |
| Reporting group description:<br>Subjects received ASTX295 at an oral dose of 520 mg, administered QD in each 28-day cycle under fasted condition, up to a maximum of 42.4 months.                                  |                                      |
| Reporting group title                                                                                                                                                                                              | Dose Escalation: Phase 1a: Cohort 7  |
| Reporting group description:<br>Subjects received ASTX295 at an oral dose of 415 mg, administered QD in each 28-day cycle under fed state, up to a maximum of 22.5 months.                                         |                                      |
| Reporting group title                                                                                                                                                                                              | Dose Escalation: Phase 1a: Cohort 8  |
| Reporting group description:<br>Subjects received ASTX295 at an oral dose of 200 mg, administered twice daily (BID) in each 28-day cycle under fasted condition, up to a maximum of 17.4 months.                   |                                      |
| Reporting group title                                                                                                                                                                                              | Dose Escalation: Phase 1a: Cohort 9  |
| Reporting group description:<br>Subjects received ASTX295 at an oral dose of 320 mg, administered BID in each 28-day cycle under fasted condition, up to a maximum of 27.5 months.                                 |                                      |
| Reporting group title                                                                                                                                                                                              | Dose Escalation: Phase 1a: Cohort 10 |
| Reporting group description:<br>Subjects received ASTX295 at an oral dose of 520 mg (5 days on, 2 days off), administered QD in each 28-day cycle, with or without food, up to a maximum of 12 months.             |                                      |
| Reporting group title                                                                                                                                                                                              | Dose Escalation: Phase 1a: Cohort 11 |
| Reporting group description:<br>Subjects received ASTX295 at an oral dose of 520 mg (3 days on, 4 days off), administered QD in each 28-day cycle, with or without food, up to a maximum of 1.8 months.            |                                      |
| Reporting group title                                                                                                                                                                                              | Dose Escalation: Phase 1a: Cohort 12 |
| Reporting group description:<br>Subjects received ASTX295 at an oral dose of 660 mg, administered QD, twice a week, in each 28-day cycle, with or without food, up to a maximum of 11.7 months.                    |                                      |
| Reporting group title                                                                                                                                                                                              | Dose Escalation: Phase 1a: Cohort 13 |
| Reporting group description:<br>Subjects received ASTX295 at an oral dose of 660 mg (3 days on, 4 days off), administered QD, in each 28-day cycle, with or without food, up to a maximum of 18.5 months.          |                                      |

|                                                                                                                                                                                                 |                                      |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------|
| Reporting group title                                                                                                                                                                           | Dose Escalation: Phase 1a: Cohort 14 |
| Reporting group description:<br>Subjects received ASTX295 at an oral dose of 800 mg, administered QD, twice a week, in each 28-day cycle, with or without food, up to a maximum of 6 months.    |                                      |
| Reporting group title                                                                                                                                                                           | Dose Expansion: Phase 1b: Cohort 1   |
| Reporting group description:<br>Subjects received ASTX295 at an oral dose of 400 mg, administered daily, in each 28-day cycle, with or without food, up to a maximum of 14.7 months.            |                                      |
| Reporting group title                                                                                                                                                                           | Dose Expansion: Phase 1b: Cohort 2   |
| Reporting group description:<br>Subjects received ASTX295 at an oral dose of 660 mg, administered QD, twice a week, in each 28-day cycle, with or without food, up to a maximum of 14.2 months. |                                      |

### Primary: Phase 1a and 1b: Number of Subjects with Treatment Emergent Adverse Events (TEAEs), and Serious TEAEs

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                      |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | Phase 1a and 1b: Number of Subjects with Treatment Emergent Adverse Events (TEAEs), and Serious TEAEs <sup>[1]</sup> |
| End point description:<br>An adverse event (AE) is any untoward medical occurrence in a subject or clinical study subject, temporally associated with the use of study treatment, whether or not considered related to the study treatment. TEAEs are defined as events that first occur or worsen on or after the date of the first study treatment Cycle 1 Day 1 (C1D1) until 30 days after the last dose of study treatment. Serious TEAE is defined as any untoward medical occurrence that, at any dose result in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent disability/incapacity, or is a congenital anomaly/birth defect. Safety analysis set included all subjects who received at least one dose of study drug. |                                                                                                                      |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Primary                                                                                                              |
| End point timeframe:<br>Up to approximately 61.3 months                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                      |
| Notes:<br>[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.<br>Justification: Descriptive statistics were provided for this endpoint.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                      |

| End point values            | Dose Escalation: Phase 1a: Cohort 1 | Dose Escalation: Phase 1a: Cohort 2 | Dose Escalation: Phase 1a: Cohort 3 | Dose Escalation: Phase 1a: Cohort 4 |
|-----------------------------|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|
| Subject group type          | Reporting group                     | Reporting group                     | Reporting group                     | Reporting group                     |
| Number of subjects analysed | 1                                   | 3                                   | 4                                   | 4                                   |
| Units: subjects             |                                     |                                     |                                     |                                     |
| TEAEs                       | 1                                   | 3                                   | 4                                   | 4                                   |
| SAEs                        | 0                                   | 0                                   | 2                                   | 0                                   |

| End point values            | Dose Escalation: Phase 1a: Cohort 5 | Dose Escalation: Phase 1a: Cohort 6 | Dose Escalation: Phase 1a: Cohort 7 | Dose Escalation: Phase 1a: Cohort 8 |
|-----------------------------|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|
| Subject group type          | Reporting group                     | Reporting group                     | Reporting group                     | Reporting group                     |
| Number of subjects analysed | 9                                   | 8                                   | 5                                   | 6                                   |
| Units: subjects             |                                     |                                     |                                     |                                     |
| TEAEs                       | 9                                   | 8                                   | 5                                   | 6                                   |

|      |   |   |   |   |
|------|---|---|---|---|
| SAEs | 2 | 1 | 1 | 2 |
|------|---|---|---|---|

| End point values            | Dose Escalation: Phase 1a: Cohort 9 | Dose Escalation: Phase 1a: Cohort 10 | Dose Escalation: Phase 1a: Cohort 11 | Dose Escalation: Phase 1a: Cohort 12 |
|-----------------------------|-------------------------------------|--------------------------------------|--------------------------------------|--------------------------------------|
| Subject group type          | Reporting group                     | Reporting group                      | Reporting group                      | Reporting group                      |
| Number of subjects analysed | 7                                   | 8                                    | 4                                    | 9                                    |
| Units: subjects             |                                     |                                      |                                      |                                      |
| TEAEs                       | 7                                   | 8                                    | 4                                    | 9                                    |
| SAEs                        | 0                                   | 1                                    | 0                                    | 4                                    |

| End point values            | Dose Escalation: Phase 1a: Cohort 13 | Dose Escalation: Phase 1a: Cohort 14 | Dose Expansion: Phase 1b: Cohort 1 | Dose Expansion: Phase 1b: Cohort 2 |
|-----------------------------|--------------------------------------|--------------------------------------|------------------------------------|------------------------------------|
| Subject group type          | Reporting group                      | Reporting group                      | Reporting group                    | Reporting group                    |
| Number of subjects analysed | 8                                    | 6                                    | 12                                 | 12                                 |
| Units: subjects             |                                      |                                      |                                    |                                    |
| TEAEs                       | 8                                    | 6                                    | 12                                 | 12                                 |
| SAEs                        | 1                                    | 4                                    | 6                                  | 4                                  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Phase 1a: Number of Subjects with Dose-limiting Toxicities (DLTs)

|                 |                                                                                                 |
|-----------------|-------------------------------------------------------------------------------------------------|
| End point title | Phase 1a: Number of Subjects with Dose-limiting Toxicities (DLTs) <sup>[2]</sup> <sup>[3]</sup> |
|-----------------|-------------------------------------------------------------------------------------------------|

End point description:

Dose-limiting toxicities (DLTs) were AEs graded by National Cancer Institute [NCI] Common Terminology Criteria for Adverse Events [CTCAE] version 5.0 criteria that occurred during first cycle of treatment & represent any 1 of the following: grade 4 thrombocytopenia of any duration; grade 3 thrombocytopenia lasting more than 7 days; ≥grade 3 hematologic toxicity with complications; febrile neutropenia of any duration; grade 4 neutropenia lasting more than 5 days; liver-associated abnormalities; ≥grade 3 nonhematologic AE; event leading to unacceptable risk after dose escalation as suggested by data and safety review committee (DSRC); clinically significant toxicities that persist or occur beyond Cycle 1. Dose escalation evaluable population included all subjects in the dose escalation who either experienced a DLT during the first cycle of treatment, or who completed the first cycle without experiencing a DLT and with at least 85% of planned study treatments administered.

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

End point timeframe:

During Cycle 1 (cycle length= 28 days)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics were provided for this endpoint.

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the

baseline period arms will be reported on when providing values for an end point on the baseline period.  
Justification: Descriptive statistics were provided for this endpoint.

| <b>End point values</b>     | Dose Escalation:<br>Phase 1a:<br>Cohort 1 | Dose Escalation:<br>Phase 1a:<br>Cohort 2 | Dose Escalation:<br>Phase 1a:<br>Cohort 3 | Dose Escalation:<br>Phase 1a:<br>Cohort 4 |
|-----------------------------|-------------------------------------------|-------------------------------------------|-------------------------------------------|-------------------------------------------|
| Subject group type          | Reporting group                           | Reporting group                           | Reporting group                           | Reporting group                           |
| Number of subjects analysed | 1                                         | 3                                         | 4                                         | 4                                         |
| Units: subjects             |                                           |                                           |                                           |                                           |
| DLTs                        | 0                                         | 0                                         | 0                                         | 0                                         |

| <b>End point values</b>     | Dose Escalation:<br>Phase 1a:<br>Cohort 5 | Dose Escalation:<br>Phase 1a:<br>Cohort 6 | Dose Escalation:<br>Phase 1a:<br>Cohort 7 | Dose Escalation:<br>Phase 1a:<br>Cohort 8 |
|-----------------------------|-------------------------------------------|-------------------------------------------|-------------------------------------------|-------------------------------------------|
| Subject group type          | Reporting group                           | Reporting group                           | Reporting group                           | Reporting group                           |
| Number of subjects analysed | 9                                         | 8                                         | 5                                         | 6                                         |
| Units: subjects             |                                           |                                           |                                           |                                           |
| DLTs                        | 0                                         | 1                                         | 1                                         | 1                                         |

| <b>End point values</b>     | Dose Escalation:<br>Phase 1a:<br>Cohort 9 | Dose Escalation:<br>Phase 1a:<br>Cohort 10 | Dose Escalation:<br>Phase 1a:<br>Cohort 11 | Dose Escalation:<br>Phase 1a:<br>Cohort 12 |
|-----------------------------|-------------------------------------------|--------------------------------------------|--------------------------------------------|--------------------------------------------|
| Subject group type          | Reporting group                           | Reporting group                            | Reporting group                            | Reporting group                            |
| Number of subjects analysed | 7                                         | 8                                          | 4                                          | 9                                          |
| Units: subjects             |                                           |                                            |                                            |                                            |
| DLTs                        | 2                                         | 2                                          | 0                                          | 0                                          |

| <b>End point values</b>     | Dose Escalation:<br>Phase 1a:<br>Cohort 13 | Dose Escalation:<br>Phase 1a:<br>Cohort 14 |  |  |
|-----------------------------|--------------------------------------------|--------------------------------------------|--|--|
| Subject group type          | Reporting group                            | Reporting group                            |  |  |
| Number of subjects analysed | 8                                          | 6                                          |  |  |
| Units: subjects             |                                            |                                            |  |  |
| DLTs                        | 0                                          | 0                                          |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 1a and 1b: Disease Control Rate (DCR)

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                             |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Phase 1a and 1b: Disease Control Rate (DCR) |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                             |
| DCR was defined as proportion of subjects who have a complete response (CR), partial response (PR)/stable disease at Week 16 according to response evaluation criteria in solid tumors (RECIST) 1.1/modified RECIST (mRECIST) 1.1 (for malignant pleural mesothelioma [MPM]) as assessed by investigator. CR: Disappearance of all target lesions. Any pathological lymph nodes (whether target or nontarget) must have reduction in short axis to <10 mm. PR: At least 30% decrease in sum of diameters of target lesions, taking as reference baseline sum diameters. Stable disease: Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease, taking as reference smallest sum diameters while on study. Efficacy analysis set included all subjects who received any amount of study treatment. DCR was based on subjects who were in this set & who had disease assessment at baseline & at least 1 follow-up disease assessment/subjects who died/stopped treatment. |                                             |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Secondary                                   |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                             |
| Up to approximately 61.3 months                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                             |

| End point values              | Dose Escalation: Phase 1a: Cohort 1 | Dose Escalation: Phase 1a: Cohort 2 | Dose Escalation: Phase 1a: Cohort 3 | Dose Escalation: Phase 1a: Cohort 4 |
|-------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|
| Subject group type            | Reporting group                     | Reporting group                     | Reporting group                     | Reporting group                     |
| Number of subjects analysed   | 1                                   | 3                                   | 3                                   | 4                                   |
| Units: percentage of subjects |                                     |                                     |                                     |                                     |
| number (not applicable)       | 100                                 | 100                                 | 0                                   | 75.0                                |

| End point values              | Dose Escalation: Phase 1a: Cohort 5 | Dose Escalation: Phase 1a: Cohort 6 | Dose Escalation: Phase 1a: Cohort 7 | Dose Escalation: Phase 1a: Cohort 8 |
|-------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|
| Subject group type            | Reporting group                     | Reporting group                     | Reporting group                     | Reporting group                     |
| Number of subjects analysed   | 8                                   | 8                                   | 5                                   | 5                                   |
| Units: percentage of subjects |                                     |                                     |                                     |                                     |
| number (not applicable)       | 62.5                                | 75.0                                | 80.0                                | 80.0                                |

| End point values              | Dose Escalation: Phase 1a: Cohort 9 | Dose Escalation: Phase 1a: Cohort 10 | Dose Escalation: Phase 1a: Cohort 11 | Dose Escalation: Phase 1a: Cohort 12 |
|-------------------------------|-------------------------------------|--------------------------------------|--------------------------------------|--------------------------------------|
| Subject group type            | Reporting group                     | Reporting group                      | Reporting group                      | Reporting group                      |
| Number of subjects analysed   | 4                                   | 7                                    | 4                                    | 8                                    |
| Units: percentage of subjects |                                     |                                      |                                      |                                      |
| number (not applicable)       | 50.0                                | 71.4                                 | 25.0                                 | 75.0                                 |

| End point values | Dose Escalation: Phase 1a: | Dose Escalation: Phase 1a: | Dose Expansion: Phase 1b: | Dose Expansion: Phase 1b: |
|------------------|----------------------------|----------------------------|---------------------------|---------------------------|
|------------------|----------------------------|----------------------------|---------------------------|---------------------------|

|                               | Cohort 13       | Cohort 14       | Cohort 1        | Cohort 2        |
|-------------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type            | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed   | 7               | 5               | 11              | 10              |
| Units: percentage of subjects |                 |                 |                 |                 |
| number (not applicable)       | 71.4            | 60.0            | 72.7            | 50.0            |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase 1a and 1b: Objective Response Rate (ORR)

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Phase 1a and 1b: Objective Response Rate (ORR) |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                |
| ORR was defined as the proportion of subjects whose best response was CR or PR according to RECIST 1.1 or mRECIST 1.1 (for MPM) as assessed by the investigator. CR: Disappearance of all target lesions. Any pathological lymph nodes (whether target or nontarget) must have reduction in short axis to <10 mm. PR: At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. Efficacy analysis set included all subjects who received any amount of study treatment. ORR was based on subjects who were in this set & who had disease assessment at baseline and at least 1 follow-up disease assessment or subjects who died or stopped treatment before the first scheduled disease assessment due to clinical progression or toxicity. |                                                |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | Secondary                                      |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                |
| Up to approximately 61.3 months                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                |

| End point values              | Dose Escalation: Phase 1a: Cohort 1 | Dose Escalation: Phase 1a: Cohort 2 | Dose Escalation: Phase 1a: Cohort 3 | Dose Escalation: Phase 1a: Cohort 4 |
|-------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|
| Subject group type            | Reporting group                     | Reporting group                     | Reporting group                     | Reporting group                     |
| Number of subjects analysed   | 1                                   | 3                                   | 3                                   | 4                                   |
| Units: percentage of subjects |                                     |                                     |                                     |                                     |
| number (not applicable)       | 0                                   | 0                                   | 0                                   | 0                                   |

| End point values              | Dose Escalation: Phase 1a: Cohort 5 | Dose Escalation: Phase 1a: Cohort 6 | Dose Escalation: Phase 1a: Cohort 7 | Dose Escalation: Phase 1a: Cohort 8 |
|-------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|
| Subject group type            | Reporting group                     | Reporting group                     | Reporting group                     | Reporting group                     |
| Number of subjects analysed   | 8                                   | 8                                   | 5                                   | 5                                   |
| Units: percentage of subjects |                                     |                                     |                                     |                                     |
| number (not applicable)       | 12.5                                | 12.5                                | 0                                   | 0                                   |

| End point values | Dose Escalation: | Dose Escalation: | Dose Escalation: | Dose Escalation: |
|------------------|------------------|------------------|------------------|------------------|
|------------------|------------------|------------------|------------------|------------------|

|                               | Phase 1a:<br>Cohort 9 | Phase 1a:<br>Cohort 10 | Phase 1a:<br>Cohort 11 | Phase 1a:<br>Cohort 12 |
|-------------------------------|-----------------------|------------------------|------------------------|------------------------|
| Subject group type            | Reporting group       | Reporting group        | Reporting group        | Reporting group        |
| Number of subjects analysed   | 4                     | 7                      | 4                      | 8                      |
| Units: percentage of subjects |                       |                        |                        |                        |
| number (not applicable)       | 0                     | 0                      | 0                      | 12.5                   |

| End point values              | Dose<br>Escalation:<br>Phase 1a:<br>Cohort 13 | Dose<br>Escalation:<br>Phase 1a:<br>Cohort 14 | Dose<br>Expansion:<br>Phase 1b:<br>Cohort 1 | Dose<br>Expansion:<br>Phase 1b:<br>Cohort 2 |
|-------------------------------|-----------------------------------------------|-----------------------------------------------|---------------------------------------------|---------------------------------------------|
| Subject group type            | Reporting group                               | Reporting group                               | Reporting group                             | Reporting group                             |
| Number of subjects analysed   | 7                                             | 5                                             | 11                                          | 10                                          |
| Units: percentage of subjects |                                               |                                               |                                             |                                             |
| number (not applicable)       | 0                                             | 0                                             | 0                                           | 0                                           |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase 1a and 1b: Area Under the Concentration-time Curve From Time Zero to Time of Last Measurable Concentration (AUClast) of ASTX295

|                 |                                                                                                                                                      |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Phase 1a and 1b: Area Under the Concentration-time Curve From Time Zero to Time of Last Measurable Concentration (AUClast) of ASTX295 <sup>[4]</sup> |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

PK analysis set included all subjects who received the study drug and have post baseline plasma concentration data. Here, '99999' indicates that values were not measurable due to low number of subjects for the specified arms. 'Subjects analysed' indicates number of subjects with data available for analyses and 'n' indicates number of subjects with data available for analyses at the specified timepoint.

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

End point timeframe:

Pre-dose on Day 1 and Day 2 of Cycles 1 and 2, and at multiple timepoints post-dose on Day 1 of Cycles 1 and 2 (Cycle length = 28 days).

Notes:

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

| End point values                                    | Dose<br>Escalation:<br>Phase 1a:<br>Cohort 1 | Dose<br>Escalation:<br>Phase 1a:<br>Cohort 2 | Dose<br>Escalation:<br>Phase 1a:<br>Cohort 3 | Dose<br>Escalation:<br>Phase 1a:<br>Cohort 4 |
|-----------------------------------------------------|----------------------------------------------|----------------------------------------------|----------------------------------------------|----------------------------------------------|
| Subject group type                                  | Reporting group                              | Reporting group                              | Reporting group                              | Reporting group                              |
| Number of subjects analysed                         | 1                                            | 3                                            | 4                                            | 4                                            |
| Units: hours*nanograms/millilitres (h*ng/mL)        |                                              |                                              |                                              |                                              |
| geometric mean (geometric coefficient of variation) |                                              |                                              |                                              |                                              |
| C1D1<br>(n=1,3,4,4,9,8,5,5,7,8,4,9,8,6,12,12)       | 28.7 (± 99999)                               | 60.0 (± 81.8)                                | 1230 (± 222.2)                               | 1140 (± 50.7)                                |

|                                              |                |              |               |               |
|----------------------------------------------|----------------|--------------|---------------|---------------|
| C2D1<br>(n=1,3,2,3,7,5,1,5,2,7,3,6,6,4,11,9) | 24.6 (± 99999) | 113 (± 82.8) | 1480 (± 77.2) | 2270 (± 34.7) |
|----------------------------------------------|----------------|--------------|---------------|---------------|

| End point values                                    | Dose Escalation:<br>Phase 1a:<br>Cohort 5 | Dose Escalation:<br>Phase 1a:<br>Cohort 6 | Dose Escalation:<br>Phase 1a:<br>Cohort 8 | Dose Escalation:<br>Phase 1a:<br>Cohort 9 |
|-----------------------------------------------------|-------------------------------------------|-------------------------------------------|-------------------------------------------|-------------------------------------------|
| Subject group type                                  | Reporting group                           | Reporting group                           | Reporting group                           | Reporting group                           |
| Number of subjects analysed                         | 9                                         | 8                                         | 5                                         | 7                                         |
| Units: hours*nanograms/millilitres (h*ng/mL)        |                                           |                                           |                                           |                                           |
| geometric mean (geometric coefficient of variation) |                                           |                                           |                                           |                                           |
| C1D1<br>(n=1,3,4,4,9,8,5,5,7,8,4,9,8,6,12,12)       | 3850 (± 135.8)                            | 3500 (± 140.7)                            | 844 (± 82.8)                              | 2180 (± 133.1)                            |
| C2D1<br>(n=1,3,2,3,7,5,1,5,2,7,3,6,6,4,11,9)        | 3540 (± 58.7)                             | 1710 (± 180.2)                            | 1790 (± 28.2)                             | 4600 (± 65.3)                             |

| End point values                                    | Dose Escalation:<br>Phase 1a:<br>Cohort 10 | Dose Escalation:<br>Phase 1a:<br>Cohort 11 | Dose Escalation:<br>Phase 1a:<br>Cohort 12 | Dose Escalation:<br>Phase 1a:<br>Cohort 13 |
|-----------------------------------------------------|--------------------------------------------|--------------------------------------------|--------------------------------------------|--------------------------------------------|
| Subject group type                                  | Reporting group                            | Reporting group                            | Reporting group                            | Reporting group                            |
| Number of subjects analysed                         | 8                                          | 4                                          | 9                                          | 8                                          |
| Units: hours*nanograms/millilitres (h*ng/mL)        |                                            |                                            |                                            |                                            |
| geometric mean (geometric coefficient of variation) |                                            |                                            |                                            |                                            |
| C1D1<br>(n=1,3,4,4,9,8,5,5,7,8,4,9,8,6,12,12)       | 11200 (± 145.8)                            | 3270 (± 64.4)                              | 10600 (± 161.2)                            | 7870 (± 222.9)                             |
| C2D1<br>(n=1,3,2,3,7,5,1,5,2,7,3,6,6,4,11,9)        | 12700 (± 131.5)                            | 2890 (± 40.2)                              | 10500 (± 237.4)                            | 8640 (± 186.7)                             |

| End point values                                    | Dose Escalation:<br>Phase 1a:<br>Cohort 14 | Dose Expansion:<br>Phase 1b:<br>Cohort 1 | Dose Expansion:<br>Phase 1b:<br>Cohort 2 |  |
|-----------------------------------------------------|--------------------------------------------|------------------------------------------|------------------------------------------|--|
| Subject group type                                  | Reporting group                            | Reporting group                          | Reporting group                          |  |
| Number of subjects analysed                         | 6                                          | 12                                       | 12                                       |  |
| Units: hours*nanograms/millilitres (h*ng/mL)        |                                            |                                          |                                          |  |
| geometric mean (geometric coefficient of variation) |                                            |                                          |                                          |  |
| C1D1<br>(n=1,3,4,4,9,8,5,5,7,8,4,9,8,6,12,12)       | 9310 (± 102.1)                             | 3020 (± 72.4)                            | 11600 (± 200.3)                          |  |
| C2D1<br>(n=1,3,2,3,7,5,1,5,2,7,3,6,6,4,11,9)        | 11000 (± 52.2)                             | 4440 (± 50.9)                            | 4730 (± 262.4)                           |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 1a and 1b: Maximum Observed Plasma Concentration (Cmax) of ASTX295

|                 |                                                                                         |
|-----------------|-----------------------------------------------------------------------------------------|
| End point title | Phase 1a and 1b: Maximum Observed Plasma Concentration (Cmax) of ASTX295 <sup>[5]</sup> |
|-----------------|-----------------------------------------------------------------------------------------|

End point description:

PK analysis set included all subjects who received the study drug and have post baseline plasma concentration data. Here, '99999' indicates that dispersion values were not measurable due to low number of subjects for the specified arms. 'Subjects analysed' indicates number of subjects with data available for analyses and 'n' indicates number of subjects with data available for analyses at the specified timepoint.

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

End point timeframe:

Pre-dose on Day 1 and Day 2 of Cycles 1 and 2, and at multiple timepoints post-dose on Day 1 of Cycles 1 and 2 (Cycle length = 28 days).

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Descriptive statistics were provided for this endpoint.

| End point values                                    | Dose Escalation: Phase 1a: Cohort 1 | Dose Escalation: Phase 1a: Cohort 2 | Dose Escalation: Phase 1a: Cohort 3 | Dose Escalation: Phase 1a: Cohort 4 |
|-----------------------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|
| Subject group type                                  | Reporting group                     | Reporting group                     | Reporting group                     | Reporting group                     |
| Number of subjects analysed                         | 1                                   | 3                                   | 4                                   | 4                                   |
| Units: nanogram(s)/millilitre (ng/mL)               |                                     |                                     |                                     |                                     |
| geometric mean (geometric coefficient of variation) |                                     |                                     |                                     |                                     |
| C1D1<br>(n=1,3,4,4,9,8,5,7,8,4,9,8,6,12,12)         | 19.1 (± 99999)                      | 27.3 (± 9.2)                        | 367 (± 189.9)                       | 448 (± 69.7)                        |
| C2D1<br>(n=1,3,2,3,7,5,5,2,7,4,5,6,4,11,9)          | 15.3 (± 99999)                      | 40.4 (± 108.1)                      | 318 (± 49.7)                        | 937 (± 63.3)                        |

| End point values                                    | Dose Escalation: Phase 1a: Cohort 5 | Dose Escalation: Phase 1a: Cohort 6 | Dose Escalation: Phase 1a: Cohort 8 | Dose Escalation: Phase 1a: Cohort 9 |
|-----------------------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|
| Subject group type                                  | Reporting group                     | Reporting group                     | Reporting group                     | Reporting group                     |
| Number of subjects analysed                         | 9                                   | 8                                   | 5                                   | 7                                   |
| Units: nanogram(s)/millilitre (ng/mL)               |                                     |                                     |                                     |                                     |
| geometric mean (geometric coefficient of variation) |                                     |                                     |                                     |                                     |
| C1D1<br>(n=1,3,4,4,9,8,5,7,8,4,9,8,6,12,12)         | 963 (± 109.0)                       | 758 (± 224.2)                       | 307 (± 67.6)                        | 924 (± 123.5)                       |
| C2D1<br>(n=1,3,2,3,7,5,5,2,7,4,5,6,4,11,9)          | 963 (± 81.8)                        | 497 (± 196.3)                       | 544 (± 52.2)                        | 1800 (± 54.8)                       |

| End point values | Dose | Dose | Dose | Dose |
|------------------|------|------|------|------|
|------------------|------|------|------|------|

|                                                     | Escalation:<br>Phase 1a:<br>Cohort 10 | Escalation:<br>Phase 1a:<br>Cohort 11 | Escalation:<br>Phase 1a:<br>Cohort 12 | Escalation:<br>Phase 1a:<br>Cohort 13 |
|-----------------------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|
| Subject group type                                  | Reporting group                       | Reporting group                       | Reporting group                       | Reporting group                       |
| Number of subjects analysed                         | 8                                     | 4                                     | 9                                     | 8                                     |
| Units: nanogram(s)/millilitre (ng/mL)               |                                       |                                       |                                       |                                       |
| geometric mean (geometric coefficient of variation) |                                       |                                       |                                       |                                       |
| C1D1<br>(n=1,3,4,4,9,8,5,7,8,4,9,8,6,12,12)         | 2670 (± 133.0)                        | 936 (± 70.9)                          | 2210 (± 189.7)                        | 1830 (± 228.8)                        |
| C2D1<br>(n=1,3,2,3,7,5,5,2,7,4,5,6,4,11,9)          | 2870 (± 87.6)                         | 1010 (± 89.3)                         | 1620 (± 334)                          | 2100 (± 165.2)                        |

| End point values                                    | Dose<br>Escalation:<br>Phase 1a:<br>Cohort 14 | Dose<br>Expansion:<br>Phase 1b:<br>Cohort 1 | Dose<br>Expansion:<br>Phase 1b:<br>Cohort 2 |  |
|-----------------------------------------------------|-----------------------------------------------|---------------------------------------------|---------------------------------------------|--|
| Subject group type                                  | Reporting group                               | Reporting group                             | Reporting group                             |  |
| Number of subjects analysed                         | 6                                             | 12                                          | 12                                          |  |
| Units: nanogram(s)/millilitre (ng/mL)               |                                               |                                             |                                             |  |
| geometric mean (geometric coefficient of variation) |                                               |                                             |                                             |  |
| C1D1<br>(n=1,3,4,4,9,8,5,7,8,4,9,8,6,12,12)         | 2600 (± 90.3)                                 | 786 (± 63.0)                                | 3010 (± 207.2)                              |  |
| C2D1<br>(n=1,3,2,3,7,5,5,2,7,4,5,6,4,11,9)          | 3490 (± 53.8)                                 | 942 (± 50.8)                                | 1370 (± 192.1)                              |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase 1a and 1b: Minimum Observed Plasma Concentration (Cmin) of ASTX295

|                 |                                                                                         |
|-----------------|-----------------------------------------------------------------------------------------|
| End point title | Phase 1a and 1b: Minimum Observed Plasma Concentration (Cmin) of ASTX295 <sup>[6]</sup> |
|-----------------|-----------------------------------------------------------------------------------------|

End point description:

PK analysis set included all subjects who received the study drug and have post baseline plasma concentration data. Here, '99999' indicates that dispersion values were not measurable due to low number of subjects for the specified arms. 'Subjects analysed' indicates number of subjects with data available for analyses.

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

End point timeframe:

Pre-dose on Day 1 and Day 2 of Cycles 1 and 2, and at multiple timepoints post-dose on Day 1 of Cycles 1 and 2 (Cycle length = 28 days).

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Descriptive statistics were provided for this endpoint.

| End point values                                    | Dose Escalation:<br>Phase 1a:<br>Cohort 1 | Dose Escalation:<br>Phase 1a:<br>Cohort 2 | Dose Escalation:<br>Phase 1a:<br>Cohort 3 | Dose Escalation:<br>Phase 1a:<br>Cohort 4 |
|-----------------------------------------------------|-------------------------------------------|-------------------------------------------|-------------------------------------------|-------------------------------------------|
| Subject group type                                  | Reporting group                           | Reporting group                           | Reporting group                           | Reporting group                           |
| Number of subjects analysed                         | 1                                         | 3                                         | 2                                         | 3                                         |
| Units: ng/mL                                        |                                           |                                           |                                           |                                           |
| geometric mean (geometric coefficient of variation) |                                           |                                           |                                           |                                           |
| C2D1                                                | 99999 ( $\pm$ 99999)                      | 99999 ( $\pm$ 99999)                      | 14.17 ( $\pm$ 151.8)                      | 33.56 ( $\pm$ 48.7)                       |

| End point values                                    | Dose Escalation:<br>Phase 1a:<br>Cohort 5 | Dose Escalation:<br>Phase 1a:<br>Cohort 6 | Dose Escalation:<br>Phase 1a:<br>Cohort 8 | Dose Escalation:<br>Phase 1a:<br>Cohort 9 |
|-----------------------------------------------------|-------------------------------------------|-------------------------------------------|-------------------------------------------|-------------------------------------------|
| Subject group type                                  | Reporting group                           | Reporting group                           | Reporting group                           | Reporting group                           |
| Number of subjects analysed                         | 7                                         | 7                                         | 5                                         | 2                                         |
| Units: ng/mL                                        |                                           |                                           |                                           |                                           |
| geometric mean (geometric coefficient of variation) |                                           |                                           |                                           |                                           |
| C2D1                                                | 40.00 ( $\pm$ 67.3)                       | 99999 ( $\pm$ 99999)                      | 59.04 ( $\pm$ 64.0)                       | 129.4 ( $\pm$ 6.0)                        |

| End point values                                    | Dose Escalation:<br>Phase 1a:<br>Cohort 10 | Dose Escalation:<br>Phase 1a:<br>Cohort 11 | Dose Escalation:<br>Phase 1a:<br>Cohort 12 | Dose Escalation:<br>Phase 1a:<br>Cohort 13 |
|-----------------------------------------------------|--------------------------------------------|--------------------------------------------|--------------------------------------------|--------------------------------------------|
| Subject group type                                  | Reporting group                            | Reporting group                            | Reporting group                            | Reporting group                            |
| Number of subjects analysed                         | 7                                          | 4                                          | 7                                          | 6                                          |
| Units: ng/mL                                        |                                            |                                            |                                            |                                            |
| geometric mean (geometric coefficient of variation) |                                            |                                            |                                            |                                            |
| C2D1                                                | 134 ( $\pm$ 99999)                         | 99999 ( $\pm$ 99999)                       | 99999 ( $\pm$ 99999)                       | 99999 ( $\pm$ 99999)                       |

| End point values                                    | Dose Escalation:<br>Phase 1a:<br>Cohort 14 | Dose Expansion:<br>Phase 1b:<br>Cohort 1 | Dose Expansion:<br>Phase 1b:<br>Cohort 2 |  |
|-----------------------------------------------------|--------------------------------------------|------------------------------------------|------------------------------------------|--|
| Subject group type                                  | Reporting group                            | Reporting group                          | Reporting group                          |  |
| Number of subjects analysed                         | 5                                          | 11                                       | 10                                       |  |
| Units: ng/mL                                        |                                            |                                          |                                          |  |
| geometric mean (geometric coefficient of variation) |                                            |                                          |                                          |  |
| C2D1                                                | 14.44 ( $\pm$ 113.3)                       | 99999 ( $\pm$ 99999)                     | 26.78 ( $\pm$ 256.5)                     |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 1a and 1b: Time to Maximum Observed Plasma Concentration (Tmax) of ASTX295

|                 |                                                                                                 |
|-----------------|-------------------------------------------------------------------------------------------------|
| End point title | Phase 1a and 1b: Time to Maximum Observed Plasma Concentration (Tmax) of ASTX295 <sup>[7]</sup> |
|-----------------|-------------------------------------------------------------------------------------------------|

End point description:

PK analysis set included all subjects who received the study drug and have post baseline plasma concentration data. Here, '99999' indicates that dispersion values were not measurable due to low number of subjects for the specified arms. 'Subjects analysed' indicates number of subjects with data available for analyses and 'n' indicates number of subjects with data available for analyses at the specified timepoint.

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

End point timeframe:

Pre-dose on Day 1 and Day 2 of Cycles 1 and 2, and at multiple timepoints post-dose on Day 1 of Cycles 1 and 2 (Cycle length = 28 days).

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Descriptive statistics were provided for this endpoint.

| End point values                              | Dose Escalation: Phase 1a: Cohort 1 | Dose Escalation: Phase 1a: Cohort 2 | Dose Escalation: Phase 1a: Cohort 3 | Dose Escalation: Phase 1a: Cohort 4 |
|-----------------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|
| Subject group type                            | Reporting group                     | Reporting group                     | Reporting group                     | Reporting group                     |
| Number of subjects analysed                   | 1                                   | 3                                   | 4                                   | 4                                   |
| Units: hours                                  |                                     |                                     |                                     |                                     |
| median (full range (min-max))                 |                                     |                                     |                                     |                                     |
| C1D1<br>(n=1,3,4,4,9,8,5,5,7,8,4,9,8,6,12,12) | 0.95 (-99999 to 99999)              | 1.00 (1.00 to 3.83)                 | 1.52 (1.00 to 3.83)                 | 1.47 (1.00 to 2.00)                 |
| C2D1<br>(n=1,3,2,3,7,5,1,5,2,7,4,6,6,4,11,9)  | 1.00 (-99999 to 99999)              | 3.08 (0.50 to 3.92)                 | 1.51 (1.00 to 2.02)                 | 2.83 (1.97 to 2.90)                 |

| End point values                              | Dose Escalation: Phase 1a: Cohort 5 | Dose Escalation: Phase 1a: Cohort 6 | Dose Escalation: Phase 1a: Cohort 8 | Dose Escalation: Phase 1a: Cohort 9 |
|-----------------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|
| Subject group type                            | Reporting group                     | Reporting group                     | Reporting group                     | Reporting group                     |
| Number of subjects analysed                   | 9                                   | 8                                   | 5                                   | 7                                   |
| Units: hours                                  |                                     |                                     |                                     |                                     |
| median (full range (min-max))                 |                                     |                                     |                                     |                                     |
| C1D1<br>(n=1,3,4,4,9,8,5,5,7,8,4,9,8,6,12,12) | 3.95 (2.00 to 4.00)                 | 3.01 (2.93 to 4.15)                 | 2.97 (1.98 to 5.7)                  | 3.02 (2.13 to 4.17)                 |

|                                              |                     |                     |                     |                     |
|----------------------------------------------|---------------------|---------------------|---------------------|---------------------|
| C2D1<br>(n=1,3,2,3,7,5,1,5,2,7,4,6,6,4,11,9) | 2.85 (2.00 to 3.02) | 3.02 (1.00 to 4.03) | 2.90 (2.05 to 3.88) | 2.42 (2.17 to 2.67) |
|----------------------------------------------|---------------------|---------------------|---------------------|---------------------|

| End point values                              | Dose Escalation:<br>Phase 1a:<br>Cohort 10 | Dose Escalation:<br>Phase 1a:<br>Cohort 11 | Dose Escalation:<br>Phase 1a:<br>Cohort 12 | Dose Escalation:<br>Phase 1a:<br>Cohort 13 |
|-----------------------------------------------|--------------------------------------------|--------------------------------------------|--------------------------------------------|--------------------------------------------|
| Subject group type                            | Reporting group                            | Reporting group                            | Reporting group                            | Reporting group                            |
| Number of subjects analysed                   | 8                                          | 4                                          | 9                                          | 8                                          |
| Units: hours                                  |                                            |                                            |                                            |                                            |
| median (full range (min-max))                 |                                            |                                            |                                            |                                            |
| C1D1<br>(n=1,3,4,4,9,8,5,5,7,8,4,9,8,6,12,12) | 3.00 (0.52 to 6.03)                        | 2.46 (1.00 to 3.17)                        | 2.98 (1.02 to 6.00)                        | 2.93 (1.98 to 5.85)                        |
| C2D1<br>(n=1,3,2,3,7,5,1,5,2,7,4,6,6,4,11,9)  | 3.05 (2.07 to 5.67)                        | 2.55 (1.97 to 3.22)                        | 3.48 (2.00 to 4.05)                        | 3.45 (1.98 to 5.9)                         |

| End point values                              | Dose Escalation:<br>Phase 1a:<br>Cohort 14 | Dose Expansion:<br>Phase 1b:<br>Cohort 1 | Dose Expansion:<br>Phase 1b:<br>Cohort 2 |  |
|-----------------------------------------------|--------------------------------------------|------------------------------------------|------------------------------------------|--|
| Subject group type                            | Reporting group                            | Reporting group                          | Reporting group                          |  |
| Number of subjects analysed                   | 6                                          | 12                                       | 12                                       |  |
| Units: hours                                  |                                            |                                          |                                          |  |
| median (full range (min-max))                 |                                            |                                          |                                          |  |
| C1D1<br>(n=1,3,4,4,9,8,5,5,7,8,4,9,8,6,12,12) | 3.49 (1.98 to 3.97)                        | 3.42 (0.97 to 6.02)                      | 2.92 (1.02 to 5.77)                      |  |
| C2D1<br>(n=1,3,2,3,7,5,1,5,2,7,4,6,6,4,11,9)  | 3.39 (1.98 to 3.98)                        | 3.00 (1.02 to 5.98)                      | 2.97 (1.92 to 5.82)                      |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase 1a and 1b: Elimination Half-life (t<sub>1/2</sub>) of ASTX295

|                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                      |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                  | Phase 1a and 1b: Elimination Half-life (t <sub>1/2</sub> ) of ASTX295 <sup>[8]</sup> |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                      |
| PK analysis set included all subjects who received the study drug and have post baseline plasma concentration data. Here, '99999' indicates that dispersion values were not measurable due to low number of subjects for the specified arms. 'Subjects analysed' indicates number of subjects with data available for analyses and 'n' indicates number of subjects with data available for analyses at the specified timepoint. |                                                                                      |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                   | Secondary                                                                            |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                      |
| Pre-dose on Day 1 and Day 2 of Cycles 1 and 2, and at multiple timepoints post-dose on Day 1 of Cycles 1 and 2 (Cycle length = 28 days).                                                                                                                                                                                                                                                                                         |                                                                                      |

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.  
Justification: Descriptive statistics were provided for this endpoint.

| End point values                                    | Dose Escalation: Phase 1a: Cohort 1 | Dose Escalation: Phase 1a: Cohort 2 | Dose Escalation: Phase 1a: Cohort 3 | Dose Escalation: Phase 1a: Cohort 4 |
|-----------------------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|
| Subject group type                                  | Reporting group                     | Reporting group                     | Reporting group                     | Reporting group                     |
| Number of subjects analysed                         | 0 <sup>[9]</sup>                    | 1                                   | 2                                   | 4                                   |
| Units: hours                                        |                                     |                                     |                                     |                                     |
| geometric mean (geometric coefficient of variation) |                                     |                                     |                                     |                                     |
| C1D1<br>(n=0,0,2,4,5,7,3,3,3,6,4,6,7,6,7,9)         | ()                                  | 99999 (± 99999)                     | 3.14 (± 37.8)                       | 2.42 (± 68.9)                       |
| C2D1<br>(n=0,1,2,2,6,4,0,1,2,4,3,3,4,4,7,5)         | ()                                  | 3.14 (± 99999)                      | 7.86 (± 46.7)                       | 4.46 (± 268.9)                      |

Notes:

[9] - Data was not reported as no subjects were available for analyses at the specified timepoint.

| End point values                                    | Dose Escalation: Phase 1a: Cohort 5 | Dose Escalation: Phase 1a: Cohort 6 | Dose Escalation: Phase 1a: Cohort 8 | Dose Escalation: Phase 1a: Cohort 9 |
|-----------------------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|
| Subject group type                                  | Reporting group                     | Reporting group                     | Reporting group                     | Reporting group                     |
| Number of subjects analysed                         | 5                                   | 7                                   | 3                                   | 3                                   |
| Units: hours                                        |                                     |                                     |                                     |                                     |
| geometric mean (geometric coefficient of variation) |                                     |                                     |                                     |                                     |
| C1D1<br>(n=0,0,2,4,5,7,3,3,3,6,4,6,7,6,7,9)         | 4.50 (± 35.0)                       | 4.86 (± 66.4)                       | 1.73 (± 39.5)                       | 1.35 (± 16.7)                       |
| C2D1<br>(n=0,1,2,2,6,4,0,1,2,4,3,3,4,4,7,5)         | 4.50 (± 106.4)                      | 3.81 (± 52.3)                       | 1.93 (± 99999)                      | 2.49 (± 68.4)                       |

| End point values                                    | Dose Escalation: Phase 1a: Cohort 10 | Dose Escalation: Phase 1a: Cohort 11 | Dose Escalation: Phase 1a: Cohort 12 | Dose Escalation: Phase 1a: Cohort 13 |
|-----------------------------------------------------|--------------------------------------|--------------------------------------|--------------------------------------|--------------------------------------|
| Subject group type                                  | Reporting group                      | Reporting group                      | Reporting group                      | Reporting group                      |
| Number of subjects analysed                         | 6                                    | 4                                    | 6                                    | 7                                    |
| Units: hours                                        |                                      |                                      |                                      |                                      |
| geometric mean (geometric coefficient of variation) |                                      |                                      |                                      |                                      |
| C1D1<br>(n=0,0,2,4,5,7,3,3,3,6,4,6,7,6,7,9)         | 3.74 (± 74.9)                        | 5.55 (± 15.1)                        | 4.39 (± 28.8)                        | 5.10 (± 39.6)                        |
| C2D1<br>(n=0,1,2,2,6,4,0,1,2,4,3,3,4,4,7,5)         | 3.59 (± 116.8)                       | 8.06 (± 3.6)                         | 4.48 (± 19.8)                        | 4.44 (± 20.0)                        |

| End point values | Dose Escalation: Phase 1a: Cohort 14 | Dose Expansion: Phase 1b: Cohort 1 | Dose Expansion: Phase 1b: Cohort 2 |  |
|------------------|--------------------------------------|------------------------------------|------------------------------------|--|
|------------------|--------------------------------------|------------------------------------|------------------------------------|--|

| Subject group type                                  | Reporting group | Reporting group | Reporting group |  |
|-----------------------------------------------------|-----------------|-----------------|-----------------|--|
| Number of subjects analysed                         | 6               | 7               | 9               |  |
| Units: hours                                        |                 |                 |                 |  |
| geometric mean (geometric coefficient of variation) |                 |                 |                 |  |
| C1D1<br>(n=0,0,2,4,5,7,3,3,3,6,4,6,7,6,7,9)         | 3.52 (± 60.0)   | 4.99 (± 58.8)   | 3.32 (± 58.3)   |  |
| C2D1<br>(n=0,1,2,2,6,4,0,1,2,4,3,3,4,4,7,5)         | 3.60 (± 14.4)   | 6.01 (± 18.7)   | 4.20 (± 23.2)   |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase 1a and 1b: Area Under the Concentration-time Curve From Time Zero to 24 Hours (AUC0-24) of ASTX295

|                 |                                                                                                                          |
|-----------------|--------------------------------------------------------------------------------------------------------------------------|
| End point title | Phase 1a and 1b: Area Under the Concentration-time Curve From Time Zero to 24 Hours (AUC0-24) of ASTX295 <sup>[10]</sup> |
|-----------------|--------------------------------------------------------------------------------------------------------------------------|

End point description:

Pharmacokinetics (PK) analysis set included all subjects who received the study drug and have post baseline plasma concentration data. Here, C1D1 represents Cycle 1 Day 1, and C2D1 represents Cycle 2 Day 1, '99999' indicates that values were not measurable due to low number of subjects for the specified arms. 'Subjects analysed' indicates number of subjects with data available for analyses and 'n' indicates number of subjects with data available for analyses at the specified timepoint.

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

End point timeframe:

Pre-dose on Day 1 and 2 of Cycles 1 and 2, and at multiple timepoints post-dose on Day 1 of Cycles 1 and 2 (Cycle length = 28 days).

Notes:

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

Justification: Descriptive statistics were provided for this endpoint.

| End point values                                    | Dose Escalation: Phase 1a: Cohort 1 | Dose Escalation: Phase 1a: Cohort 2 | Dose Escalation: Phase 1a: Cohort 3 | Dose Escalation: Phase 1a: Cohort 4 |
|-----------------------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|
| Subject group type                                  | Reporting group                     | Reporting group                     | Reporting group                     | Reporting group                     |
| Number of subjects analysed                         | 1                                   | 0 <sup>[11]</sup>                   | 4                                   | 4                                   |
| Units: hours*nanograms/millilitres (h*ng/mL)        |                                     |                                     |                                     |                                     |
| geometric mean (geometric coefficient of variation) |                                     |                                     |                                     |                                     |
| C1D1<br>(n=0,0,3,3,7,8,5,0,0,8,4,8,8,6,11,12)       | 99999 (± 99999)                     | ()                                  | 2040 (± 148.9)                      | 1380 (± 53.6)                       |
| C2D1<br>(n=1,0,2,2,7,4,0,0,0,7,3,6,4,4,9,6)         | 27.7 (± 99999)                      | ()                                  | 1500 (± 76.3)                       | 2170 (± 39.8)                       |

Notes:

[11] - Data was not reported as AUC(0-24) could not be calculated.

| End point values | Dose Escalation: Phase 1a: Cohort 5 | Dose Escalation: Phase 1a: Cohort 6 | Dose Escalation: Phase 1a: Cohort 8 | Dose Escalation: Phase 1a: Cohort 9 |
|------------------|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|
|------------------|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|

| Subject group type                                  | Reporting group | Reporting group | Reporting group   | Reporting group   |
|-----------------------------------------------------|-----------------|-----------------|-------------------|-------------------|
| Number of subjects analysed                         | 9               | 8               | 0 <sup>[12]</sup> | 0 <sup>[13]</sup> |
| Units: hours*nanograms/millilitres (h*ng/mL)        |                 |                 |                   |                   |
| geometric mean (geometric coefficient of variation) |                 |                 |                   |                   |
| C1D1<br>(n=0,0,3,3,7,8,5,0,0,8,4,8,8,6,11,12)       | 4450 (± 59.0)   | 3520 (± 140.5)  | ()                | ()                |
| C2D1<br>(n=1,0,2,2,7,4,0,0,0,7,3,6,4,4,9,6)         | 3610 (± 60.4)   | 2760 (± 82.8)   | ()                | ()                |

Notes:

[12] - Since this cohort was dosed every 12 hours, therefore AUC0-24 could not be calculated.

[13] - Since this cohort was dosed every 12 hours, therefore AUC0-24 could not be calculated.

| End point values                                    | Dose Escalation:<br>Phase 1a:<br>Cohort 10 | Dose Escalation:<br>Phase 1a:<br>Cohort 11 | Dose Escalation:<br>Phase 1a:<br>Cohort 12 | Dose Escalation:<br>Phase 1a:<br>Cohort 13 |
|-----------------------------------------------------|--------------------------------------------|--------------------------------------------|--------------------------------------------|--------------------------------------------|
| Subject group type                                  | Reporting group                            | Reporting group                            | Reporting group                            | Reporting group                            |
| Number of subjects analysed                         | 8                                          | 4                                          | 8                                          | 8                                          |
| Units: hours*nanograms/millilitres (h*ng/mL)        |                                            |                                            |                                            |                                            |
| geometric mean (geometric coefficient of variation) |                                            |                                            |                                            |                                            |
| C1D1<br>(n=0,0,3,3,7,8,5,0,0,8,4,8,8,6,11,12)       | 11300 (± 137.8)                            | 3280 (± 64.4)                              | 11500 (± 173.4)                            | 7860 (± 223.2)                             |
| C2D1<br>(n=1,0,2,2,7,4,0,0,0,7,3,6,4,4,9,6)         | 12700 (± 129.8)                            | 2890 (± 40.2)                              | 10500 (± 238.6)                            | 10400 (± 175.0)                            |

| End point values                                    | Dose Escalation:<br>Phase 1a:<br>Cohort 14 | Dose Expansion:<br>Phase 1b:<br>Cohort 1 | Dose Expansion:<br>Phase 1b:<br>Cohort 2 |  |
|-----------------------------------------------------|--------------------------------------------|------------------------------------------|------------------------------------------|--|
| Subject group type                                  | Reporting group                            | Reporting group                          | Reporting group                          |  |
| Number of subjects analysed                         | 6                                          | 12                                       | 12                                       |  |
| Units: hours*nanograms/millilitres (h*ng/mL)        |                                            |                                          |                                          |  |
| geometric mean (geometric coefficient of variation) |                                            |                                          |                                          |  |
| C1D1<br>(n=0,0,3,3,7,8,5,0,0,8,4,8,8,6,11,12)       | 9360 (± 101.3)                             | 2930 (± 74.3)                            | 11800 (± 195.7)                          |  |
| C2D1<br>(n=1,0,2,2,7,4,0,0,0,7,3,6,4,4,9,6)         | 11000 (± 52.5)                             | 4180 (± 52.6)                            | 8940 (± 203.4)                           |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase 1a and 1b: Area Under the Concentration-time Curve From Time Zero to Infinity (AUC0-inf) of ASTX295

|                 |                                                                                                                           |
|-----------------|---------------------------------------------------------------------------------------------------------------------------|
| End point title | Phase 1a and 1b: Area Under the Concentration-time Curve From Time Zero to Infinity (AUC0-inf) of ASTX295 <sup>[14]</sup> |
|-----------------|---------------------------------------------------------------------------------------------------------------------------|

End point description:

PK analysis set included all subjects who received the study drug and have post baseline plasma concentration data. Here, '99999' indicates that values were not measurable due to low number of subjects for the specified arms. 'Subjects analysed' indicates number of subjects with data available for analyses and 'n' indicates number of subjects with data available for analyses at the specified timepoint.

End point type Secondary

End point timeframe:

Pre-dose on Day 1 and Day 2 of Cycles 1 and 2, and at multiple timepoints post-dose on Day 1 of Cycles 1 and 2 (Cycle length = 28 days).

Notes:

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

Justification: Descriptive statistics were provided for this endpoint.

| End point values                                    | Dose Escalation: Phase 1a: Cohort 1 | Dose Escalation: Phase 1a: Cohort 2 | Dose Escalation: Phase 1a: Cohort 3 | Dose Escalation: Phase 1a: Cohort 4 |
|-----------------------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|
| Subject group type                                  | Reporting group                     | Reporting group                     | Reporting group                     | Reporting group                     |
| Number of subjects analysed                         | 0 <sup>[15]</sup>                   | 1                                   | 4                                   | 4                                   |
| Units: h*ng/mL                                      |                                     |                                     |                                     |                                     |
| geometric mean (geometric coefficient of variation) |                                     |                                     |                                     |                                     |
| C1D1<br>(n=0,0,2,4,5,7,3,3,6,4,6,7,6,7,9)           | ()                                  | 99999 (± 99999)                     | 1550 (± 986.8)                      | 1250 (± 42.5)                       |
| C2D1<br>(n=0,1,2,2,6,4,0,1,2,4,3,3,4,4,7,5)         | ()                                  | 261 (± 99999)                       | 1660 (± 90.1)                       | 2330 (± 51.5)                       |

Notes:

[15] - Data was not reported as no subjects were available for analyses at the specified timepoint.

| End point values                                    | Dose Escalation: Phase 1a: Cohort 5 | Dose Escalation: Phase 1a: Cohort 6 | Dose Escalation: Phase 1a: Cohort 8 | Dose Escalation: Phase 1a: Cohort 9 |
|-----------------------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|
| Subject group type                                  | Reporting group                     | Reporting group                     | Reporting group                     | Reporting group                     |
| Number of subjects analysed                         | 9                                   | 8                                   | 5                                   | 7                                   |
| Units: h*ng/mL                                      |                                     |                                     |                                     |                                     |
| geometric mean (geometric coefficient of variation) |                                     |                                     |                                     |                                     |
| C1D1<br>(n=0,0,2,4,5,7,3,3,3,6,4,6,7,6,7,9)         | 3670 (± 40.8)                       | 3300 (± 138.5)                      | 1190 (± 43.0)                       | 4350 (± 211.2)                      |
| C2D1<br>(n=0,1,2,2,6,4,0,1,2,4,3,3,4,4,7,5)         | 4400 (± 50.6)                       | 2820 (± 83.3)                       | 2160 (± 99999)                      | 5250 (± 49.4)                       |

| End point values                                    | Dose Escalation: Phase 1a: Cohort 10 | Dose Escalation: Phase 1a: Cohort 11 | Dose Escalation: Phase 1a: Cohort 12 | Dose Escalation: Phase 1a: Cohort 13 |
|-----------------------------------------------------|--------------------------------------|--------------------------------------|--------------------------------------|--------------------------------------|
| Subject group type                                  | Reporting group                      | Reporting group                      | Reporting group                      | Reporting group                      |
| Number of subjects analysed                         | 8                                    | 4                                    | 9                                    | 8                                    |
| Units: h*ng/mL                                      |                                      |                                      |                                      |                                      |
| geometric mean (geometric coefficient of variation) |                                      |                                      |                                      |                                      |

|                                             |                 |               |                 |                 |
|---------------------------------------------|-----------------|---------------|-----------------|-----------------|
| C1D1<br>(n=0,0,2,4,5,7,3,3,3,6,4,6,7,6,7,9) | 13000 (± 190.6) | 3380 (± 63.3) | 10200 (± 215.9) | 9680 (± 221.2)  |
| C2D1<br>(n=0,1,2,2,6,4,0,1,2,4,3,3,4,4,7,5) | 16700 (± 112.8) | 3150 (± 36.1) | 13500 (± 75.4)  | 10800 (± 179.3) |

| End point values                                    | Dose Escalation:<br>Phase 1a:<br>Cohort 14 | Dose Expansion:<br>Phase 1b:<br>Cohort 1 | Dose Expansion:<br>Phase 1b:<br>Cohort 2 |  |
|-----------------------------------------------------|--------------------------------------------|------------------------------------------|------------------------------------------|--|
| Subject group type                                  | Reporting group                            | Reporting group                          | Reporting group                          |  |
| Number of subjects analysed                         | 6                                          | 12                                       | 12                                       |  |
| Units: h*ng/mL                                      |                                            |                                          |                                          |  |
| geometric mean (geometric coefficient of variation) |                                            |                                          |                                          |  |
| C1D1<br>(n=0,0,2,4,5,7,3,3,3,6,4,6,7,6,7,9)         | 9540 (± 101.0)                             | 2390 (± 74.6)                            | 13500 (± 176.3)                          |  |
| C2D1<br>(n=0,1,2,2,6,4,0,1,2,4,3,3,4,4,7,5)         | 11200 (± 51.8)                             | 4590 (± 46.1)                            | 12400 (± 169.9)                          |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase 1a: AUC0-24 of ASTX295 Under Fed State

|                 |                                                              |
|-----------------|--------------------------------------------------------------|
| End point title | Phase 1a: AUC0-24 of ASTX295 Under Fed State <sup>[16]</sup> |
|-----------------|--------------------------------------------------------------|

End point description:

PK analysis set included all subjects who received the study drug and have post baseline plasma concentration data. Here, '99999' indicates that values were not measurable due to low number of subjects for the specified arms. 'Subjects analysed' indicates number of subjects with data available for analyses and 'n' indicates number of subjects with data available for analyses at the specified timepoint.

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

End point timeframe:

Pre-dose on Day 1 and Day 2 of Cycles 1 and 2, and at multiple timepoints post-dose on Day 1 of Cycles 1 and 2 (Cycle length = 28 days).

Notes:

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

Justification: Descriptive statistics were provided for this endpoint.

| End point values                                    | Dose Escalation:<br>Phase 1a:<br>Cohort 7 |  |  |  |
|-----------------------------------------------------|-------------------------------------------|--|--|--|
| Subject group type                                  | Reporting group                           |  |  |  |
| Number of subjects analysed                         | 5                                         |  |  |  |
| Units: h*ng/mL                                      |                                           |  |  |  |
| geometric mean (geometric coefficient of variation) |                                           |  |  |  |
| C1D1 (n=5)                                          | 5730 (± 57.9)                             |  |  |  |
| C2D1 (n=0)                                          | 99999 (± 99999)                           |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 1a: AUClast of ASTX295 Under Fed State

|                 |                                                              |
|-----------------|--------------------------------------------------------------|
| End point title | Phase 1a: AUClast of ASTX295 Under Fed State <sup>[17]</sup> |
|-----------------|--------------------------------------------------------------|

End point description:

PK analysis set included all subjects who received the study drug and have post baseline plasma concentration data. Here, '99999' indicates that values were not measurable due to low number of subjects for the specified arms. 'Subjects analysed' indicates number of subjects with data available for analyses and 'n' indicates number of subjects with data available for analyses at the specified timepoint.

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

End point timeframe:

Pre-dose on Day 1 and Day 2 of Cycles 1 and 2, and at multiple timepoints post-dose on Day 1 of Cycles 1 and 2 (Cycle length = 28 days).

Notes:

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

Justification: Descriptive statistics were provided for this endpoint.

| End point values                                    | Dose Escalation: Phase 1a: Cohort 7 |  |  |  |
|-----------------------------------------------------|-------------------------------------|--|--|--|
| Subject group type                                  | Reporting group                     |  |  |  |
| Number of subjects analysed                         | 5                                   |  |  |  |
| Units: h*ng/mL                                      |                                     |  |  |  |
| geometric mean (geometric coefficient of variation) |                                     |  |  |  |
| C1D1 (n=5)                                          | 5720 (± 58.3)                       |  |  |  |
| C2D1 (n=1)                                          | 427 (± 99999)                       |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 1a: AUC0-inf of ASTX295 Under Fed State

|                 |                                                               |
|-----------------|---------------------------------------------------------------|
| End point title | Phase 1a: AUC0-inf of ASTX295 Under Fed State <sup>[18]</sup> |
|-----------------|---------------------------------------------------------------|

End point description:

PK analysis set included all subjects who received the study drug and have post baseline plasma concentration data. Here, '99999' indicates that values were not measurable due to low number of subjects for the specified arms. 'Subjects analysed' indicates number of subjects with data available for analyses and 'n' indicates number of subjects with data available for analyses at the specified timepoint.

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

End point timeframe:

Pre-dose on Day 1 and Day 2 of Cycles 1 and 2, and at multiple timepoints post-dose on Day 1 of Cycles 1 and 2 (Cycle length = 28 days).

Notes:

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

Justification: Descriptive statistics were provided for this endpoint.

| End point values                                    | Dose Escalation: Phase 1a: Cohort 7 |  |  |  |
|-----------------------------------------------------|-------------------------------------|--|--|--|
| Subject group type                                  | Reporting group                     |  |  |  |
| Number of subjects analysed                         | 5                                   |  |  |  |
| Units: h*ng/mL                                      |                                     |  |  |  |
| geometric mean (geometric coefficient of variation) |                                     |  |  |  |
| C1D1 (n=3)                                          | 7200 ( $\pm$ 26.9)                  |  |  |  |
| C2D1 (n=0)                                          | 99999 ( $\pm$ 99999)                |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase 1a: Cmax of ASTX295 Under Fed State

|                 |                                                           |
|-----------------|-----------------------------------------------------------|
| End point title | Phase 1a: Cmax of ASTX295 Under Fed State <sup>[19]</sup> |
|-----------------|-----------------------------------------------------------|

End point description:

PK analysis set included all subjects who received the study drug and have post baseline plasma concentration data. Here, '99999' indicates that dispersion values were not measurable due to low number of subjects for the specified arms. 'Subjects analysed' indicates number of subjects with data available for analyses and 'n' indicates number of subjects with data available for analyses at the specified timepoint.

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

End point timeframe:

Pre-dose on Day 1 and Day 2 of Cycles 1 and 2, and at multiple timepoints post-dose on Day 1 of Cycles 1 and 2 (Cycle length = 28 days).

Notes:

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

Justification: Descriptive statistics were provided for this endpoint.

| End point values                                    | Dose Escalation: Phase 1a: Cohort 7 |  |  |  |
|-----------------------------------------------------|-------------------------------------|--|--|--|
| Subject group type                                  | Reporting group                     |  |  |  |
| Number of subjects analysed                         | 5                                   |  |  |  |
| Units: ng/mL                                        |                                     |  |  |  |
| geometric mean (geometric coefficient of variation) |                                     |  |  |  |
| C1D1 (n=5)                                          | 1970 ( $\pm$ 88.4)                  |  |  |  |
| C2D1 (n=1)                                          | 43.1 ( $\pm$ 99999)                 |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 1a: Cmin of ASTX295 Under Fed State

|                 |                                                           |
|-----------------|-----------------------------------------------------------|
| End point title | Phase 1a: Cmin of ASTX295 Under Fed State <sup>[20]</sup> |
|-----------------|-----------------------------------------------------------|

End point description:

PK analysis set included all subjects who received the study drug and have post baseline plasma concentration data. Here, '99999' indicates that dispersion values were not measurable due to low number of subjects. 'Subjects analysed' indicates number of subjects with data available for analyses.

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

End point timeframe:

Pre-dose on Day 1 and Day 2 of Cycles 1 and 2, and at multiple timepoints post-dose on Day 1 of Cycles 1 and 2 (Cycle length = 28 days).

Notes:

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

Justification: Descriptive statistics were provided for this endpoint.

| End point values                                    | Dose Escalation: Phase 1a: Cohort 7 |  |  |  |
|-----------------------------------------------------|-------------------------------------|--|--|--|
| Subject group type                                  | Reporting group                     |  |  |  |
| Number of subjects analysed                         | 1                                   |  |  |  |
| Units: ng/mL                                        |                                     |  |  |  |
| geometric mean (geometric coefficient of variation) |                                     |  |  |  |
| C2D1                                                | 5.88 (± 99999)                      |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 1a: Tmax of ASTX295 Under Fed State

|                 |                                                           |
|-----------------|-----------------------------------------------------------|
| End point title | Phase 1a: Tmax of ASTX295 Under Fed State <sup>[21]</sup> |
|-----------------|-----------------------------------------------------------|

End point description:

PK analysis set included all subjects who received the study drug and have post baseline plasma concentration data. Here, '99999' indicates that dispersion values were not measurable due to low number of subjects for the specified arms. 'Subjects analysed' indicates number of subjects with data available for analyses and 'n' indicates number of subjects with data available for analyses at the specified timepoint.

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

End point timeframe:

Pre-dose on Day 1 and Day 2 of Cycles 1 and 2, and at multiple timepoints post-dose on Day 1 of Cycles 1 and 2 (Cycle length = 28 days).

Notes:

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

Justification: Descriptive statistics were provided for this endpoint.

| End point values              | Dose Escalation:<br>Phase 1a:<br>Cohort 7 |  |  |  |
|-------------------------------|-------------------------------------------|--|--|--|
| Subject group type            | Reporting group                           |  |  |  |
| Number of subjects analysed   | 5                                         |  |  |  |
| Units: hours                  |                                           |  |  |  |
| median (full range (min-max)) |                                           |  |  |  |
| C1D1 (n=5)                    | 3.87 (1.02 to 4.17)                       |  |  |  |
| C2D1 (n=1)                    | 7.33 (-99999 to 99999)                    |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase 1a: The t1/2 of ASTX295 Under Fed State

|                 |                                                               |
|-----------------|---------------------------------------------------------------|
| End point title | Phase 1a: The t1/2 of ASTX295 Under Fed State <sup>[22]</sup> |
|-----------------|---------------------------------------------------------------|

End point description:

PK analysis set included all subjects who received the study drug and have post baseline plasma concentration data. Here, '99999' indicates that dispersion values were not measurable due to low number of subjects for the specified arms. 'Subjects analysed' indicates number of subjects with data available for analyses and 'n' indicates number of subjects with data available for analyses at the specified timepoint.

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

End point timeframe:

Pre-dose on Day 1 and Day 2 of Cycles 1 and 2, and at multiple timepoints post-dose on Day 1 of Cycles 1 and 2 (Cycle length = 28 days).

Notes:

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

Justification: Descriptive statistics were provided for this endpoint.

| End point values                                    | Dose Escalation:<br>Phase 1a:<br>Cohort 7 |  |  |  |
|-----------------------------------------------------|-------------------------------------------|--|--|--|
| Subject group type                                  | Reporting group                           |  |  |  |
| Number of subjects analysed                         | 3                                         |  |  |  |
| Units: hours                                        |                                           |  |  |  |
| geometric mean (geometric coefficient of variation) |                                           |  |  |  |
| C1D1 (n=3)                                          | 6.55 (± 36.7)                             |  |  |  |
| C2D1 (n=0)                                          | 99999 (± 99999)                           |  |  |  |

## **Statistical analyses**

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to approximately 61.3 months

Adverse event reporting additional description:

Safety analysis set included all subjects who received at least one dose of study drug.

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 27.0 |
|--------------------|------|

### Reporting groups

|                       |                                     |
|-----------------------|-------------------------------------|
| Reporting group title | Dose Escalation: Phase 1a: Cohort 1 |
|-----------------------|-------------------------------------|

Reporting group description:

Subjects received ASTX295 at starting dose of 15 milligrams (mg), orally, administered once daily (QD) in each 28-day cycle under fasted condition, up to a maximum of 1.8 months.

|                       |                                     |
|-----------------------|-------------------------------------|
| Reporting group title | Dose Escalation: Phase 1a: Cohort 2 |
|-----------------------|-------------------------------------|

Reporting group description:

Subjects received ASTX295 at an oral dose of 45 mg, administered QD in each 28-day cycle under fasted condition, up to a maximum of 17.4 months.

|                       |                                     |
|-----------------------|-------------------------------------|
| Reporting group title | Dose Escalation: Phase 1a: Cohort 3 |
|-----------------------|-------------------------------------|

Reporting group description:

Subjects received ASTX295 at an oral dose of 120 mg, administered QD in each 28-day cycle under fasted condition, up to a maximum of 1.8 months.

|                       |                                     |
|-----------------------|-------------------------------------|
| Reporting group title | Dose Escalation: Phase 1a: Cohort 4 |
|-----------------------|-------------------------------------|

Reporting group description:

Subjects received ASTX295 at an oral dose of 240 mg, administered QD in each 28-day cycle under fasted condition, up to a maximum of 6.4 months.

|                       |                                     |
|-----------------------|-------------------------------------|
| Reporting group title | Dose Escalation: Phase 1a: Cohort 5 |
|-----------------------|-------------------------------------|

Reporting group description:

Subjects received ASTX295 at an oral dose of 420 mg, administered QD in each 28-day cycle under fasted condition, up to a maximum of 14.7 months.

|                       |                                     |
|-----------------------|-------------------------------------|
| Reporting group title | Dose Escalation: Phase 1a: Cohort 6 |
|-----------------------|-------------------------------------|

Reporting group description:

Subjects received ASTX295 at an oral dose of 520 mg, administered QD in each 28-day cycle under fasted condition, up to a maximum of 42.4 months.

|                       |                                     |
|-----------------------|-------------------------------------|
| Reporting group title | Dose Escalation: Phase 1a: Cohort 7 |
|-----------------------|-------------------------------------|

Reporting group description:

Subjects received ASTX295 at an oral dose of 415 mg, administered QD in each 28-day cycle under fed state, up to a maximum of 22.5 months.

|                       |                                     |
|-----------------------|-------------------------------------|
| Reporting group title | Dose Escalation: Phase 1a: Cohort 8 |
|-----------------------|-------------------------------------|

Reporting group description:

Subjects received ASTX295 at an oral dose of 200 mg, administered twice daily (BID) in each 28-day cycle under fasted condition, up to a maximum of 17.4 months.

|                       |                                     |
|-----------------------|-------------------------------------|
| Reporting group title | Dose Escalation: Phase 1a: Cohort 9 |
|-----------------------|-------------------------------------|

Reporting group description:

Subjects received ASTX295 at an oral dose of 320 mg, administered BID in each 28-day cycle under fasted condition, up to a maximum of 27.5 months.

|                       |                                      |
|-----------------------|--------------------------------------|
| Reporting group title | Dose Escalation: Phase 1a: Cohort 10 |
|-----------------------|--------------------------------------|

Reporting group description:

Subjects received ASTX295 at an oral dose of 520 mg (5 days on, 2 days off), administered QD in each 28-day cycle, with or without food, up to a maximum of 12 months.

|                       |                                      |
|-----------------------|--------------------------------------|
| Reporting group title | Dose Escalation: Phase 1a: Cohort 11 |
|-----------------------|--------------------------------------|

Reporting group description:

Subjects received ASTX295 at an oral dose of 520 mg (3 days on, 4 days off), administered QD in each 28-day cycle, with or without food, up to a maximum of 1.8 months.

|                       |                                      |
|-----------------------|--------------------------------------|
| Reporting group title | Dose Escalation: Phase 1a: Cohort 12 |
|-----------------------|--------------------------------------|

Reporting group description:

Subjects received ASTX295 at an oral dose of 660 mg, administered QD, twice a week, in each 28-day cycle, with or without food, up to a maximum of 11.7 months.

|                       |                                      |
|-----------------------|--------------------------------------|
| Reporting group title | Dose Escalation: Phase 1a: Cohort 13 |
|-----------------------|--------------------------------------|

Reporting group description:

Subjects received ASTX295 at an oral dose of 660 mg (3 days on, 4 days off), administered QD, in each 28-day cycle, with or without food, up to a maximum of 18.5 months.

|                       |                                      |
|-----------------------|--------------------------------------|
| Reporting group title | Dose Escalation: Phase 1a: Cohort 14 |
|-----------------------|--------------------------------------|

Reporting group description:

Subjects received ASTX295 at an oral dose of 800 mg, administered QD, twice a week, in each 28-day cycle, with or without food, up to a maximum of 6 months.

|                       |                                    |
|-----------------------|------------------------------------|
| Reporting group title | Dose Expansion: Phase 1b: Cohort 1 |
|-----------------------|------------------------------------|

Reporting group description:

Subjects received ASTX295 at an oral dose of 400 mg, administered daily, in each 28-day cycle, with or without food, up to a maximum of 14.7 months.

|                       |                                    |
|-----------------------|------------------------------------|
| Reporting group title | Dose Expansion: Phase 1b: Cohort 2 |
|-----------------------|------------------------------------|

Reporting group description:

Subjects received ASTX295 at an oral dose of 660 mg, administered QD, twice a week, in each 28-day cycle, with or without food, up to a maximum of 14.2 months.

| Serious adverse events                            | Dose Escalation:<br>Phase 1a: Cohort 1 | Dose Escalation:<br>Phase 1a: Cohort 2 | Dose Escalation:<br>Phase 1a: Cohort 3 |
|---------------------------------------------------|----------------------------------------|----------------------------------------|----------------------------------------|
| Total subjects affected by serious adverse events |                                        |                                        |                                        |
| subjects affected / exposed                       | 0 / 1 (0.00%)                          | 0 / 3 (0.00%)                          | 2 / 4 (50.00%)                         |
| number of deaths (all causes)                     | 1                                      | 0                                      | 2                                      |
| number of deaths resulting from adverse events    | 0                                      | 0                                      | 0                                      |
| Investigations                                    |                                        |                                        |                                        |
| Alanine aminotransferase increased                |                                        |                                        |                                        |
| subjects affected / exposed                       | 0 / 1 (0.00%)                          | 0 / 3 (0.00%)                          | 0 / 4 (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    |                                        |                                        |                                        |
| Fall                                              |                                        |                                        |                                        |
| subjects affected / exposed                       | 0 / 1 (0.00%)                          | 0 / 3 (0.00%)                          | 0 / 4 (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                                  |
| Abdominal wall wound                              |                                        |                                        |                                        |

|                                                      |               |               |                |
|------------------------------------------------------|---------------|---------------|----------------|
| subjects affected / exposed                          | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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                                   |               |               |                |
| Hypotension                                          |               |               |                |
| subjects affected / exposed                          | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 0         | 0 / 0         | 0 / 0          |
| Cardiac disorders                                    |               |               |                |
| Atrial fibrillation                                  |               |               |                |
| subjects affected / exposed                          | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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          |
| Pericardial effusion                                 |               |               |                |
| subjects affected / exposed                          | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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                             |               |               |                |
| Loss of consciousness                                |               |               |                |
| subjects affected / exposed                          | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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          |
| Seizure                                              |               |               |                |
| subjects affected / exposed                          | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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          |
| Hemiparesis                                          |               |               |                |
| subjects affected / exposed                          | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |               |               |                |
| Asthenia                                             |               |               |                |

|                                                 |               |               |               |
|-------------------------------------------------|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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         |
| Blood and lymphatic system disorders            |               |               |               |
| Anaemia                                         |               |               |               |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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                      |               |               |               |
| Gastrointestinal haemorrhage                    |               |               |               |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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         |
| Small intestinal obstruction                    |               |               |               |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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         |
| Abdominal pain                                  |               |               |               |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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         |
| Oesophageal obstruction                         |               |               |               |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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         |
| Haemoperitoneum                                 |               |               |               |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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         |
| Hepatobiliary disorders                         |               |               |               |

|                                                 |               |               |                |
|-------------------------------------------------|---------------|---------------|----------------|
| Hyperbilirubinaemia                             |               |               |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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          |
| Respiratory, thoracic and mediastinal disorders |               |               |                |
| Haemoptysis                                     |               |               |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Pleural effusion                                |               |               |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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          |
| Dyspnoea                                        |               |               |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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          |
| Tracheal fistula                                |               |               |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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          |
| Pulmonary embolism                              |               |               |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 haemorrhage                               |               |               |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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<br>Pneumonia<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all | 0 / 1 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 4 (25.00%)<br>0 / 1<br>0 / 0 |
| Abdominal abscess<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                        | 0 / 1 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 4 (0.00%)<br>0 / 0<br>0 / 0  |
| Septic shock<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                             | 0 / 1 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 4 (0.00%)<br>0 / 0<br>0 / 0  |
| Skin bacterial infection<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                 | 0 / 1 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 4 (0.00%)<br>0 / 0<br>0 / 0  |
| Urinary tract infection<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                  | 0 / 1 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 4 (0.00%)<br>0 / 0<br>0 / 0  |
| Urosepsis<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                                | 0 / 1 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 4 (0.00%)<br>0 / 0<br>0 / 0  |

| <b>Serious adverse events</b>                     | Dose Escalation:<br>Phase 1a: Cohort 4 | Dose Escalation:<br>Phase 1a: Cohort 5 | Dose Escalation:<br>Phase 1a: Cohort 6 |
|---------------------------------------------------|----------------------------------------|----------------------------------------|----------------------------------------|
| Total subjects affected by serious adverse events |                                        |                                        |                                        |
| subjects affected / exposed                       | 0 / 4 (0.00%)                          | 2 / 9 (22.22%)                         | 1 / 8 (12.50%)                         |
| number of deaths (all causes)                     | 2                                      | 4                                      | 6                                      |
| number of deaths resulting from adverse events    | 0                                      | 0                                      | 0                                      |
| Investigations                                    |                                        |                                        |                                        |
| Alanine aminotransferase increased                |                                        |                                        |                                        |

|                                                 |               |                |                |
|-------------------------------------------------|---------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 1 / 8 (12.50%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Injury, poisoning and procedural complications  |               |                |                |
| Fall                                            |               |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 1 / 8 (12.50%) |
| 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 wall wound                            |               |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (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                              |               |                |                |
| Hypotension                                     |               |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (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                               |               |                |                |
| Atrial fibrillation                             |               |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (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          |
| Pericardial effusion                            |               |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (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                        |               |                |                |
| Loss of consciousness                           |               |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 1 / 9 (11.11%) | 0 / 8 (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          |
| Seizure                                         |               |                |                |

|                                                      |               |                |                |
|------------------------------------------------------|---------------|----------------|----------------|
| subjects affected / exposed                          | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (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          |
| Hemiparesis                                          |               |                |                |
| subjects affected / exposed                          | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (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 |               |                |                |
| Asthenia                                             |               |                |                |
| subjects affected / exposed                          | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (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 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (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          |
| Blood and lymphatic system disorders                 |               |                |                |
| Anaemia                                              |               |                |                |
| subjects affected / exposed                          | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (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                           |               |                |                |
| Gastrointestinal haemorrhage                         |               |                |                |
| subjects affected / exposed                          | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (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          |
| Small intestinal obstruction                         |               |                |                |
| subjects affected / exposed                          | 0 / 4 (0.00%) | 1 / 9 (11.11%) | 0 / 8 (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          |
| Abdominal pain                                       |               |                |                |
| subjects affected / exposed                          | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 1 / 8 (12.50%) |
| occurrences causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 0         | 0 / 0          | 0 / 0          |

|                                                 |               |                |                |
|-------------------------------------------------|---------------|----------------|----------------|
| Oesophageal obstruction                         |               |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 1 / 9 (11.11%) | 0 / 8 (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          |
| Haemoperitoneum                                 |               |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (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          |
| Hepatobiliary disorders                         |               |                |                |
| Hyperbilirubinaemia                             |               |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 1 / 8 (12.50%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Respiratory, thoracic and mediastinal disorders |               |                |                |
| Haemoptysis                                     |               |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (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          |
| Pleural effusion                                |               |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 1 / 9 (11.11%) | 0 / 8 (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          |
| Dyspnoea                                        |               |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (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          |
| Tracheal fistula                                |               |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (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          |
| Pulmonary embolism                              |               |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (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 / 9 (0.00%) | 0 / 8 (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 haemorrhage                               |               |               |               |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 9 (0.00%) | 0 / 8 (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                     |               |               |               |
| Pneumonia                                       |               |               |               |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 9 (0.00%) | 0 / 8 (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         |
| Abdominal abscess                               |               |               |               |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 9 (0.00%) | 0 / 8 (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         |
| Septic shock                                    |               |               |               |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 9 (0.00%) | 0 / 8 (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         |
| Skin bacterial infection                        |               |               |               |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 9 (0.00%) | 0 / 8 (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 infection                         |               |               |               |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 9 (0.00%) | 0 / 8 (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         |
| Urosepsis                                       |               |               |               |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 9 (0.00%) | 0 / 8 (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         |

| <b>Serious adverse events</b>                     | Dose Escalation:<br>Phase 1a: Cohort 7 | Dose Escalation:<br>Phase 1a: Cohort 8 | Dose Escalation:<br>Phase 1a: Cohort 9 |
|---------------------------------------------------|----------------------------------------|----------------------------------------|----------------------------------------|
| Total subjects affected by serious adverse events |                                        |                                        |                                        |
| subjects affected / exposed                       | 1 / 5 (20.00%)                         | 2 / 6 (33.33%)                         | 0 / 7 (0.00%)                          |
| number of deaths (all causes)                     | 3                                      | 4                                      | 3                                      |
| number of deaths resulting from adverse events    | 1                                      | 1                                      | 0                                      |
| Investigations                                    |                                        |                                        |                                        |
| Alanine aminotransferase increased                |                                        |                                        |                                        |
| subjects affected / exposed                       | 0 / 5 (0.00%)                          | 0 / 6 (0.00%)                          | 0 / 7 (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    |                                        |                                        |                                        |
| Fall                                              |                                        |                                        |                                        |
| subjects affected / exposed                       | 0 / 5 (0.00%)                          | 0 / 6 (0.00%)                          | 0 / 7 (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                                  |
| Abdominal wall wound                              |                                        |                                        |                                        |
| subjects affected / exposed                       | 0 / 5 (0.00%)                          | 0 / 6 (0.00%)                          | 0 / 7 (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                                |                                        |                                        |                                        |
| Hypotension                                       |                                        |                                        |                                        |
| subjects affected / exposed                       | 0 / 5 (0.00%)                          | 0 / 6 (0.00%)                          | 0 / 7 (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                                 |                                        |                                        |                                        |
| Atrial fibrillation                               |                                        |                                        |                                        |
| subjects affected / exposed                       | 0 / 5 (0.00%)                          | 0 / 6 (0.00%)                          | 0 / 7 (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                                  |
| Pericardial effusion                              |                                        |                                        |                                        |
| subjects affected / exposed                       | 0 / 5 (0.00%)                          | 0 / 6 (0.00%)                          | 0 / 7 (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                          |                                        |                                        |                                        |

|                                                      |                |               |               |
|------------------------------------------------------|----------------|---------------|---------------|
| Loss of consciousness                                |                |               |               |
| subjects affected / exposed                          | 0 / 5 (0.00%)  | 0 / 6 (0.00%) | 0 / 7 (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         |
| Seizure                                              |                |               |               |
| subjects affected / exposed                          | 0 / 5 (0.00%)  | 0 / 6 (0.00%) | 0 / 7 (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         |
| Hemiparesis                                          |                |               |               |
| subjects affected / exposed                          | 0 / 5 (0.00%)  | 0 / 6 (0.00%) | 0 / 7 (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 |                |               |               |
| Asthenia                                             |                |               |               |
| subjects affected / exposed                          | 0 / 5 (0.00%)  | 0 / 6 (0.00%) | 0 / 7 (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 / 5 (0.00%)  | 0 / 6 (0.00%) | 0 / 7 (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         |
| Blood and lymphatic system disorders                 |                |               |               |
| Anaemia                                              |                |               |               |
| subjects affected / exposed                          | 0 / 5 (0.00%)  | 0 / 6 (0.00%) | 0 / 7 (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                           |                |               |               |
| Gastrointestinal haemorrhage                         |                |               |               |
| subjects affected / exposed                          | 1 / 5 (20.00%) | 0 / 6 (0.00%) | 0 / 7 (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                     | 1 / 5 (20.00%) | 1 / 6 (16.67%) | 0 / 7 (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         |
| Abdominal pain                                  |                |                |               |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (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         |
| Oesophageal obstruction                         |                |                |               |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (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         |
| Haemoperitoneum                                 |                |                |               |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (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         |
| Hepatobiliary disorders                         |                |                |               |
| Hyperbilirubinaemia                             |                |                |               |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (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         |
| Respiratory, thoracic and mediastinal disorders |                |                |               |
| Haemoptysis                                     |                |                |               |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (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         |
| Pleural effusion                                |                |                |               |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (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         |
| Dyspnoea                                        |                |                |               |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 1 / 6 (16.67%) | 0 / 7 (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         |

|                                                 |               |                |               |
|-------------------------------------------------|---------------|----------------|---------------|
| Tracheal fistula                                |               |                |               |
| subjects affected / exposed                     | 0 / 5 (0.00%) | 1 / 6 (16.67%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 1          | 0 / 0         |
| Pulmonary embolism                              |               |                |               |
| subjects affected / exposed                     | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (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 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (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 haemorrhage                               |               |                |               |
| subjects affected / exposed                     | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (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                     |               |                |               |
| Pneumonia                                       |               |                |               |
| subjects affected / exposed                     | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (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         |
| Abdominal abscess                               |               |                |               |
| subjects affected / exposed                     | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (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         |
| Septic shock                                    |               |                |               |
| subjects affected / exposed                     | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (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         |
| Skin bacterial infection                        |               |                |               |
| subjects affected / exposed                     | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (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 infection                         |               |               |               |
| subjects affected / exposed                     | 0 / 5 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (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         |
| Urosepsis                                       |               |               |               |
| subjects affected / exposed                     | 0 / 5 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (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         |

| <b>Serious adverse events</b>                     | Dose Escalation:<br>Phase 1a: Cohort 10 | Dose Escalation:<br>Phase 1a: Cohort 11 | Dose Escalation:<br>Phase 1a: Cohort 12 |
|---------------------------------------------------|-----------------------------------------|-----------------------------------------|-----------------------------------------|
| Total subjects affected by serious adverse events |                                         |                                         |                                         |
| subjects affected / exposed                       | 1 / 8 (12.50%)                          | 0 / 4 (0.00%)                           | 4 / 9 (44.44%)                          |
| number of deaths (all causes)                     | 6                                       | 4                                       | 6                                       |
| number of deaths resulting from adverse events    | 0                                       | 0                                       | 0                                       |
| Investigations                                    |                                         |                                         |                                         |
| Alanine aminotransferase increased                |                                         |                                         |                                         |
| subjects affected / exposed                       | 0 / 8 (0.00%)                           | 0 / 4 (0.00%)                           | 0 / 9 (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    |                                         |                                         |                                         |
| Fall                                              |                                         |                                         |                                         |
| subjects affected / exposed                       | 0 / 8 (0.00%)                           | 0 / 4 (0.00%)                           | 0 / 9 (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                                   |
| Abdominal wall wound                              |                                         |                                         |                                         |
| subjects affected / exposed                       | 0 / 8 (0.00%)                           | 0 / 4 (0.00%)                           | 0 / 9 (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                                |                                         |                                         |                                         |
| Hypotension                                       |                                         |                                         |                                         |
| subjects affected / exposed                       | 0 / 8 (0.00%)                           | 0 / 4 (0.00%)                           | 0 / 9 (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                                 |                                         |                                         |                                         |
| Atrial fibrillation                               |                                         |                                         |                                         |

|                                                      |               |               |                |
|------------------------------------------------------|---------------|---------------|----------------|
| subjects affected / exposed                          | 0 / 8 (0.00%) | 0 / 4 (0.00%) | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 2          |
| deaths causally related to treatment / all           | 0 / 0         | 0 / 0         | 0 / 0          |
| Pericardial effusion                                 |               |               |                |
| subjects affected / exposed                          | 0 / 8 (0.00%) | 0 / 4 (0.00%) | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 0         | 0 / 0         | 0 / 0          |
| Nervous system disorders                             |               |               |                |
| Loss of consciousness                                |               |               |                |
| subjects affected / exposed                          | 0 / 8 (0.00%) | 0 / 4 (0.00%) | 0 / 9 (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          |
| Seizure                                              |               |               |                |
| subjects affected / exposed                          | 0 / 8 (0.00%) | 0 / 4 (0.00%) | 0 / 9 (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          |
| Hemiparesis                                          |               |               |                |
| subjects affected / exposed                          | 0 / 8 (0.00%) | 0 / 4 (0.00%) | 0 / 9 (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 |               |               |                |
| Asthenia                                             |               |               |                |
| subjects affected / exposed                          | 0 / 8 (0.00%) | 0 / 4 (0.00%) | 0 / 9 (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 / 8 (0.00%) | 0 / 4 (0.00%) | 0 / 9 (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          |
| Blood and lymphatic system disorders                 |               |               |                |
| Anaemia                                              |               |               |                |
| subjects affected / exposed                          | 0 / 8 (0.00%) | 0 / 4 (0.00%) | 0 / 9 (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                      |               |               |               |
| Gastrointestinal haemorrhage                    |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 4 (0.00%) | 0 / 9 (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         |
| Small intestinal obstruction                    |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 4 (0.00%) | 0 / 9 (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         |
| Abdominal pain                                  |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 4 (0.00%) | 0 / 9 (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         |
| Oesophageal obstruction                         |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 4 (0.00%) | 0 / 9 (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         |
| Haemoperitoneum                                 |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 4 (0.00%) | 0 / 9 (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         |
| Hepatobiliary disorders                         |               |               |               |
| Hyperbilirubinaemia                             |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 4 (0.00%) | 0 / 9 (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         |
| Respiratory, thoracic and mediastinal disorders |               |               |               |
| Haemoptysis                                     |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 4 (0.00%) | 0 / 9 (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         |
| Pleural effusion                                |               |               |               |

|                                                 |                |               |                |
|-------------------------------------------------|----------------|---------------|----------------|
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Dyspnoea                                        |                |               |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Tracheal fistula                                |                |               |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (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          |
| Pulmonary embolism                              |                |               |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (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 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (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 haemorrhage                               |                |               |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (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                     |                |               |                |
| Pneumonia                                       |                |               |                |
| subjects affected / exposed                     | 1 / 8 (12.50%) | 0 / 4 (0.00%) | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Abdominal abscess                               |                |               |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Septic shock                                    |                |               |                |

|                                                 |               |               |                |
|-------------------------------------------------|---------------|---------------|----------------|
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 4 (0.00%) | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Skin bacterial infection                        |               |               |                |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 4 (0.00%) | 0 / 9 (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 infection                         |               |               |                |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 4 (0.00%) | 0 / 9 (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          |
| Urosepsis                                       |               |               |                |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 4 (0.00%) | 0 / 9 (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          |

| <b>Serious adverse events</b>                     | Dose Escalation:<br>Phase 1a: Cohort 13 | Dose Escalation:<br>Phase 1a: Cohort 14 | Dose Expansion:<br>Phase 1b: Cohort 1 |
|---------------------------------------------------|-----------------------------------------|-----------------------------------------|---------------------------------------|
| Total subjects affected by serious adverse events |                                         |                                         |                                       |
| subjects affected / exposed                       | 1 / 8 (12.50%)                          | 4 / 6 (66.67%)                          | 6 / 12 (50.00%)                       |
| number of deaths (all causes)                     | 5                                       | 5                                       | 4                                     |
| number of deaths resulting from adverse events    | 0                                       | 1                                       | 0                                     |
| Investigations                                    |                                         |                                         |                                       |
| Alanine aminotransferase increased                |                                         |                                         |                                       |
| subjects affected / exposed                       | 0 / 8 (0.00%)                           | 0 / 6 (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                                 |
| Injury, poisoning and procedural complications    |                                         |                                         |                                       |
| Fall                                              |                                         |                                         |                                       |
| subjects affected / exposed                       | 0 / 8 (0.00%)                           | 0 / 6 (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                                 |
| Abdominal wall wound                              |                                         |                                         |                                       |

|                                                      |                |                |                |
|------------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                          | 0 / 8 (0.00%)  | 0 / 6 (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          |
| Vascular disorders                                   |                |                |                |
| Hypotension                                          |                |                |                |
| subjects affected / exposed                          | 0 / 8 (0.00%)  | 0 / 6 (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          |
| Cardiac disorders                                    |                |                |                |
| Atrial fibrillation                                  |                |                |                |
| subjects affected / exposed                          | 0 / 8 (0.00%)  | 0 / 6 (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          |
| Pericardial effusion                                 |                |                |                |
| subjects affected / exposed                          | 0 / 8 (0.00%)  | 0 / 6 (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          |
| Nervous system disorders                             |                |                |                |
| Loss of consciousness                                |                |                |                |
| subjects affected / exposed                          | 0 / 8 (0.00%)  | 0 / 6 (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          |
| Seizure                                              |                |                |                |
| subjects affected / exposed                          | 0 / 8 (0.00%)  | 1 / 6 (16.67%) | 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          |
| Hemiparesis                                          |                |                |                |
| subjects affected / exposed                          | 1 / 8 (12.50%) | 0 / 6 (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          |
| General disorders and administration site conditions |                |                |                |
| Asthenia                                             |                |                |                |

|                                                 |               |                |                |
|-------------------------------------------------|---------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 6 (0.00%)  | 1 / 12 (8.33%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Oedema                                          |               |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 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          |
| Blood and lymphatic system disorders            |               |                |                |
| Anaemia                                         |               |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 6 (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                      |               |                |                |
| Gastrointestinal haemorrhage                    |               |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 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          |
| Small intestinal obstruction                    |               |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 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          |
| Abdominal pain                                  |               |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 6 (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          |
| Oesophageal obstruction                         |               |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 6 (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          |
| Haemoperitoneum                                 |               |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 6 (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          |
| Hepatobiliary disorders                         |               |                |                |

|                                                 |               |                |                 |
|-------------------------------------------------|---------------|----------------|-----------------|
| Hyperbilirubinaemia                             |               |                |                 |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 6 (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           |
| Respiratory, thoracic and mediastinal disorders |               |                |                 |
| Haemoptysis                                     |               |                |                 |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 6 (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           |
| Pleural effusion                                |               |                |                 |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 6 (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           |
| Dyspnoea                                        |               |                |                 |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 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           |
| Tracheal fistula                                |               |                |                 |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 6 (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           |
| Pulmonary embolism                              |               |                |                 |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 6 (0.00%)  | 2 / 12 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Renal and urinary disorders                     |               |                |                 |
| Acute kidney injury                             |               |                |                 |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 6 (0.00%)  | 2 / 12 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Renal haemorrhage                               |               |                |                 |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 6 (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<br>Pneumonia<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all | 0 / 8 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 6 (16.67%)<br>0 / 1<br>0 / 1 | 0 / 12 (0.00%)<br>0 / 0<br>0 / 0 |
| Abdominal abscess<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                        | 0 / 8 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 6 (0.00%)<br>0 / 0<br>0 / 0  | 0 / 12 (0.00%)<br>0 / 0<br>0 / 0 |
| Septic shock<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                             | 0 / 8 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 6 (0.00%)<br>0 / 0<br>0 / 0  | 0 / 12 (0.00%)<br>0 / 0<br>0 / 0 |
| Skin bacterial infection<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                 | 0 / 8 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 6 (0.00%)<br>0 / 0<br>0 / 0  | 1 / 12 (8.33%)<br>0 / 1<br>0 / 0 |
| Urinary tract infection<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                  | 0 / 8 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 6 (0.00%)<br>0 / 0<br>0 / 0  | 1 / 12 (8.33%)<br>0 / 1<br>0 / 0 |
| Urosepsis<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                                | 0 / 8 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 6 (0.00%)<br>0 / 0<br>0 / 0  | 1 / 12 (8.33%)<br>0 / 1<br>0 / 0 |

|                                                   |                                       |  |  |
|---------------------------------------------------|---------------------------------------|--|--|
| <b>Serious adverse events</b>                     | Dose Expansion:<br>Phase 1b: Cohort 2 |  |  |
| Total subjects affected by serious adverse events |                                       |  |  |
| subjects affected / exposed                       | 4 / 12 (33.33%)                       |  |  |
| number of deaths (all causes)                     | 3                                     |  |  |
| number of deaths resulting from adverse events    | 0                                     |  |  |
| Investigations                                    |                                       |  |  |
| Alanine aminotransferase increased                |                                       |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed                     | 0 / 12 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Injury, poisoning and procedural complications  |                |  |  |
| Fall                                            |                |  |  |
| subjects affected / exposed                     | 0 / 12 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Abdominal wall wound                            |                |  |  |
| subjects affected / exposed                     | 0 / 12 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Vascular disorders                              |                |  |  |
| Hypotension                                     |                |  |  |
| subjects affected / exposed                     | 0 / 12 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Cardiac disorders                               |                |  |  |
| Atrial fibrillation                             |                |  |  |
| subjects affected / exposed                     | 1 / 12 (8.33%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Pericardial effusion                            |                |  |  |
| subjects affected / exposed                     | 0 / 12 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Nervous system disorders                        |                |  |  |
| Loss of consciousness                           |                |  |  |
| subjects affected / exposed                     | 0 / 12 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Seizure                                         |                |  |  |

|                                                      |                |  |  |
|------------------------------------------------------|----------------|--|--|
| subjects affected / exposed                          | 0 / 12 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Hemiparesis                                          |                |  |  |
| subjects affected / exposed                          | 0 / 12 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| General disorders and administration site conditions |                |  |  |
| Asthenia                                             |                |  |  |
| subjects affected / exposed                          | 0 / 12 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Oedema                                               |                |  |  |
| subjects affected / exposed                          | 0 / 12 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Blood and lymphatic system disorders                 |                |  |  |
| Anaemia                                              |                |  |  |
| subjects affected / exposed                          | 1 / 12 (8.33%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Gastrointestinal disorders                           |                |  |  |
| Gastrointestinal haemorrhage                         |                |  |  |
| subjects affected / exposed                          | 0 / 12 (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 / 12 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Abdominal pain                                       |                |  |  |
| subjects affected / exposed                          | 1 / 12 (8.33%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| Oesophageal obstruction                         |                |  |  |
| subjects affected / exposed                     | 0 / 12 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Haemoperitoneum                                 |                |  |  |
| subjects affected / exposed                     | 1 / 12 (8.33%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Hepatobiliary disorders                         |                |  |  |
| Hyperbilirubinaemia                             |                |  |  |
| subjects affected / exposed                     | 0 / 12 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Respiratory, thoracic and mediastinal disorders |                |  |  |
| Haemoptysis                                     |                |  |  |
| subjects affected / exposed                     | 0 / 12 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Pleural effusion                                |                |  |  |
| subjects affected / exposed                     | 0 / 12 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Dyspnoea                                        |                |  |  |
| subjects affected / exposed                     | 0 / 12 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Tracheal fistula                                |                |  |  |
| subjects affected / exposed                     | 0 / 12 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Pulmonary embolism                              |                |  |  |
| subjects affected / exposed                     | 0 / 12 (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 / 12 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Renal haemorrhage                               |                |  |  |
| subjects affected / exposed                     | 1 / 12 (8.33%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Infections and infestations                     |                |  |  |
| Pneumonia                                       |                |  |  |
| subjects affected / exposed                     | 0 / 12 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Abdominal abscess                               |                |  |  |
| subjects affected / exposed                     | 0 / 12 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Septic shock                                    |                |  |  |
| subjects affected / exposed                     | 0 / 12 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Skin bacterial infection                        |                |  |  |
| subjects affected / exposed                     | 0 / 12 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Urinary tract infection                         |                |  |  |
| subjects affected / exposed                     | 0 / 12 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Urosepsis                                       |                |  |  |
| subjects affected / exposed                     | 0 / 12 (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 %

| <b>Non-serious adverse events</b>                                                                                                      | Dose Escalation:<br>Phase 1a: Cohort 1 | Dose Escalation:<br>Phase 1a: Cohort 2 | Dose Escalation:<br>Phase 1a: Cohort 3 |
|----------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------|----------------------------------------|----------------------------------------|
| Total subjects affected by non-serious adverse events<br>subjects affected / exposed                                                   | 1 / 1 (100.00%)                        | 3 / 3 (100.00%)                        | 4 / 4 (100.00%)                        |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps)<br>Cancer pain<br>subjects affected / exposed<br>occurrences (all) | 0 / 1 (0.00%)<br>0                     | 0 / 3 (0.00%)<br>0                     | 2 / 4 (50.00%)<br>2                    |
| Tumour pain<br>subjects affected / exposed<br>occurrences (all)                                                                        | 0 / 1 (0.00%)<br>0                     | 0 / 3 (0.00%)<br>0                     | 0 / 4 (0.00%)<br>0                     |
| Vascular disorders<br>Hypotension<br>subjects affected / exposed<br>occurrences (all)                                                  | 0 / 1 (0.00%)<br>0                     | 0 / 3 (0.00%)<br>0                     | 0 / 4 (0.00%)<br>0                     |
| Deep vein thrombosis<br>subjects affected / exposed<br>occurrences (all)                                                               | 0 / 1 (0.00%)<br>0                     | 0 / 3 (0.00%)<br>0                     | 0 / 4 (0.00%)<br>0                     |
| Hypertension<br>subjects affected / exposed<br>occurrences (all)                                                                       | 0 / 1 (0.00%)<br>0                     | 0 / 3 (0.00%)<br>0                     | 0 / 4 (0.00%)<br>0                     |
| Embolism<br>subjects affected / exposed<br>occurrences (all)                                                                           | 0 / 1 (0.00%)<br>0                     | 0 / 3 (0.00%)<br>0                     | 0 / 4 (0.00%)<br>0                     |
| Hot flush<br>subjects affected / exposed<br>occurrences (all)                                                                          | 0 / 1 (0.00%)<br>0                     | 0 / 3 (0.00%)<br>0                     | 0 / 4 (0.00%)<br>0                     |
| Pallor<br>subjects affected / exposed<br>occurrences (all)                                                                             | 0 / 1 (0.00%)<br>0                     | 0 / 3 (0.00%)<br>0                     | 0 / 4 (0.00%)<br>0                     |
| Peripheral embolism                                                                                                                    |                                        |                                        |                                        |

|                                                      |               |                |                |
|------------------------------------------------------|---------------|----------------|----------------|
| subjects affected / exposed                          | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                                    | 0             | 0              | 0              |
| General disorders and administration site conditions |               |                |                |
| Pyrexia                                              |               |                |                |
| subjects affected / exposed                          | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 1 / 4 (25.00%) |
| occurrences (all)                                    | 0             | 0              | 1              |
| Fatigue                                              |               |                |                |
| subjects affected / exposed                          | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 2 / 4 (50.00%) |
| occurrences (all)                                    | 0             | 0              | 4              |
| Asthenia                                             |               |                |                |
| subjects affected / exposed                          | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                                    | 0             | 0              | 0              |
| Gait disturbance                                     |               |                |                |
| subjects affected / exposed                          | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                                    | 0             | 0              | 0              |
| Influenza like illness                               |               |                |                |
| subjects affected / exposed                          | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                                    | 0             | 0              | 0              |
| Non-cardiac chest pain                               |               |                |                |
| subjects affected / exposed                          | 0 / 1 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (0.00%)  |
| occurrences (all)                                    | 0             | 1              | 0              |
| Oedema peripheral                                    |               |                |                |
| subjects affected / exposed                          | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                                    | 0             | 0              | 0              |
| Chest discomfort                                     |               |                |                |
| subjects affected / exposed                          | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                                    | 0             | 0              | 0              |
| Chest pain                                           |               |                |                |
| subjects affected / exposed                          | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                                    | 0             | 0              | 0              |
| Chills                                               |               |                |                |
| subjects affected / exposed                          | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                                    | 0             | 0              | 0              |
| Early satiety                                        |               |                |                |

|                                                 |                 |               |                |
|-------------------------------------------------|-----------------|---------------|----------------|
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 3 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                               | 0               | 0             | 0              |
| Infusion site extravasation                     |                 |               |                |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 3 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                               | 0               | 0             | 0              |
| Pain                                            |                 |               |                |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 3 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                               | 0               | 0             | 0              |
| Performance status decreased                    |                 |               |                |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 3 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                               | 0               | 0             | 0              |
| Physical deconditioning                         |                 |               |                |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 3 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                               | 0               | 0             | 0              |
| Peripheral swelling                             |                 |               |                |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 3 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                               | 0               | 0             | 0              |
| Immune system disorders                         |                 |               |                |
| Contrast media reaction                         |                 |               |                |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 3 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                               | 0               | 0             | 0              |
| Reproductive system and breast disorders        |                 |               |                |
| Erectile dysfunction                            |                 |               |                |
| subjects affected / exposed                     | 1 / 1 (100.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                               | 1               | 0             | 0              |
| Vaginal haemorrhage                             |                 |               |                |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 3 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                               | 0               | 0             | 0              |
| Respiratory, thoracic and mediastinal disorders |                 |               |                |
| Cough                                           |                 |               |                |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 3 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                               | 0               | 0             | 0              |
| Dyspnoea                                        |                 |               |                |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all)                               | 0               | 0             | 1              |
| Oropharyngeal pain                              |                 |               |                |

|                                                    |               |               |               |
|----------------------------------------------------|---------------|---------------|---------------|
| subjects affected / exposed                        | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                                  | 0             | 0             | 0             |
| Wheezing                                           |               |               |               |
| subjects affected / exposed                        | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                                  | 0             | 0             | 0             |
| Atelectasis                                        |               |               |               |
| subjects affected / exposed                        | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                                  | 0             | 0             | 0             |
| Pleural effusion                                   |               |               |               |
| subjects affected / exposed                        | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                                  | 0             | 0             | 0             |
| Acute respiratory distress syndrome                |               |               |               |
| subjects affected / exposed                        | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                                  | 0             | 0             | 0             |
| Nasal congestion                                   |               |               |               |
| subjects affected / exposed                        | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                                  | 0             | 0             | 0             |
| Pulmonary embolism                                 |               |               |               |
| subjects affected / exposed                        | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                                  | 0             | 0             | 0             |
| Rhinorrhoea                                        |               |               |               |
| subjects affected / exposed                        | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                                  | 0             | 0             | 0             |
| Upper respiratory tract congestion                 |               |               |               |
| subjects affected / exposed                        | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                                  | 0             | 0             | 0             |
| Increased viscosity of upper respiratory secretion |               |               |               |
| subjects affected / exposed                        | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                                  | 0             | 0             | 0             |
| Pneumothorax                                       |               |               |               |
| subjects affected / exposed                        | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                                  | 0             | 0             | 0             |
| Productive cough                                   |               |               |               |
| subjects affected / exposed                        | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                                  | 0             | 0             | 0             |

|                                      |               |                |                |
|--------------------------------------|---------------|----------------|----------------|
| Psychiatric disorders                |               |                |                |
| Depression                           |               |                |                |
| subjects affected / exposed          | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Hallucination, auditory              |               |                |                |
| subjects affected / exposed          | 0 / 1 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0             | 1              | 0              |
| Insomnia                             |               |                |                |
| subjects affected / exposed          | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Anxiety                              |               |                |                |
| subjects affected / exposed          | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Confusional state                    |               |                |                |
| subjects affected / exposed          | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Irritability                         |               |                |                |
| subjects affected / exposed          | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Product issues                       |               |                |                |
| Device breakage                      |               |                |                |
| subjects affected / exposed          | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Investigations                       |               |                |                |
| Blood alkaline phosphatase increased |               |                |                |
| subjects affected / exposed          | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 1 / 4 (25.00%) |
| occurrences (all)                    | 0             | 0              | 1              |
| Blood creatinine increased           |               |                |                |
| subjects affected / exposed          | 0 / 1 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0             | 2              | 0              |
| Alanine aminotransferase increased   |               |                |                |
| subjects affected / exposed          | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 1 / 4 (25.00%) |
| occurrences (all)                    | 0             | 0              | 1              |
| Aspartate aminotransferase increased |               |                |                |
| subjects affected / exposed          | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 1 / 4 (25.00%) |
| occurrences (all)                    | 0             | 0              | 1              |

|                                        |               |                |                |
|----------------------------------------|---------------|----------------|----------------|
| Blood bilirubin increased              |               |                |                |
| subjects affected / exposed            | 0 / 1 (0.00%) | 1 / 3 (33.33%) | 1 / 4 (25.00%) |
| occurrences (all)                      | 0             | 1              | 1              |
| Blood cholesterol increased            |               |                |                |
| subjects affected / exposed            | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0             | 0              | 0              |
| Blood lactate dehydrogenase decreased  |               |                |                |
| subjects affected / exposed            | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0             | 0              | 0              |
| Blood phosphorus decreased             |               |                |                |
| subjects affected / exposed            | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0             | 0              | 0              |
| Electrocardiogram QT interval abnormal |               |                |                |
| subjects affected / exposed            | 0 / 1 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0             | 2              | 0              |
| Electrocardiogram QT prolonged         |               |                |                |
| subjects affected / exposed            | 0 / 1 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0             | 1              | 0              |
| Gamma-glutamyltransferase increased    |               |                |                |
| subjects affected / exposed            | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0             | 0              | 0              |
| Lymphocyte count decreased             |               |                |                |
| subjects affected / exposed            | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0             | 0              | 0              |
| Neutrophil count decreased             |               |                |                |
| subjects affected / exposed            | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0             | 0              | 0              |
| Weight decreased                       |               |                |                |
| subjects affected / exposed            | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0             | 0              | 0              |
| Weight increased                       |               |                |                |
| subjects affected / exposed            | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0             | 0              | 0              |
| White blood cell count decreased       |               |                |                |

|                                                |               |               |               |
|------------------------------------------------|---------------|---------------|---------------|
| subjects affected / exposed                    | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                              | 0             | 0             | 0             |
| Blood creatine phosphokinase increased         |               |               |               |
| subjects affected / exposed                    | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                              | 0             | 0             | 0             |
| Blood creatinine decreased                     |               |               |               |
| subjects affected / exposed                    | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                              | 0             | 0             | 0             |
| Blood lactate dehydrogenase increased          |               |               |               |
| subjects affected / exposed                    | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                              | 0             | 0             | 0             |
| Blood sodium decreased                         |               |               |               |
| subjects affected / exposed                    | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                              | 0             | 0             | 0             |
| Eosinophil count decreased                     |               |               |               |
| subjects affected / exposed                    | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                              | 0             | 0             | 0             |
| Platelet count decreased                       |               |               |               |
| subjects affected / exposed                    | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                              | 0             | 0             | 0             |
| White blood cell count increased               |               |               |               |
| subjects affected / exposed                    | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                              | 0             | 0             | 0             |
| Ejection fraction decreased                    |               |               |               |
| subjects affected / exposed                    | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                              | 0             | 0             | 0             |
| Blood albumin decreased                        |               |               |               |
| subjects affected / exposed                    | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                              | 0             | 0             | 0             |
| Carbon dioxide decreased                       |               |               |               |
| subjects affected / exposed                    | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                              | 0             | 0             | 0             |
| Injury, poisoning and procedural complications |               |               |               |

|                                                                                 |                    |                    |                    |
|---------------------------------------------------------------------------------|--------------------|--------------------|--------------------|
| Spinal compression fracture<br>subjects affected / exposed<br>occurrences (all) | 0 / 1 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0 |
| Contusion<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 1 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0 |
| Fall<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 1 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0 |
| Stoma prolapse<br>subjects affected / exposed<br>occurrences (all)              | 0 / 1 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0 |
| Skin laceration<br>subjects affected / exposed<br>occurrences (all)             | 0 / 1 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0 |
| Pelvic fracture<br>subjects affected / exposed<br>occurrences (all)             | 0 / 1 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0 |
| Procedural pain<br>subjects affected / exposed<br>occurrences (all)             | 0 / 1 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0 |
| Rib fracture<br>subjects affected / exposed<br>occurrences (all)                | 0 / 1 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0 |
| Ulna fracture<br>subjects affected / exposed<br>occurrences (all)               | 0 / 1 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0 |
| Cardiac disorders                                                               |                    |                    |                    |
| Sinus tachycardia<br>subjects affected / exposed<br>occurrences (all)           | 0 / 1 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0 |
| Atrial fibrillation<br>subjects affected / exposed<br>occurrences (all)         | 0 / 1 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0 |
| Palpitations                                                                    |                    |                    |                    |

|                                     |               |                |               |
|-------------------------------------|---------------|----------------|---------------|
| subjects affected / exposed         | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                   | 0             | 0              | 0             |
| Pericardial effusion                |               |                |               |
| subjects affected / exposed         | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                   | 0             | 0              | 0             |
| Sinus bradycardia                   |               |                |               |
| subjects affected / exposed         | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                   | 0             | 0              | 0             |
| Atrial thrombosis                   |               |                |               |
| subjects affected / exposed         | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                   | 0             | 0              | 0             |
| Atrioventricular block first degree |               |                |               |
| subjects affected / exposed         | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                   | 0             | 0              | 0             |
| Tachycardia                         |               |                |               |
| subjects affected / exposed         | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                   | 0             | 0              | 0             |
| Nervous system disorders            |               |                |               |
| Dizziness                           |               |                |               |
| subjects affected / exposed         | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                   | 0             | 0              | 0             |
| Ageusia                             |               |                |               |
| subjects affected / exposed         | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                   | 0             | 0              | 0             |
| Anosmia                             |               |                |               |
| subjects affected / exposed         | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                   | 0             | 0              | 0             |
| Dysgeusia                           |               |                |               |
| subjects affected / exposed         | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                   | 0             | 0              | 0             |
| Headache                            |               |                |               |
| subjects affected / exposed         | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                   | 0             | 0              | 0             |
| Hypoaesthesia                       |               |                |               |
| subjects affected / exposed         | 0 / 1 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (0.00%) |
| occurrences (all)                   | 0             | 1              | 0             |

|                             |               |               |               |
|-----------------------------|---------------|---------------|---------------|
| Sensory loss                |               |               |               |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Syncope                     |               |               |               |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Paraesthesia                |               |               |               |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Brain oedema                |               |               |               |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Neuropathy peripheral       |               |               |               |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Post herpetic neuralgia     |               |               |               |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Taste disorder              |               |               |               |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Tremor                      |               |               |               |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Coordination abnormal       |               |               |               |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Cognitive disorder          |               |               |               |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Disturbance in attention    |               |               |               |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Parosmia                    |               |               |               |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |

|                                      |               |                |                |
|--------------------------------------|---------------|----------------|----------------|
| Blood and lymphatic system disorders |               |                |                |
| Anaemia                              |               |                |                |
| subjects affected / exposed          | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 1 / 4 (25.00%) |
| occurrences (all)                    | 0             | 0              | 1              |
| Leukocytosis                         |               |                |                |
| subjects affected / exposed          | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 1 / 4 (25.00%) |
| occurrences (all)                    | 0             | 0              | 1              |
| Leukopenia                           |               |                |                |
| subjects affected / exposed          | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Thrombocytopenia                     |               |                |                |
| subjects affected / exposed          | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Lymphopenia                          |               |                |                |
| subjects affected / exposed          | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Neutropenia                          |               |                |                |
| subjects affected / exposed          | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Ear and labyrinth disorders          |               |                |                |
| Tinnitus                             |               |                |                |
| subjects affected / exposed          | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Hyperacusis                          |               |                |                |
| subjects affected / exposed          | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Eye disorders                        |               |                |                |
| Vision blurred                       |               |                |                |
| subjects affected / exposed          | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Conjunctival haemorrhage             |               |                |                |
| subjects affected / exposed          | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Eye pain                             |               |                |                |
| subjects affected / exposed          | 0 / 1 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0             | 1              | 0              |
| Vitreous floaters                    |               |                |                |

|                             |                 |                |                |
|-----------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 3 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0              |
| Diplopia                    |                 |                |                |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 3 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0              |
| Gastrointestinal disorders  |                 |                |                |
| Nausea                      |                 |                |                |
| subjects affected / exposed | 0 / 1 (0.00%)   | 1 / 3 (33.33%) | 2 / 4 (50.00%) |
| occurrences (all)           | 0               | 1              | 2              |
| Vomiting                    |                 |                |                |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 3 (0.00%)  | 1 / 4 (25.00%) |
| occurrences (all)           | 0               | 0              | 2              |
| Abdominal pain              |                 |                |                |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 3 (0.00%)  | 1 / 4 (25.00%) |
| occurrences (all)           | 0               | 0              | 1              |
| Constipation                |                 |                |                |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 3 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0              |
| Diarrhoea                   |                 |                |                |
| subjects affected / exposed | 1 / 1 (100.00%) | 1 / 3 (33.33%) | 1 / 4 (25.00%) |
| occurrences (all)           | 1               | 2              | 1              |
| Abdominal distension        |                 |                |                |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 3 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0              |
| Dry mouth                   |                 |                |                |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 3 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0              |
| Haematochezia               |                 |                |                |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 3 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0              |
| Retching                    |                 |                |                |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 3 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0              |
| Anal incontinence           |                 |                |                |
| subjects affected / exposed | 1 / 1 (100.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 1               | 0              | 0              |

|                                  |               |               |                |
|----------------------------------|---------------|---------------|----------------|
| Dyspepsia                        |               |               |                |
| subjects affected / exposed      | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |
| Dysphagia                        |               |               |                |
| subjects affected / exposed      | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |
| Faeces soft                      |               |               |                |
| subjects affected / exposed      | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |
| Flatulence                       |               |               |                |
| subjects affected / exposed      | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |
| Gastrooesophageal reflux disease |               |               |                |
| subjects affected / exposed      | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all)                | 0             | 0             | 1              |
| Salivary hypersecretion          |               |               |                |
| subjects affected / exposed      | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |
| Stomatitis                       |               |               |                |
| subjects affected / exposed      | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |
| Abdominal pain upper             |               |               |                |
| subjects affected / exposed      | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |
| Colitis                          |               |               |                |
| subjects affected / exposed      | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |
| Food poisoning                   |               |               |                |
| subjects affected / exposed      | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |
| Tooth discolouration             |               |               |                |
| subjects affected / exposed      | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |
| Ascites                          |               |               |                |
| subjects affected / exposed      | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |

|                                                                                                                    |                    |                    |                     |
|--------------------------------------------------------------------------------------------------------------------|--------------------|--------------------|---------------------|
| Parotid gland enlargement<br>subjects affected / exposed<br>occurrences (all)                                      | 0 / 1 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0  |
| Rectal haemorrhage<br>subjects affected / exposed<br>occurrences (all)                                             | 0 / 1 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0  |
| Tooth erosion<br>subjects affected / exposed<br>occurrences (all)                                                  | 0 / 1 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0  |
| Tooth loss<br>subjects affected / exposed<br>occurrences (all)                                                     | 0 / 1 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0  |
| Hepatobiliary disorders<br>Hyperbilirubinaemia<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 1 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0 | 1 / 4 (25.00%)<br>2 |
| Hepatitis acute<br>subjects affected / exposed<br>occurrences (all)                                                | 0 / 1 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0  |
| Biliary dilatation<br>subjects affected / exposed<br>occurrences (all)                                             | 0 / 1 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0  |
| Skin and subcutaneous tissue disorders<br>Dermatitis acneiform<br>subjects affected / exposed<br>occurrences (all) | 0 / 1 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0  |
| Pruritus<br>subjects affected / exposed<br>occurrences (all)                                                       | 0 / 1 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0 | 1 / 4 (25.00%)<br>1 |
| Rash maculo-papular<br>subjects affected / exposed<br>occurrences (all)                                            | 0 / 1 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0  |
| Dermatitis contact<br>subjects affected / exposed<br>occurrences (all)                                             | 0 / 1 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0  |
| Night sweats                                                                                                       |                    |                    |                     |

|                                        |               |                |               |
|----------------------------------------|---------------|----------------|---------------|
| subjects affected / exposed            | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                      | 0             | 0              | 0             |
| Rash                                   |               |                |               |
| subjects affected / exposed            | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                      | 0             | 0              | 0             |
| Rash macular                           |               |                |               |
| subjects affected / exposed            | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                      | 0             | 0              | 0             |
| Skin lesion                            |               |                |               |
| subjects affected / exposed            | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                      | 0             | 0              | 0             |
| Hyperhidrosis                          |               |                |               |
| subjects affected / exposed            | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                      | 0             | 0              | 0             |
| Renal and urinary disorders            |               |                |               |
| Ketonuria                              |               |                |               |
| subjects affected / exposed            | 0 / 1 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (0.00%) |
| occurrences (all)                      | 0             | 1              | 0             |
| Urinary incontinence                   |               |                |               |
| subjects affected / exposed            | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                      | 0             | 0              | 0             |
| Haematuria                             |               |                |               |
| subjects affected / exposed            | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                      | 0             | 0              | 0             |
| Proteinuria                            |               |                |               |
| subjects affected / exposed            | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                      | 0             | 0              | 0             |
| Renal colic                            |               |                |               |
| subjects affected / exposed            | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                      | 0             | 0              | 0             |
| Glycosuria                             |               |                |               |
| subjects affected / exposed            | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                      | 0             | 0              | 0             |
| Endocrine disorders                    |               |                |               |
| Pituitary-dependent Cushing's syndrome |               |                |               |

|                                                 |                 |                |               |
|-------------------------------------------------|-----------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 3 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0               | 0              | 0             |
| Hypothyroidism                                  |                 |                |               |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 3 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0               | 0              | 0             |
| Musculoskeletal and connective tissue disorders |                 |                |               |
| Back pain                                       |                 |                |               |
| subjects affected / exposed                     | 1 / 1 (100.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 1               | 0              | 0             |
| Myalgia                                         |                 |                |               |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 3 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0               | 0              | 0             |
| Arthralgia                                      |                 |                |               |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 1 / 3 (33.33%) | 0 / 4 (0.00%) |
| occurrences (all)                               | 0               | 1              | 0             |
| Groin pain                                      |                 |                |               |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 1 / 3 (33.33%) | 0 / 4 (0.00%) |
| occurrences (all)                               | 0               | 1              | 0             |
| Muscle spasms                                   |                 |                |               |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 3 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0               | 0              | 0             |
| Musculoskeletal pain                            |                 |                |               |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 3 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0               | 0              | 0             |
| Osteoarthritis                                  |                 |                |               |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 1 / 3 (33.33%) | 0 / 4 (0.00%) |
| occurrences (all)                               | 0               | 1              | 0             |
| Fistula                                         |                 |                |               |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 3 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0               | 0              | 0             |
| Musculoskeletal chest pain                      |                 |                |               |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 3 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0               | 0              | 0             |
| Osteoporosis                                    |                 |                |               |

|                             |                 |               |               |
|-----------------------------|-----------------|---------------|---------------|
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0               | 0             | 0             |
| Pain in extremity           |                 |               |               |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0               | 0             | 0             |
| Coccydynia                  |                 |               |               |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0               | 0             | 0             |
| Infections and infestations |                 |               |               |
| COVID-19                    |                 |               |               |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0               | 0             | 0             |
| Pneumonia                   |                 |               |               |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0               | 0             | 0             |
| Urinary tract infection     |                 |               |               |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0               | 0             | 0             |
| Respiratory tract infection |                 |               |               |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0               | 0             | 0             |
| Cellulitis                  |                 |               |               |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0               | 0             | 0             |
| Onychomycosis               |                 |               |               |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0               | 0             | 0             |
| Oral candidiasis            |                 |               |               |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0               | 0             | 0             |
| Pneumonia aspiration        |                 |               |               |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0               | 0             | 0             |
| Skin infection              |                 |               |               |
| subjects affected / exposed | 1 / 1 (100.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 1               | 0             | 0             |

|                                                                                       |                    |                     |                     |
|---------------------------------------------------------------------------------------|--------------------|---------------------|---------------------|
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 0 / 1 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Candida infection<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 1 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Herpes zoster<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 1 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 1 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Vaginal infection<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 1 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Coronavirus infection<br>subjects affected / exposed<br>occurrences (all)             | 0 / 1 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Influenza<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 1 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Metabolism and nutrition disorders                                                    |                    |                     |                     |
| Decreased appetite<br>subjects affected / exposed<br>occurrences (all)                | 0 / 1 (0.00%)<br>0 | 1 / 3 (33.33%)<br>1 | 1 / 4 (25.00%)<br>1 |
| Hypercalcaemia<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 1 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Hyperkalaemia<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 1 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Hypomagnesaemia<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 1 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Dehydration                                                                           |                    |                     |                     |

|                             |               |                |               |
|-----------------------------|---------------|----------------|---------------|
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Gout                        |               |                |               |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Hyperglycaemia              |               |                |               |
| subjects affected / exposed | 0 / 1 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 1              | 0             |
| Hyperlipidaemia             |               |                |               |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Hypokalaemia                |               |                |               |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Hyponatraemia               |               |                |               |
| subjects affected / exposed | 0 / 1 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 1              | 0             |
| Hypophosphataemia           |               |                |               |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Vitamin B12 deficiency      |               |                |               |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Vitamin D deficiency        |               |                |               |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Hypoalbuminaemia            |               |                |               |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Hypocalcaemia               |               |                |               |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Hypoglycaemia               |               |                |               |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Hyperuricaemia              |               |                |               |

|                             |               |               |               |
|-----------------------------|---------------|---------------|---------------|
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Malnutrition                |               |               |               |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |

| <b>Non-serious adverse events</b>                                   | Dose Escalation:<br>Phase 1a: Cohort 4 | Dose Escalation:<br>Phase 1a: Cohort 5 | Dose Escalation:<br>Phase 1a: Cohort 6 |
|---------------------------------------------------------------------|----------------------------------------|----------------------------------------|----------------------------------------|
| Total subjects affected by non-serious adverse events               |                                        |                                        |                                        |
| subjects affected / exposed                                         | 4 / 4 (100.00%)                        | 9 / 9 (100.00%)                        | 8 / 8 (100.00%)                        |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                        |                                        |                                        |
| Cancer pain                                                         |                                        |                                        |                                        |
| subjects affected / exposed                                         | 0 / 4 (0.00%)                          | 0 / 9 (0.00%)                          | 0 / 8 (0.00%)                          |
| occurrences (all)                                                   | 0                                      | 0                                      | 0                                      |
| Tumour pain                                                         |                                        |                                        |                                        |
| subjects affected / exposed                                         | 0 / 4 (0.00%)                          | 0 / 9 (0.00%)                          | 1 / 8 (12.50%)                         |
| occurrences (all)                                                   | 0                                      | 0                                      | 1                                      |
| Vascular disorders                                                  |                                        |                                        |                                        |
| Hypotension                                                         |                                        |                                        |                                        |
| subjects affected / exposed                                         | 0 / 4 (0.00%)                          | 1 / 9 (11.11%)                         | 0 / 8 (0.00%)                          |
| occurrences (all)                                                   | 0                                      | 1                                      | 0                                      |
| Deep vein thrombosis                                                |                                        |                                        |                                        |
| subjects affected / exposed                                         | 0 / 4 (0.00%)                          | 0 / 9 (0.00%)                          | 0 / 8 (0.00%)                          |
| occurrences (all)                                                   | 0                                      | 0                                      | 0                                      |
| Hypertension                                                        |                                        |                                        |                                        |
| subjects affected / exposed                                         | 0 / 4 (0.00%)                          | 0 / 9 (0.00%)                          | 0 / 8 (0.00%)                          |
| occurrences (all)                                                   | 0                                      | 0                                      | 0                                      |
| Embolism                                                            |                                        |                                        |                                        |
| subjects affected / exposed                                         | 0 / 4 (0.00%)                          | 0 / 9 (0.00%)                          | 0 / 8 (0.00%)                          |
| occurrences (all)                                                   | 0                                      | 0                                      | 0                                      |
| Hot flush                                                           |                                        |                                        |                                        |
| subjects affected / exposed                                         | 0 / 4 (0.00%)                          | 0 / 9 (0.00%)                          | 0 / 8 (0.00%)                          |
| occurrences (all)                                                   | 0                                      | 0                                      | 0                                      |
| Pallor                                                              |                                        |                                        |                                        |
| subjects affected / exposed                                         | 0 / 4 (0.00%)                          | 0 / 9 (0.00%)                          | 0 / 8 (0.00%)                          |
| occurrences (all)                                                   | 0                                      | 0                                      | 0                                      |
| Peripheral embolism                                                 |                                        |                                        |                                        |

|                                                      |                |                |                |
|------------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                          | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                                    | 0              | 0              | 0              |
| General disorders and administration site conditions |                |                |                |
| Pyrexia                                              |                |                |                |
| subjects affected / exposed                          | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                                    | 0              | 0              | 1              |
| Fatigue                                              |                |                |                |
| subjects affected / exposed                          | 2 / 4 (50.00%) | 3 / 9 (33.33%) | 4 / 8 (50.00%) |
| occurrences (all)                                    | 2              | 3              | 10             |
| Asthenia                                             |                |                |                |
| subjects affected / exposed                          | 0 / 4 (0.00%)  | 1 / 9 (11.11%) | 0 / 8 (0.00%)  |
| occurrences (all)                                    | 0              | 1              | 0              |
| Gait disturbance                                     |                |                |                |
| subjects affected / exposed                          | 0 / 4 (0.00%)  | 1 / 9 (11.11%) | 0 / 8 (0.00%)  |
| occurrences (all)                                    | 0              | 1              | 0              |
| Influenza like illness                               |                |                |                |
| subjects affected / exposed                          | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                                    | 0              | 0              | 1              |
| Non-cardiac chest pain                               |                |                |                |
| subjects affected / exposed                          | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                                    | 0              | 0              | 1              |
| Oedema peripheral                                    |                |                |                |
| subjects affected / exposed                          | 0 / 4 (0.00%)  | 1 / 9 (11.11%) | 2 / 8 (25.00%) |
| occurrences (all)                                    | 0              | 1              | 2              |
| Chest discomfort                                     |                |                |                |
| subjects affected / exposed                          | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                                    | 0              | 0              | 0              |
| Chest pain                                           |                |                |                |
| subjects affected / exposed                          | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                                    | 0              | 0              | 0              |
| Chills                                               |                |                |                |
| subjects affected / exposed                          | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                                    | 0              | 0              | 0              |
| Early satiety                                        |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Infusion site extravasation                     |                |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Pain                                            |                |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Performance status decreased                    |                |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Physical deconditioning                         |                |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Peripheral swelling                             |                |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Immune system disorders                         |                |                |                |
| Contrast media reaction                         |                |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Reproductive system and breast disorders        |                |                |                |
| Erectile dysfunction                            |                |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Vaginal haemorrhage                             |                |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Respiratory, thoracic and mediastinal disorders |                |                |                |
| Cough                                           |                |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Dyspnoea                                        |                |                |                |
| subjects affected / exposed                     | 1 / 4 (25.00%) | 1 / 9 (11.11%) | 1 / 8 (12.50%) |
| occurrences (all)                               | 1              | 1              | 1              |
| Oropharyngeal pain                              |                |                |                |

|                                                    |               |                |                |
|----------------------------------------------------|---------------|----------------|----------------|
| subjects affected / exposed                        | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                                  | 0             | 0              | 0              |
| Wheezing                                           |               |                |                |
| subjects affected / exposed                        | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                                  | 0             | 0              | 0              |
| Atelectasis                                        |               |                |                |
| subjects affected / exposed                        | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                                  | 0             | 0              | 1              |
| Pleural effusion                                   |               |                |                |
| subjects affected / exposed                        | 0 / 4 (0.00%) | 1 / 9 (11.11%) | 0 / 8 (0.00%)  |
| occurrences (all)                                  | 0             | 1              | 0              |
| Acute respiratory distress syndrome                |               |                |                |
| subjects affected / exposed                        | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                                  | 0             | 0              | 0              |
| Nasal congestion                                   |               |                |                |
| subjects affected / exposed                        | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                                  | 0             | 0              | 0              |
| Pulmonary embolism                                 |               |                |                |
| subjects affected / exposed                        | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                                  | 0             | 0              | 0              |
| Rhinorrhoea                                        |               |                |                |
| subjects affected / exposed                        | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                                  | 0             | 0              | 0              |
| Upper respiratory tract congestion                 |               |                |                |
| subjects affected / exposed                        | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                                  | 0             | 0              | 0              |
| Increased viscosity of upper respiratory secretion |               |                |                |
| subjects affected / exposed                        | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                                  | 0             | 0              | 0              |
| Pneumothorax                                       |               |                |                |
| subjects affected / exposed                        | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                                  | 0             | 0              | 0              |
| Productive cough                                   |               |                |                |
| subjects affected / exposed                        | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                                  | 0             | 0              | 0              |

|                                      |                |                |                |
|--------------------------------------|----------------|----------------|----------------|
| Psychiatric disorders                |                |                |                |
| Depression                           |                |                |                |
| subjects affected / exposed          | 0 / 4 (0.00%)  | 1 / 9 (11.11%) | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0              | 1              | 0              |
| Hallucination, auditory              |                |                |                |
| subjects affected / exposed          | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Insomnia                             |                |                |                |
| subjects affected / exposed          | 0 / 4 (0.00%)  | 2 / 9 (22.22%) | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0              | 2              | 0              |
| Anxiety                              |                |                |                |
| subjects affected / exposed          | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Confusional state                    |                |                |                |
| subjects affected / exposed          | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Irritability                         |                |                |                |
| subjects affected / exposed          | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Product issues                       |                |                |                |
| Device breakage                      |                |                |                |
| subjects affected / exposed          | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Investigations                       |                |                |                |
| Blood alkaline phosphatase increased |                |                |                |
| subjects affected / exposed          | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Blood creatinine increased           |                |                |                |
| subjects affected / exposed          | 1 / 4 (25.00%) | 1 / 9 (11.11%) | 1 / 8 (12.50%) |
| occurrences (all)                    | 1              | 1              | 1              |
| Alanine aminotransferase increased   |                |                |                |
| subjects affected / exposed          | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                    | 0              | 0              | 4              |
| Aspartate aminotransferase increased |                |                |                |
| subjects affected / exposed          | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                    | 0              | 0              | 6              |

|                                                                                               |                     |                     |                     |
|-----------------------------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| Blood bilirubin increased<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 4 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Blood cholesterol increased<br>subjects affected / exposed<br>occurrences (all)               | 0 / 4 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  | 1 / 8 (12.50%)<br>1 |
| Blood lactate dehydrogenase<br>decreased<br>subjects affected / exposed<br>occurrences (all)  | 0 / 4 (0.00%)<br>0  | 1 / 9 (11.11%)<br>1 | 0 / 8 (0.00%)<br>0  |
| Blood phosphorus decreased<br>subjects affected / exposed<br>occurrences (all)                | 0 / 4 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  | 1 / 8 (12.50%)<br>1 |
| Electrocardiogram QT interval<br>abnormal<br>subjects affected / exposed<br>occurrences (all) | 0 / 4 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Electrocardiogram QT prolonged<br>subjects affected / exposed<br>occurrences (all)            | 0 / 4 (0.00%)<br>0  | 2 / 9 (22.22%)<br>3 | 0 / 8 (0.00%)<br>0  |
| Gamma-glutamyltransferase<br>increased<br>subjects affected / exposed<br>occurrences (all)    | 0 / 4 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  | 1 / 8 (12.50%)<br>2 |
| Lymphocyte count decreased<br>subjects affected / exposed<br>occurrences (all)                | 0 / 4 (0.00%)<br>0  | 1 / 9 (11.11%)<br>1 | 0 / 8 (0.00%)<br>0  |
| Neutrophil count decreased<br>subjects affected / exposed<br>occurrences (all)                | 0 / 4 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  | 1 / 8 (12.50%)<br>2 |
| Weight decreased<br>subjects affected / exposed<br>occurrences (all)                          | 1 / 4 (25.00%)<br>1 | 0 / 9 (0.00%)<br>0  | 2 / 8 (25.00%)<br>2 |
| Weight increased<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 4 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  | 1 / 8 (12.50%)<br>1 |
| White blood cell count decreased                                                              |                     |                     |                     |

|                                                |               |               |                |
|------------------------------------------------|---------------|---------------|----------------|
| subjects affected / exposed                    | 0 / 4 (0.00%) | 0 / 9 (0.00%) | 2 / 8 (25.00%) |
| occurrences (all)                              | 0             | 0             | 4              |
| Blood creatine phosphokinase increased         |               |               |                |
| subjects affected / exposed                    | 0 / 4 (0.00%) | 0 / 9 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0              |
| Blood creatinine decreased                     |               |               |                |
| subjects affected / exposed                    | 0 / 4 (0.00%) | 0 / 9 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0              |
| Blood lactate dehydrogenase increased          |               |               |                |
| subjects affected / exposed                    | 0 / 4 (0.00%) | 0 / 9 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0              |
| Blood sodium decreased                         |               |               |                |
| subjects affected / exposed                    | 0 / 4 (0.00%) | 0 / 9 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0              |
| Eosinophil count decreased                     |               |               |                |
| subjects affected / exposed                    | 0 / 4 (0.00%) | 0 / 9 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0              |
| Platelet count decreased                       |               |               |                |
| subjects affected / exposed                    | 0 / 4 (0.00%) | 0 / 9 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0              |
| White blood cell count increased               |               |               |                |
| subjects affected / exposed                    | 0 / 4 (0.00%) | 0 / 9 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0              |
| Ejection fraction decreased                    |               |               |                |
| subjects affected / exposed                    | 0 / 4 (0.00%) | 0 / 9 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0              |
| Blood albumin decreased                        |               |               |                |
| subjects affected / exposed                    | 0 / 4 (0.00%) | 0 / 9 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0              |
| Carbon dioxide decreased                       |               |               |                |
| subjects affected / exposed                    | 0 / 4 (0.00%) | 0 / 9 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0              |
| Injury, poisoning and procedural complications |               |               |                |

|                                                                                            |                    |                     |                    |
|--------------------------------------------------------------------------------------------|--------------------|---------------------|--------------------|
| Spinal compression fracture<br>subjects affected / exposed<br>occurrences (all)            | 0 / 4 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0 |
| Contusion<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 4 (0.00%)<br>0 | 1 / 9 (11.11%)<br>1 | 0 / 8 (0.00%)<br>0 |
| Fall<br>subjects affected / exposed<br>occurrences (all)                                   | 0 / 4 (0.00%)<br>0 | 1 / 9 (11.11%)<br>1 | 0 / 8 (0.00%)<br>0 |
| Stoma prolapse<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 4 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0 |
| Skin laceration<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 4 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0 |
| Pelvic fracture<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 4 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0 |
| Procedural pain<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 4 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0 |
| Rib fracture<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 4 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0 |
| Ulna fracture<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 4 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0 |
| Cardiac disorders<br>Sinus tachycardia<br>subjects affected / exposed<br>occurrences (all) | 0 / 4 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0 |
| Atrial fibrillation<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 4 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0 |
| Palpitations                                                                               |                    |                     |                    |

|                                     |                |                |                |
|-------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed         | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                   | 0              | 0              | 0              |
| Pericardial effusion                |                |                |                |
| subjects affected / exposed         | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                   | 0              | 0              | 0              |
| Sinus bradycardia                   |                |                |                |
| subjects affected / exposed         | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                   | 0              | 0              | 0              |
| Atrial thrombosis                   |                |                |                |
| subjects affected / exposed         | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                   | 0              | 0              | 0              |
| Atrioventricular block first degree |                |                |                |
| subjects affected / exposed         | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                   | 0              | 0              | 0              |
| Tachycardia                         |                |                |                |
| subjects affected / exposed         | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                   | 0              | 0              | 0              |
| Nervous system disorders            |                |                |                |
| Dizziness                           |                |                |                |
| subjects affected / exposed         | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                   | 0              | 0              | 1              |
| Ageusia                             |                |                |                |
| subjects affected / exposed         | 0 / 4 (0.00%)  | 1 / 9 (11.11%) | 0 / 8 (0.00%)  |
| occurrences (all)                   | 0              | 1              | 0              |
| Anosmia                             |                |                |                |
| subjects affected / exposed         | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                   | 0              | 0              | 0              |
| Dysgeusia                           |                |                |                |
| subjects affected / exposed         | 1 / 4 (25.00%) | 2 / 9 (22.22%) | 0 / 8 (0.00%)  |
| occurrences (all)                   | 1              | 3              | 0              |
| Headache                            |                |                |                |
| subjects affected / exposed         | 0 / 4 (0.00%)  | 1 / 9 (11.11%) | 1 / 8 (12.50%) |
| occurrences (all)                   | 0              | 2              | 2              |
| Hypoaesthesia                       |                |                |                |
| subjects affected / exposed         | 0 / 4 (0.00%)  | 1 / 9 (11.11%) | 0 / 8 (0.00%)  |
| occurrences (all)                   | 0              | 1              | 0              |

|                             |               |                |                |
|-----------------------------|---------------|----------------|----------------|
| Sensory loss                |               |                |                |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 9 (11.11%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0             | 1              | 0              |
| Syncope                     |               |                |                |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)           | 0             | 0              | 1              |
| Paraesthesia                |               |                |                |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Brain oedema                |               |                |                |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Neuropathy peripheral       |               |                |                |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Post herpetic neuralgia     |               |                |                |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Taste disorder              |               |                |                |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Tremor                      |               |                |                |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Coordination abnormal       |               |                |                |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Cognitive disorder          |               |                |                |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Disturbance in attention    |               |                |                |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Parosmia                    |               |                |                |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |

|                                      |               |                |                |
|--------------------------------------|---------------|----------------|----------------|
| Blood and lymphatic system disorders |               |                |                |
| Anaemia                              |               |                |                |
| subjects affected / exposed          | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                    | 0             | 0              | 1              |
| Leukocytosis                         |               |                |                |
| subjects affected / exposed          | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Leukopenia                           |               |                |                |
| subjects affected / exposed          | 0 / 4 (0.00%) | 1 / 9 (11.11%) | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0             | 1              | 0              |
| Thrombocytopenia                     |               |                |                |
| subjects affected / exposed          | 0 / 4 (0.00%) | 1 / 9 (11.11%) | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0             | 1              | 0              |
| Lymphopenia                          |               |                |                |
| subjects affected / exposed          | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Neutropenia                          |               |                |                |
| subjects affected / exposed          | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Ear and labyrinth disorders          |               |                |                |
| Tinnitus                             |               |                |                |
| subjects affected / exposed          | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Hyperacusis                          |               |                |                |
| subjects affected / exposed          | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Eye disorders                        |               |                |                |
| Vision blurred                       |               |                |                |
| subjects affected / exposed          | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Conjunctival haemorrhage             |               |                |                |
| subjects affected / exposed          | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                    | 0             | 0              | 1              |
| Eye pain                             |               |                |                |
| subjects affected / exposed          | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Vitreous floaters                    |               |                |                |

|                             |                 |                 |                |
|-----------------------------|-----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%)   | 1 / 9 (11.11%)  | 0 / 8 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0              |
| Diplopia                    |                 |                 |                |
| subjects affected / exposed | 0 / 4 (0.00%)   | 0 / 9 (0.00%)   | 0 / 8 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0              |
| Gastrointestinal disorders  |                 |                 |                |
| Nausea                      |                 |                 |                |
| subjects affected / exposed | 3 / 4 (75.00%)  | 7 / 9 (77.78%)  | 5 / 8 (62.50%) |
| occurrences (all)           | 4               | 16              | 13             |
| Vomiting                    |                 |                 |                |
| subjects affected / exposed | 2 / 4 (50.00%)  | 5 / 9 (55.56%)  | 4 / 8 (50.00%) |
| occurrences (all)           | 2               | 10              | 5              |
| Abdominal pain              |                 |                 |                |
| subjects affected / exposed | 0 / 4 (0.00%)   | 1 / 9 (11.11%)  | 2 / 8 (25.00%) |
| occurrences (all)           | 0               | 1               | 2              |
| Constipation                |                 |                 |                |
| subjects affected / exposed | 0 / 4 (0.00%)   | 0 / 9 (0.00%)   | 1 / 8 (12.50%) |
| occurrences (all)           | 0               | 0               | 1              |
| Diarrhoea                   |                 |                 |                |
| subjects affected / exposed | 4 / 4 (100.00%) | 9 / 9 (100.00%) | 7 / 8 (87.50%) |
| occurrences (all)           | 10              | 15              | 17             |
| Abdominal distension        |                 |                 |                |
| subjects affected / exposed | 0 / 4 (0.00%)   | 1 / 9 (11.11%)  | 0 / 8 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0              |
| Dry mouth                   |                 |                 |                |
| subjects affected / exposed | 1 / 4 (25.00%)  | 0 / 9 (0.00%)   | 0 / 8 (0.00%)  |
| occurrences (all)           | 1               | 0               | 0              |
| Haematochezia               |                 |                 |                |
| subjects affected / exposed | 0 / 4 (0.00%)   | 0 / 9 (0.00%)   | 0 / 8 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0              |
| Retching                    |                 |                 |                |
| subjects affected / exposed | 0 / 4 (0.00%)   | 0 / 9 (0.00%)   | 0 / 8 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0              |
| Anal incontinence           |                 |                 |                |
| subjects affected / exposed | 0 / 4 (0.00%)   | 0 / 9 (0.00%)   | 0 / 8 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0              |

|                                  |                |                |                |
|----------------------------------|----------------|----------------|----------------|
| Dyspepsia                        |                |                |                |
| subjects affected / exposed      | 0 / 4 (0.00%)  | 1 / 9 (11.11%) | 0 / 8 (0.00%)  |
| occurrences (all)                | 0              | 1              | 0              |
| Dysphagia                        |                |                |                |
| subjects affected / exposed      | 0 / 4 (0.00%)  | 2 / 9 (22.22%) | 0 / 8 (0.00%)  |
| occurrences (all)                | 0              | 2              | 0              |
| Faeces soft                      |                |                |                |
| subjects affected / exposed      | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                | 0              | 0              | 1              |
| Flatulence                       |                |                |                |
| subjects affected / exposed      | 0 / 4 (0.00%)  | 2 / 9 (22.22%) | 0 / 8 (0.00%)  |
| occurrences (all)                | 0              | 2              | 0              |
| Gastrooesophageal reflux disease |                |                |                |
| subjects affected / exposed      | 1 / 4 (25.00%) | 1 / 9 (11.11%) | 1 / 8 (12.50%) |
| occurrences (all)                | 1              | 1              | 1              |
| Salivary hypersecretion          |                |                |                |
| subjects affected / exposed      | 0 / 4 (0.00%)  | 1 / 9 (11.11%) | 0 / 8 (0.00%)  |
| occurrences (all)                | 0              | 1              | 0              |
| Stomatitis                       |                |                |                |
| subjects affected / exposed      | 0 / 4 (0.00%)  | 1 / 9 (11.11%) | 0 / 8 (0.00%)  |
| occurrences (all)                | 0              | 1              | 0              |
| Abdominal pain upper             |                |                |                |
| subjects affected / exposed      | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0              |
| Colitis                          |                |                |                |
| subjects affected / exposed      | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0              |
| Food poisoning                   |                |                |                |
| subjects affected / exposed      | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0              |
| Tooth discolouration             |                |                |                |
| subjects affected / exposed      | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0              |
| Ascites                          |                |                |                |
| subjects affected / exposed      | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0              |

|                                                                                                                    |                    |                     |                     |
|--------------------------------------------------------------------------------------------------------------------|--------------------|---------------------|---------------------|
| Parotid gland enlargement<br>subjects affected / exposed<br>occurrences (all)                                      | 0 / 4 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Rectal haemorrhage<br>subjects affected / exposed<br>occurrences (all)                                             | 0 / 4 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Tooth erosion<br>subjects affected / exposed<br>occurrences (all)                                                  | 0 / 4 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Tooth loss<br>subjects affected / exposed<br>occurrences (all)                                                     | 0 / 4 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Hepatobiliary disorders<br>Hyperbilirubinaemia<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 4 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  | 1 / 8 (12.50%)<br>1 |
| Hepatitis acute<br>subjects affected / exposed<br>occurrences (all)                                                | 0 / 4 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Biliary dilatation<br>subjects affected / exposed<br>occurrences (all)                                             | 0 / 4 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Skin and subcutaneous tissue disorders<br>Dermatitis acneiform<br>subjects affected / exposed<br>occurrences (all) | 0 / 4 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Pruritus<br>subjects affected / exposed<br>occurrences (all)                                                       | 0 / 4 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Rash maculo-papular<br>subjects affected / exposed<br>occurrences (all)                                            | 0 / 4 (0.00%)<br>0 | 1 / 9 (11.11%)<br>1 | 1 / 8 (12.50%)<br>1 |
| Dermatitis contact<br>subjects affected / exposed<br>occurrences (all)                                             | 0 / 4 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Night sweats                                                                                                       |                    |                     |                     |

|                                        |               |               |               |
|----------------------------------------|---------------|---------------|---------------|
| subjects affected / exposed            | 0 / 4 (0.00%) | 0 / 9 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all)                      | 0             | 0             | 0             |
| Rash                                   |               |               |               |
| subjects affected / exposed            | 0 / 4 (0.00%) | 0 / 9 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all)                      | 0             | 0             | 0             |
| Rash macular                           |               |               |               |
| subjects affected / exposed            | 0 / 4 (0.00%) | 0 / 9 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all)                      | 0             | 0             | 0             |
| Skin lesion                            |               |               |               |
| subjects affected / exposed            | 0 / 4 (0.00%) | 0 / 9 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all)                      | 0             | 0             | 0             |
| Hyperhidrosis                          |               |               |               |
| subjects affected / exposed            | 0 / 4 (0.00%) | 0 / 9 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all)                      | 0             | 0             | 0             |
| Renal and urinary disorders            |               |               |               |
| Ketonuria                              |               |               |               |
| subjects affected / exposed            | 0 / 4 (0.00%) | 0 / 9 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all)                      | 0             | 0             | 0             |
| Urinary incontinence                   |               |               |               |
| subjects affected / exposed            | 0 / 4 (0.00%) | 0 / 9 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all)                      | 0             | 0             | 0             |
| Haematuria                             |               |               |               |
| subjects affected / exposed            | 0 / 4 (0.00%) | 0 / 9 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all)                      | 0             | 0             | 0             |
| Proteinuria                            |               |               |               |
| subjects affected / exposed            | 0 / 4 (0.00%) | 0 / 9 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all)                      | 0             | 0             | 0             |
| Renal colic                            |               |               |               |
| subjects affected / exposed            | 0 / 4 (0.00%) | 0 / 9 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all)                      | 0             | 0             | 0             |
| Glycosuria                             |               |               |               |
| subjects affected / exposed            | 0 / 4 (0.00%) | 0 / 9 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all)                      | 0             | 0             | 0             |
| Endocrine disorders                    |               |               |               |
| Pituitary-dependent Cushing's syndrome |               |               |               |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Hypothyroidism                                  |                |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Musculoskeletal and connective tissue disorders |                |                |                |
| Back pain                                       |                |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Myalgia                                         |                |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Arthralgia                                      |                |                |                |
| subjects affected / exposed                     | 1 / 4 (25.00%) | 1 / 9 (11.11%) | 0 / 8 (0.00%)  |
| occurrences (all)                               | 1              | 1              | 0              |
| Groin pain                                      |                |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Muscle spasms                                   |                |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 2 / 8 (25.00%) |
| occurrences (all)                               | 0              | 0              | 2              |
| Musculoskeletal pain                            |                |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 1 / 9 (11.11%) | 0 / 8 (0.00%)  |
| occurrences (all)                               | 0              | 1              | 0              |
| Osteoarthritis                                  |                |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Fistula                                         |                |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Musculoskeletal chest pain                      |                |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Osteoporosis                                    |                |                |                |

|                             |               |                |                |
|-----------------------------|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Pain in extremity           |               |                |                |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Coccydynia                  |               |                |                |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Infections and infestations |               |                |                |
| COVID-19                    |               |                |                |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)           | 0             | 0              | 1              |
| Pneumonia                   |               |                |                |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Urinary tract infection     |               |                |                |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Respiratory tract infection |               |                |                |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Cellulitis                  |               |                |                |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)           | 0             | 0              | 1              |
| Onychomycosis               |               |                |                |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)           | 0             | 0              | 1              |
| Oral candidiasis            |               |                |                |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)           | 0             | 0              | 2              |
| Pneumonia aspiration        |               |                |                |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 9 (11.11%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0             | 1              | 0              |
| Skin infection              |               |                |                |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |

|                                                                                       |                     |                     |                     |
|---------------------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 0 / 4 (0.00%)<br>0  | 1 / 9 (11.11%)<br>1 | 0 / 8 (0.00%)<br>0  |
| Candida infection<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 4 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Herpes zoster<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 4 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 4 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Vaginal infection<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 4 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Coronavirus infection<br>subjects affected / exposed<br>occurrences (all)             | 0 / 4 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Influenza<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 4 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Metabolism and nutrition disorders                                                    |                     |                     |                     |
| Decreased appetite<br>subjects affected / exposed<br>occurrences (all)                | 3 / 4 (75.00%)<br>3 | 3 / 9 (33.33%)<br>3 | 3 / 8 (37.50%)<br>3 |
| Hypercalcaemia<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 4 (0.00%)<br>0  | 1 / 9 (11.11%)<br>1 | 0 / 8 (0.00%)<br>0  |
| Hyperkalaemia<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 4 (0.00%)<br>0  | 1 / 9 (11.11%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Hypomagnesaemia<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 4 (0.00%)<br>0  | 1 / 9 (11.11%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Dehydration                                                                           |                     |                     |                     |

|                             |               |                |                |
|-----------------------------|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 2 / 8 (25.00%) |
| occurrences (all)           | 0             | 0              | 2              |
| Gout                        |               |                |                |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)           | 0             | 0              | 1              |
| Hyperglycaemia              |               |                |                |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 9 (11.11%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0             | 1              | 0              |
| Hyperlipidaemia             |               |                |                |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)           | 0             | 0              | 1              |
| Hypokalaemia                |               |                |                |
| subjects affected / exposed | 0 / 4 (0.00%) | 3 / 9 (33.33%) | 1 / 8 (12.50%) |
| occurrences (all)           | 0             | 3              | 1              |
| Hyponatraemia               |               |                |                |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Hypophosphataemia           |               |                |                |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 9 (22.22%) | 1 / 8 (12.50%) |
| occurrences (all)           | 0             | 2              | 1              |
| Vitamin B12 deficiency      |               |                |                |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 9 (11.11%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0             | 1              | 0              |
| Vitamin D deficiency        |               |                |                |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)           | 0             | 0              | 1              |
| Hypoalbuminaemia            |               |                |                |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Hypocalcaemia               |               |                |                |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Hypoglycaemia               |               |                |                |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 9 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Hyperuricaemia              |               |                |                |

|                             |               |               |               |
|-----------------------------|---------------|---------------|---------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 9 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Malnutrition                |               |               |               |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 9 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |

| <b>Non-serious adverse events</b>                                   | Dose Escalation:<br>Phase 1a: Cohort 7 | Dose Escalation:<br>Phase 1a: Cohort 8 | Dose Escalation:<br>Phase 1a: Cohort 9 |
|---------------------------------------------------------------------|----------------------------------------|----------------------------------------|----------------------------------------|
| Total subjects affected by non-serious adverse events               |                                        |                                        |                                        |
| subjects affected / exposed                                         | 5 / 5 (100.00%)                        | 6 / 6 (100.00%)                        | 7 / 7 (100.00%)                        |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                        |                                        |                                        |
| Cancer pain                                                         |                                        |                                        |                                        |
| subjects affected / exposed                                         | 0 / 5 (0.00%)                          | 0 / 6 (0.00%)                          | 0 / 7 (0.00%)                          |
| occurrences (all)                                                   | 0                                      | 0                                      | 0                                      |
| Tumour pain                                                         |                                        |                                        |                                        |
| subjects affected / exposed                                         | 0 / 5 (0.00%)                          | 0 / 6 (0.00%)                          | 0 / 7 (0.00%)                          |
| occurrences (all)                                                   | 0                                      | 0                                      | 0                                      |
| Vascular disorders                                                  |                                        |                                        |                                        |
| Hypotension                                                         |                                        |                                        |                                        |
| subjects affected / exposed                                         | 1 / 5 (20.00%)                         | 1 / 6 (16.67%)                         | 1 / 7 (14.29%)                         |
| occurrences (all)                                                   | 1                                      | 1                                      | 1                                      |
| Deep vein thrombosis                                                |                                        |                                        |                                        |
| subjects affected / exposed                                         | 0 / 5 (0.00%)                          | 0 / 6 (0.00%)                          | 0 / 7 (0.00%)                          |
| occurrences (all)                                                   | 0                                      | 0                                      | 0                                      |
| Hypertension                                                        |                                        |                                        |                                        |
| subjects affected / exposed                                         | 0 / 5 (0.00%)                          | 0 / 6 (0.00%)                          | 0 / 7 (0.00%)                          |
| occurrences (all)                                                   | 0                                      | 0                                      | 0                                      |
| Embolism                                                            |                                        |                                        |                                        |
| subjects affected / exposed                                         | 0 / 5 (0.00%)                          | 0 / 6 (0.00%)                          | 0 / 7 (0.00%)                          |
| occurrences (all)                                                   | 0                                      | 0                                      | 0                                      |
| Hot flush                                                           |                                        |                                        |                                        |
| subjects affected / exposed                                         | 0 / 5 (0.00%)                          | 0 / 6 (0.00%)                          | 0 / 7 (0.00%)                          |
| occurrences (all)                                                   | 0                                      | 0                                      | 0                                      |
| Pallor                                                              |                                        |                                        |                                        |
| subjects affected / exposed                                         | 0 / 5 (0.00%)                          | 0 / 6 (0.00%)                          | 0 / 7 (0.00%)                          |
| occurrences (all)                                                   | 0                                      | 0                                      | 0                                      |
| Peripheral embolism                                                 |                                        |                                        |                                        |

|                                                         |                    |                    |                    |
|---------------------------------------------------------|--------------------|--------------------|--------------------|
| subjects affected / exposed<br>occurrences (all)        | 0 / 5 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0 |
| General disorders and administration<br>site conditions |                    |                    |                    |
| Pyrexia                                                 |                    |                    |                    |
| subjects affected / exposed                             | 2 / 5 (40.00%)     | 0 / 6 (0.00%)      | 1 / 7 (14.29%)     |
| occurrences (all)                                       | 2                  | 0                  | 1                  |
| Fatigue                                                 |                    |                    |                    |
| subjects affected / exposed                             | 1 / 5 (20.00%)     | 5 / 6 (83.33%)     | 3 / 7 (42.86%)     |
| occurrences (all)                                       | 2                  | 5                  | 6                  |
| Asthenia                                                |                    |                    |                    |
| subjects affected / exposed                             | 0 / 5 (0.00%)      | 1 / 6 (16.67%)     | 0 / 7 (0.00%)      |
| occurrences (all)                                       | 0                  | 1                  | 0                  |
| Gait disturbance                                        |                    |                    |                    |
| subjects affected / exposed                             | 0 / 5 (0.00%)      | 0 / 6 (0.00%)      | 0 / 7 (0.00%)      |
| occurrences (all)                                       | 0                  | 0                  | 0                  |
| Influenza like illness                                  |                    |                    |                    |
| subjects affected / exposed                             | 0 / 5 (0.00%)      | 0 / 6 (0.00%)      | 0 / 7 (0.00%)      |
| occurrences (all)                                       | 0                  | 0                  | 0                  |
| Non-cardiac chest pain                                  |                    |                    |                    |
| subjects affected / exposed                             | 0 / 5 (0.00%)      | 1 / 6 (16.67%)     | 1 / 7 (14.29%)     |
| occurrences (all)                                       | 0                  | 1                  | 1                  |
| Oedema peripheral                                       |                    |                    |                    |
| subjects affected / exposed                             | 0 / 5 (0.00%)      | 0 / 6 (0.00%)      | 0 / 7 (0.00%)      |
| occurrences (all)                                       | 0                  | 0                  | 0                  |
| Chest discomfort                                        |                    |                    |                    |
| subjects affected / exposed                             | 0 / 5 (0.00%)      | 1 / 6 (16.67%)     | 0 / 7 (0.00%)      |
| occurrences (all)                                       | 0                  | 1                  | 0                  |
| Chest pain                                              |                    |                    |                    |
| subjects affected / exposed                             | 0 / 5 (0.00%)      | 0 / 6 (0.00%)      | 0 / 7 (0.00%)      |
| occurrences (all)                                       | 0                  | 0                  | 0                  |
| Chills                                                  |                    |                    |                    |
| subjects affected / exposed                             | 0 / 5 (0.00%)      | 1 / 6 (16.67%)     | 1 / 7 (14.29%)     |
| occurrences (all)                                       | 0                  | 1                  | 1                  |
| Early satiety                                           |                    |                    |                    |

|                                                                                                                      |                     |                     |                     |
|----------------------------------------------------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)                                                                     | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  |
| Infusion site extravasation<br>subjects affected / exposed<br>occurrences (all)                                      | 0 / 5 (0.00%)<br>0  | 1 / 6 (16.67%)<br>1 | 0 / 7 (0.00%)<br>0  |
| Pain<br>subjects affected / exposed<br>occurrences (all)                                                             | 0 / 5 (0.00%)<br>0  | 1 / 6 (16.67%)<br>1 | 0 / 7 (0.00%)<br>0  |
| Performance status decreased<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  |
| Physical deconditioning<br>subjects affected / exposed<br>occurrences (all)                                          | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  |
| Peripheral swelling<br>subjects affected / exposed<br>occurrences (all)                                              | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  |
| Immune system disorders<br>Contrast media reaction<br>subjects affected / exposed<br>occurrences (all)               | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  |
| Reproductive system and breast disorders<br>Erectile dysfunction<br>subjects affected / exposed<br>occurrences (all) | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  |
| Vaginal haemorrhage<br>subjects affected / exposed<br>occurrences (all)                                              | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  |
| Respiratory, thoracic and mediastinal disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all)         | 1 / 5 (20.00%)<br>1 | 0 / 6 (0.00%)<br>0  | 2 / 7 (28.57%)<br>2 |
| Dyspnoea<br>subjects affected / exposed<br>occurrences (all)                                                         | 1 / 5 (20.00%)<br>1 | 0 / 6 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  |
| Oropharyngeal pain                                                                                                   |                     |                     |                     |

|                                                    |                |               |                |
|----------------------------------------------------|----------------|---------------|----------------|
| subjects affected / exposed                        | 1 / 5 (20.00%) | 0 / 6 (0.00%) | 1 / 7 (14.29%) |
| occurrences (all)                                  | 1              | 0             | 1              |
| Wheezing                                           |                |               |                |
| subjects affected / exposed                        | 1 / 5 (20.00%) | 0 / 6 (0.00%) | 0 / 7 (0.00%)  |
| occurrences (all)                                  | 1              | 0             | 0              |
| Atelectasis                                        |                |               |                |
| subjects affected / exposed                        | 0 / 5 (0.00%)  | 0 / 6 (0.00%) | 0 / 7 (0.00%)  |
| occurrences (all)                                  | 0              | 0             | 0              |
| Pleural effusion                                   |                |               |                |
| subjects affected / exposed                        | 0 / 5 (0.00%)  | 0 / 6 (0.00%) | 0 / 7 (0.00%)  |
| occurrences (all)                                  | 0              | 0             | 0              |
| Acute respiratory distress syndrome                |                |               |                |
| subjects affected / exposed                        | 0 / 5 (0.00%)  | 0 / 6 (0.00%) | 0 / 7 (0.00%)  |
| occurrences (all)                                  | 0              | 0             | 0              |
| Nasal congestion                                   |                |               |                |
| subjects affected / exposed                        | 0 / 5 (0.00%)  | 0 / 6 (0.00%) | 0 / 7 (0.00%)  |
| occurrences (all)                                  | 0              | 0             | 0              |
| Pulmonary embolism                                 |                |               |                |
| subjects affected / exposed                        | 0 / 5 (0.00%)  | 0 / 6 (0.00%) | 0 / 7 (0.00%)  |
| occurrences (all)                                  | 0              | 0             | 0              |
| Rhinorrhoea                                        |                |               |                |
| subjects affected / exposed                        | 0 / 5 (0.00%)  | 0 / 6 (0.00%) | 0 / 7 (0.00%)  |
| occurrences (all)                                  | 0              | 0             | 0              |
| Upper respiratory tract congestion                 |                |               |                |
| subjects affected / exposed                        | 0 / 5 (0.00%)  | 0 / 6 (0.00%) | 0 / 7 (0.00%)  |
| occurrences (all)                                  | 0              | 0             | 0              |
| Increased viscosity of upper respiratory secretion |                |               |                |
| subjects affected / exposed                        | 0 / 5 (0.00%)  | 0 / 6 (0.00%) | 0 / 7 (0.00%)  |
| occurrences (all)                                  | 0              | 0             | 0              |
| Pneumothorax                                       |                |               |                |
| subjects affected / exposed                        | 0 / 5 (0.00%)  | 0 / 6 (0.00%) | 0 / 7 (0.00%)  |
| occurrences (all)                                  | 0              | 0             | 0              |
| Productive cough                                   |                |               |                |
| subjects affected / exposed                        | 0 / 5 (0.00%)  | 0 / 6 (0.00%) | 0 / 7 (0.00%)  |
| occurrences (all)                                  | 0              | 0             | 0              |

|                                      |                |                |                |
|--------------------------------------|----------------|----------------|----------------|
| Psychiatric disorders                |                |                |                |
| Depression                           |                |                |                |
| subjects affected / exposed          | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Hallucination, auditory              |                |                |                |
| subjects affected / exposed          | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Insomnia                             |                |                |                |
| subjects affected / exposed          | 0 / 5 (0.00%)  | 1 / 6 (16.67%) | 2 / 7 (28.57%) |
| occurrences (all)                    | 0              | 1              | 2              |
| Anxiety                              |                |                |                |
| subjects affected / exposed          | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Confusional state                    |                |                |                |
| subjects affected / exposed          | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Irritability                         |                |                |                |
| subjects affected / exposed          | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Product issues                       |                |                |                |
| Device breakage                      |                |                |                |
| subjects affected / exposed          | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Investigations                       |                |                |                |
| Blood alkaline phosphatase increased |                |                |                |
| subjects affected / exposed          | 1 / 5 (20.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                    | 1              | 0              | 0              |
| Blood creatinine increased           |                |                |                |
| subjects affected / exposed          | 1 / 5 (20.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                    | 1              | 0              | 0              |
| Alanine aminotransferase increased   |                |                |                |
| subjects affected / exposed          | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Aspartate aminotransferase increased |                |                |                |
| subjects affected / exposed          | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |

|                                        |               |                |                |
|----------------------------------------|---------------|----------------|----------------|
| Blood bilirubin increased              |               |                |                |
| subjects affected / exposed            | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                      | 0             | 0              | 0              |
| Blood cholesterol increased            |               |                |                |
| subjects affected / exposed            | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                      | 0             | 0              | 0              |
| Blood lactate dehydrogenase decreased  |               |                |                |
| subjects affected / exposed            | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                      | 0             | 0              | 0              |
| Blood phosphorus decreased             |               |                |                |
| subjects affected / exposed            | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                      | 0             | 0              | 0              |
| Electrocardiogram QT interval abnormal |               |                |                |
| subjects affected / exposed            | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                      | 0             | 0              | 0              |
| Electrocardiogram QT prolonged         |               |                |                |
| subjects affected / exposed            | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                      | 0             | 0              | 0              |
| Gamma-glutamyltransferase increased    |               |                |                |
| subjects affected / exposed            | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                      | 0             | 0              | 0              |
| Lymphocyte count decreased             |               |                |                |
| subjects affected / exposed            | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 1 / 7 (14.29%) |
| occurrences (all)                      | 0             | 0              | 2              |
| Neutrophil count decreased             |               |                |                |
| subjects affected / exposed            | 0 / 5 (0.00%) | 1 / 6 (16.67%) | 0 / 7 (0.00%)  |
| occurrences (all)                      | 0             | 1              | 0              |
| Weight decreased                       |               |                |                |
| subjects affected / exposed            | 0 / 5 (0.00%) | 1 / 6 (16.67%) | 1 / 7 (14.29%) |
| occurrences (all)                      | 0             | 2              | 1              |
| Weight increased                       |               |                |                |
| subjects affected / exposed            | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                      | 0             | 0              | 0              |
| White blood cell count decreased       |               |                |                |

|                                                |               |               |                |
|------------------------------------------------|---------------|---------------|----------------|
| subjects affected / exposed                    | 0 / 5 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0              |
| Blood creatine phosphokinase increased         |               |               |                |
| subjects affected / exposed                    | 0 / 5 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0              |
| Blood creatinine decreased                     |               |               |                |
| subjects affected / exposed                    | 0 / 5 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0              |
| Blood lactate dehydrogenase increased          |               |               |                |
| subjects affected / exposed                    | 0 / 5 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0              |
| Blood sodium decreased                         |               |               |                |
| subjects affected / exposed                    | 0 / 5 (0.00%) | 0 / 6 (0.00%) | 1 / 7 (14.29%) |
| occurrences (all)                              | 0             | 0             | 1              |
| Eosinophil count decreased                     |               |               |                |
| subjects affected / exposed                    | 0 / 5 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0              |
| Platelet count decreased                       |               |               |                |
| subjects affected / exposed                    | 0 / 5 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0              |
| White blood cell count increased               |               |               |                |
| subjects affected / exposed                    | 0 / 5 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0              |
| Ejection fraction decreased                    |               |               |                |
| subjects affected / exposed                    | 0 / 5 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0              |
| Blood albumin decreased                        |               |               |                |
| subjects affected / exposed                    | 0 / 5 (0.00%) | 0 / 6 (0.00%) | 1 / 7 (14.29%) |
| occurrences (all)                              | 0             | 0             | 1              |
| Carbon dioxide decreased                       |               |               |                |
| subjects affected / exposed                    | 0 / 5 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0              |
| Injury, poisoning and procedural complications |               |               |                |

|                                                                                 |                     |                    |                    |
|---------------------------------------------------------------------------------|---------------------|--------------------|--------------------|
| Spinal compression fracture<br>subjects affected / exposed<br>occurrences (all) | 1 / 5 (20.00%)<br>1 | 0 / 6 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0 |
| Contusion<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0 |
| Fall<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0 |
| Stoma prolapse<br>subjects affected / exposed<br>occurrences (all)              | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0 |
| Skin laceration<br>subjects affected / exposed<br>occurrences (all)             | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0 |
| Pelvic fracture<br>subjects affected / exposed<br>occurrences (all)             | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0 |
| Procedural pain<br>subjects affected / exposed<br>occurrences (all)             | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0 |
| Rib fracture<br>subjects affected / exposed<br>occurrences (all)                | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0 |
| Ulna fracture<br>subjects affected / exposed<br>occurrences (all)               | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0 |
| Cardiac disorders                                                               |                     |                    |                    |
| Sinus tachycardia<br>subjects affected / exposed<br>occurrences (all)           | 1 / 5 (20.00%)<br>1 | 0 / 6 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0 |
| Atrial fibrillation<br>subjects affected / exposed<br>occurrences (all)         | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0 |
| Palpitations                                                                    |                     |                    |                    |

|                                     |                |                |                |
|-------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed         | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                   | 0              | 0              | 0              |
| Pericardial effusion                |                |                |                |
| subjects affected / exposed         | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                   | 0              | 0              | 0              |
| Sinus bradycardia                   |                |                |                |
| subjects affected / exposed         | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                   | 0              | 0              | 0              |
| Atrial thrombosis                   |                |                |                |
| subjects affected / exposed         | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                   | 0              | 0              | 0              |
| Atrioventricular block first degree |                |                |                |
| subjects affected / exposed         | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                   | 0              | 0              | 0              |
| Tachycardia                         |                |                |                |
| subjects affected / exposed         | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                   | 0              | 0              | 0              |
| Nervous system disorders            |                |                |                |
| Dizziness                           |                |                |                |
| subjects affected / exposed         | 2 / 5 (40.00%) | 1 / 6 (16.67%) | 0 / 7 (0.00%)  |
| occurrences (all)                   | 2              | 1              | 0              |
| Ageusia                             |                |                |                |
| subjects affected / exposed         | 1 / 5 (20.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                   | 1              | 0              | 0              |
| Anosmia                             |                |                |                |
| subjects affected / exposed         | 1 / 5 (20.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                   | 1              | 0              | 0              |
| Dysgeusia                           |                |                |                |
| subjects affected / exposed         | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                   | 0              | 0              | 0              |
| Headache                            |                |                |                |
| subjects affected / exposed         | 0 / 5 (0.00%)  | 1 / 6 (16.67%) | 1 / 7 (14.29%) |
| occurrences (all)                   | 0              | 1              | 1              |
| Hypoaesthesia                       |                |                |                |
| subjects affected / exposed         | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                   | 0              | 0              | 0              |

|                             |               |                |                |
|-----------------------------|---------------|----------------|----------------|
| Sensory loss                |               |                |                |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Syncope                     |               |                |                |
| subjects affected / exposed | 0 / 5 (0.00%) | 1 / 6 (16.67%) | 1 / 7 (14.29%) |
| occurrences (all)           | 0             | 1              | 1              |
| Paraesthesia                |               |                |                |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Brain oedema                |               |                |                |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Neuropathy peripheral       |               |                |                |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Post herpetic neuralgia     |               |                |                |
| subjects affected / exposed | 0 / 5 (0.00%) | 1 / 6 (16.67%) | 0 / 7 (0.00%)  |
| occurrences (all)           | 0             | 1              | 0              |
| Taste disorder              |               |                |                |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 1 / 7 (14.29%) |
| occurrences (all)           | 0             | 0              | 1              |
| Tremor                      |               |                |                |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Coordination abnormal       |               |                |                |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Cognitive disorder          |               |                |                |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Disturbance in attention    |               |                |                |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Parosmia                    |               |                |                |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |

|                                      |                |               |               |
|--------------------------------------|----------------|---------------|---------------|
| Blood and lymphatic system disorders |                |               |               |
| Anaemia                              |                |               |               |
| subjects affected / exposed          | 1 / 5 (20.00%) | 0 / 6 (0.00%) | 0 / 7 (0.00%) |
| occurrences (all)                    | 8              | 0             | 0             |
| Leukocytosis                         |                |               |               |
| subjects affected / exposed          | 1 / 5 (20.00%) | 0 / 6 (0.00%) | 0 / 7 (0.00%) |
| occurrences (all)                    | 2              | 0             | 0             |
| Leukopenia                           |                |               |               |
| subjects affected / exposed          | 0 / 5 (0.00%)  | 0 / 6 (0.00%) | 0 / 7 (0.00%) |
| occurrences (all)                    | 0              | 0             | 0             |
| Thrombocytopenia                     |                |               |               |
| subjects affected / exposed          | 0 / 5 (0.00%)  | 0 / 6 (0.00%) | 0 / 7 (0.00%) |
| occurrences (all)                    | 0              | 0             | 0             |
| Lymphopenia                          |                |               |               |
| subjects affected / exposed          | 0 / 5 (0.00%)  | 0 / 6 (0.00%) | 0 / 7 (0.00%) |
| occurrences (all)                    | 0              | 0             | 0             |
| Neutropenia                          |                |               |               |
| subjects affected / exposed          | 0 / 5 (0.00%)  | 0 / 6 (0.00%) | 0 / 7 (0.00%) |
| occurrences (all)                    | 0              | 0             | 0             |
| Ear and labyrinth disorders          |                |               |               |
| Tinnitus                             |                |               |               |
| subjects affected / exposed          | 1 / 5 (20.00%) | 0 / 6 (0.00%) | 0 / 7 (0.00%) |
| occurrences (all)                    | 1              | 0             | 0             |
| Hyperacusis                          |                |               |               |
| subjects affected / exposed          | 0 / 5 (0.00%)  | 0 / 6 (0.00%) | 0 / 7 (0.00%) |
| occurrences (all)                    | 0              | 0             | 0             |
| Eye disorders                        |                |               |               |
| Vision blurred                       |                |               |               |
| subjects affected / exposed          | 1 / 5 (20.00%) | 0 / 6 (0.00%) | 0 / 7 (0.00%) |
| occurrences (all)                    | 1              | 0             | 0             |
| Conjunctival haemorrhage             |                |               |               |
| subjects affected / exposed          | 0 / 5 (0.00%)  | 0 / 6 (0.00%) | 0 / 7 (0.00%) |
| occurrences (all)                    | 0              | 0             | 0             |
| Eye pain                             |                |               |               |
| subjects affected / exposed          | 0 / 5 (0.00%)  | 0 / 6 (0.00%) | 0 / 7 (0.00%) |
| occurrences (all)                    | 0              | 0             | 0             |
| Vitreous floaters                    |                |               |               |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 5 (0.00%)   | 0 / 6 (0.00%)   | 0 / 7 (0.00%)   |
| occurrences (all)           | 0               | 0               | 0               |
| Diplopia                    |                 |                 |                 |
| subjects affected / exposed | 0 / 5 (0.00%)   | 0 / 6 (0.00%)   | 0 / 7 (0.00%)   |
| occurrences (all)           | 0               | 0               | 0               |
| Gastrointestinal disorders  |                 |                 |                 |
| Nausea                      |                 |                 |                 |
| subjects affected / exposed | 5 / 5 (100.00%) | 5 / 6 (83.33%)  | 7 / 7 (100.00%) |
| occurrences (all)           | 19              | 8               | 15              |
| Vomiting                    |                 |                 |                 |
| subjects affected / exposed | 5 / 5 (100.00%) | 3 / 6 (50.00%)  | 6 / 7 (85.71%)  |
| occurrences (all)           | 12              | 5               | 10              |
| Abdominal pain              |                 |                 |                 |
| subjects affected / exposed | 1 / 5 (20.00%)  | 1 / 6 (16.67%)  | 1 / 7 (14.29%)  |
| occurrences (all)           | 4               | 3               | 1               |
| Constipation                |                 |                 |                 |
| subjects affected / exposed | 2 / 5 (40.00%)  | 0 / 6 (0.00%)   | 0 / 7 (0.00%)   |
| occurrences (all)           | 3               | 0               | 0               |
| Diarrhoea                   |                 |                 |                 |
| subjects affected / exposed | 2 / 5 (40.00%)  | 6 / 6 (100.00%) | 7 / 7 (100.00%) |
| occurrences (all)           | 4               | 8               | 11              |
| Abdominal distension        |                 |                 |                 |
| subjects affected / exposed | 1 / 5 (20.00%)  | 0 / 6 (0.00%)   | 0 / 7 (0.00%)   |
| occurrences (all)           | 2               | 0               | 0               |
| Dry mouth                   |                 |                 |                 |
| subjects affected / exposed | 1 / 5 (20.00%)  | 0 / 6 (0.00%)   | 0 / 7 (0.00%)   |
| occurrences (all)           | 1               | 0               | 0               |
| Haematochezia               |                 |                 |                 |
| subjects affected / exposed | 1 / 5 (20.00%)  | 0 / 6 (0.00%)   | 0 / 7 (0.00%)   |
| occurrences (all)           | 1               | 0               | 0               |
| Retching                    |                 |                 |                 |
| subjects affected / exposed | 1 / 5 (20.00%)  | 0 / 6 (0.00%)   | 0 / 7 (0.00%)   |
| occurrences (all)           | 1               | 0               | 0               |
| Anal incontinence           |                 |                 |                 |
| subjects affected / exposed | 0 / 5 (0.00%)   | 0 / 6 (0.00%)   | 0 / 7 (0.00%)   |
| occurrences (all)           | 0               | 0               | 0               |

|                                  |               |                |               |
|----------------------------------|---------------|----------------|---------------|
| Dyspepsia                        |               |                |               |
| subjects affected / exposed      | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%) |
| occurrences (all)                | 0             | 0              | 0             |
| Dysphagia                        |               |                |               |
| subjects affected / exposed      | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%) |
| occurrences (all)                | 0             | 0              | 0             |
| Faeces soft                      |               |                |               |
| subjects affected / exposed      | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%) |
| occurrences (all)                | 0             | 0              | 0             |
| Flatulence                       |               |                |               |
| subjects affected / exposed      | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%) |
| occurrences (all)                | 0             | 0              | 0             |
| Gastrooesophageal reflux disease |               |                |               |
| subjects affected / exposed      | 0 / 5 (0.00%) | 1 / 6 (16.67%) | 0 / 7 (0.00%) |
| occurrences (all)                | 0             | 1              | 0             |
| Salivary hypersecretion          |               |                |               |
| subjects affected / exposed      | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%) |
| occurrences (all)                | 0             | 0              | 0             |
| Stomatitis                       |               |                |               |
| subjects affected / exposed      | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%) |
| occurrences (all)                | 0             | 0              | 0             |
| Abdominal pain upper             |               |                |               |
| subjects affected / exposed      | 0 / 5 (0.00%) | 1 / 6 (16.67%) | 0 / 7 (0.00%) |
| occurrences (all)                | 0             | 4              | 0             |
| Colitis                          |               |                |               |
| subjects affected / exposed      | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%) |
| occurrences (all)                | 0             | 0              | 0             |
| Food poisoning                   |               |                |               |
| subjects affected / exposed      | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%) |
| occurrences (all)                | 0             | 0              | 0             |
| Tooth discolouration             |               |                |               |
| subjects affected / exposed      | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%) |
| occurrences (all)                | 0             | 0              | 0             |
| Ascites                          |               |                |               |
| subjects affected / exposed      | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%) |
| occurrences (all)                | 0             | 0              | 0             |

|                                                                                                                    |                     |                    |                     |
|--------------------------------------------------------------------------------------------------------------------|---------------------|--------------------|---------------------|
| Parotid gland enlargement<br>subjects affected / exposed<br>occurrences (all)                                      | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  |
| Rectal haemorrhage<br>subjects affected / exposed<br>occurrences (all)                                             | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  |
| Tooth erosion<br>subjects affected / exposed<br>occurrences (all)                                                  | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  |
| Tooth loss<br>subjects affected / exposed<br>occurrences (all)                                                     | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  |
| Hepatobiliary disorders<br>Hyperbilirubinaemia<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  |
| Hepatitis acute<br>subjects affected / exposed<br>occurrences (all)                                                | 1 / 5 (20.00%)<br>1 | 0 / 6 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  |
| Biliary dilatation<br>subjects affected / exposed<br>occurrences (all)                                             | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 | 1 / 7 (14.29%)<br>1 |
| Skin and subcutaneous tissue disorders<br>Dermatitis acneiform<br>subjects affected / exposed<br>occurrences (all) | 1 / 5 (20.00%)<br>1 | 0 / 6 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  |
| Pruritus<br>subjects affected / exposed<br>occurrences (all)                                                       | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  |
| Rash maculo-papular<br>subjects affected / exposed<br>occurrences (all)                                            | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  |
| Dermatitis contact<br>subjects affected / exposed<br>occurrences (all)                                             | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  |
| Night sweats                                                                                                       |                     |                    |                     |

|                                        |               |               |                |
|----------------------------------------|---------------|---------------|----------------|
| subjects affected / exposed            | 0 / 5 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (0.00%)  |
| occurrences (all)                      | 0             | 0             | 0              |
| Rash                                   |               |               |                |
| subjects affected / exposed            | 0 / 5 (0.00%) | 0 / 6 (0.00%) | 1 / 7 (14.29%) |
| occurrences (all)                      | 0             | 0             | 1              |
| Rash macular                           |               |               |                |
| subjects affected / exposed            | 0 / 5 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (0.00%)  |
| occurrences (all)                      | 0             | 0             | 0              |
| Skin lesion                            |               |               |                |
| subjects affected / exposed            | 0 / 5 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (0.00%)  |
| occurrences (all)                      | 0             | 0             | 0              |
| Hyperhidrosis                          |               |               |                |
| subjects affected / exposed            | 0 / 5 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (0.00%)  |
| occurrences (all)                      | 0             | 0             | 0              |
| Renal and urinary disorders            |               |               |                |
| Ketonuria                              |               |               |                |
| subjects affected / exposed            | 0 / 5 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (0.00%)  |
| occurrences (all)                      | 0             | 0             | 0              |
| Urinary incontinence                   |               |               |                |
| subjects affected / exposed            | 0 / 5 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (0.00%)  |
| occurrences (all)                      | 0             | 0             | 0              |
| Haematuria                             |               |               |                |
| subjects affected / exposed            | 0 / 5 (0.00%) | 0 / 6 (0.00%) | 1 / 7 (14.29%) |
| occurrences (all)                      | 0             | 0             | 1              |
| Proteinuria                            |               |               |                |
| subjects affected / exposed            | 0 / 5 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (0.00%)  |
| occurrences (all)                      | 0             | 0             | 0              |
| Renal colic                            |               |               |                |
| subjects affected / exposed            | 0 / 5 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (0.00%)  |
| occurrences (all)                      | 0             | 0             | 0              |
| Glycosuria                             |               |               |                |
| subjects affected / exposed            | 0 / 5 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (0.00%)  |
| occurrences (all)                      | 0             | 0             | 0              |
| Endocrine disorders                    |               |               |                |
| Pituitary-dependent Cushing's syndrome |               |               |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Hypothyroidism                                  |                |                |                |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 1 / 7 (14.29%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Musculoskeletal and connective tissue disorders |                |                |                |
| Back pain                                       |                |                |                |
| subjects affected / exposed                     | 1 / 5 (20.00%) | 1 / 6 (16.67%) | 1 / 7 (14.29%) |
| occurrences (all)                               | 1              | 1              | 1              |
| Myalgia                                         |                |                |                |
| subjects affected / exposed                     | 1 / 5 (20.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                               | 1              | 0              | 0              |
| Arthralgia                                      |                |                |                |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 1 / 7 (14.29%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Groin pain                                      |                |                |                |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Muscle spasms                                   |                |                |                |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Musculoskeletal pain                            |                |                |                |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Osteoarthritis                                  |                |                |                |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Fistula                                         |                |                |                |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Musculoskeletal chest pain                      |                |                |                |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Osteoporosis                                    |                |                |                |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 1 / 7 (14.29%) |
| occurrences (all)           | 0              | 0              | 1              |
| Pain in extremity           |                |                |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Coccydynia                  |                |                |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Infections and infestations |                |                |                |
| COVID-19                    |                |                |                |
| subjects affected / exposed | 1 / 5 (20.00%) | 1 / 6 (16.67%) | 1 / 7 (14.29%) |
| occurrences (all)           | 1              | 1              | 1              |
| Pneumonia                   |                |                |                |
| subjects affected / exposed | 2 / 5 (40.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)           | 2              | 0              | 0              |
| Urinary tract infection     |                |                |                |
| subjects affected / exposed | 2 / 5 (40.00%) | 0 / 6 (0.00%)  | 1 / 7 (14.29%) |
| occurrences (all)           | 2              | 0              | 1              |
| Respiratory tract infection |                |                |                |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0              |
| Cellulitis                  |                |                |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Onychomycosis               |                |                |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Oral candidiasis            |                |                |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Pneumonia aspiration        |                |                |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Skin infection              |                |                |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |

|                                                                                       |                     |                     |                     |
|---------------------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  |
| Candida infection<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  |
| Herpes zoster<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 5 (0.00%)<br>0  | 1 / 6 (16.67%)<br>1 | 0 / 7 (0.00%)<br>0  |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  |
| Vaginal infection<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 1 / 7 (14.29%)<br>1 |
| Coronavirus infection<br>subjects affected / exposed<br>occurrences (all)             | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  |
| Influenza<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  |
| Metabolism and nutrition disorders                                                    |                     |                     |                     |
| Decreased appetite<br>subjects affected / exposed<br>occurrences (all)                | 1 / 5 (20.00%)<br>1 | 1 / 6 (16.67%)<br>1 | 2 / 7 (28.57%)<br>2 |
| Hypercalcaemia<br>subjects affected / exposed<br>occurrences (all)                    | 1 / 5 (20.00%)<br>1 | 0 / 6 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  |
| Hyperkalaemia<br>subjects affected / exposed<br>occurrences (all)                     | 1 / 5 (20.00%)<br>1 | 0 / 6 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  |
| Hypomagnesaemia<br>subjects affected / exposed<br>occurrences (all)                   | 1 / 5 (20.00%)<br>1 | 0 / 6 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  |
| Dehydration                                                                           |                     |                     |                     |

|                             |               |                |                |
|-----------------------------|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Gout                        |               |                |                |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Hyperglycaemia              |               |                |                |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Hyperlipidaemia             |               |                |                |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Hypokalaemia                |               |                |                |
| subjects affected / exposed | 0 / 5 (0.00%) | 1 / 6 (16.67%) | 1 / 7 (14.29%) |
| occurrences (all)           | 0             | 1              | 6              |
| Hyponatraemia               |               |                |                |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Hypophosphataemia           |               |                |                |
| subjects affected / exposed | 0 / 5 (0.00%) | 1 / 6 (16.67%) | 1 / 7 (14.29%) |
| occurrences (all)           | 0             | 1              | 1              |
| Vitamin B12 deficiency      |               |                |                |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Vitamin D deficiency        |               |                |                |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Hypoalbuminaemia            |               |                |                |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Hypocalcaemia               |               |                |                |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Hypoglycaemia               |               |                |                |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Hyperuricaemia              |               |                |                |

|                             |               |               |               |
|-----------------------------|---------------|---------------|---------------|
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Malnutrition                |               |               |               |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |

| <b>Non-serious adverse events</b>                                   | Dose Escalation:<br>Phase 1a: Cohort 10 | Dose Escalation:<br>Phase 1a: Cohort 11 | Dose Escalation:<br>Phase 1a: Cohort 12 |
|---------------------------------------------------------------------|-----------------------------------------|-----------------------------------------|-----------------------------------------|
| Total subjects affected by non-serious adverse events               |                                         |                                         |                                         |
| subjects affected / exposed                                         | 8 / 8 (100.00%)                         | 4 / 4 (100.00%)                         | 9 / 9 (100.00%)                         |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                         |                                         |                                         |
| Cancer pain                                                         |                                         |                                         |                                         |
| subjects affected / exposed                                         | 0 / 8 (0.00%)                           | 0 / 4 (0.00%)                           | 0 / 9 (0.00%)                           |
| occurrences (all)                                                   | 0                                       | 0                                       | 0                                       |
| Tumour pain                                                         |                                         |                                         |                                         |
| subjects affected / exposed                                         | 0 / 8 (0.00%)                           | 0 / 4 (0.00%)                           | 0 / 9 (0.00%)                           |
| occurrences (all)                                                   | 0                                       | 0                                       | 0                                       |
| Vascular disorders                                                  |                                         |                                         |                                         |
| Hypotension                                                         |                                         |                                         |                                         |
| subjects affected / exposed                                         | 0 / 8 (0.00%)                           | 0 / 4 (0.00%)                           | 0 / 9 (0.00%)                           |
| occurrences (all)                                                   | 0                                       | 0                                       | 0                                       |
| Deep vein thrombosis                                                |                                         |                                         |                                         |
| subjects affected / exposed                                         | 0 / 8 (0.00%)                           | 0 / 4 (0.00%)                           | 0 / 9 (0.00%)                           |
| occurrences (all)                                                   | 0                                       | 0                                       | 0                                       |
| Hypertension                                                        |                                         |                                         |                                         |
| subjects affected / exposed                                         | 1 / 8 (12.50%)                          | 0 / 4 (0.00%)                           | 0 / 9 (0.00%)                           |
| occurrences (all)                                                   | 2                                       | 0                                       | 0                                       |
| Embolism                                                            |                                         |                                         |                                         |
| subjects affected / exposed                                         | 0 / 8 (0.00%)                           | 0 / 4 (0.00%)                           | 0 / 9 (0.00%)                           |
| occurrences (all)                                                   | 0                                       | 0                                       | 0                                       |
| Hot flush                                                           |                                         |                                         |                                         |
| subjects affected / exposed                                         | 0 / 8 (0.00%)                           | 1 / 4 (25.00%)                          | 0 / 9 (0.00%)                           |
| occurrences (all)                                                   | 0                                       | 1                                       | 0                                       |
| Pallor                                                              |                                         |                                         |                                         |
| subjects affected / exposed                                         | 0 / 8 (0.00%)                           | 0 / 4 (0.00%)                           | 1 / 9 (11.11%)                          |
| occurrences (all)                                                   | 0                                       | 0                                       | 1                                       |
| Peripheral embolism                                                 |                                         |                                         |                                         |

|                                                      |                |                |                |
|------------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                          | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                                    | 0              | 0              | 0              |
| General disorders and administration site conditions |                |                |                |
| Pyrexia                                              |                |                |                |
| subjects affected / exposed                          | 1 / 8 (12.50%) | 0 / 4 (0.00%)  | 2 / 9 (22.22%) |
| occurrences (all)                                    | 2              | 0              | 4              |
| Fatigue                                              |                |                |                |
| subjects affected / exposed                          | 5 / 8 (62.50%) | 3 / 4 (75.00%) | 6 / 9 (66.67%) |
| occurrences (all)                                    | 9              | 3              | 11             |
| Asthenia                                             |                |                |                |
| subjects affected / exposed                          | 1 / 8 (12.50%) | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                                    | 3              | 0              | 0              |
| Gait disturbance                                     |                |                |                |
| subjects affected / exposed                          | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                                    | 0              | 0              | 0              |
| Influenza like illness                               |                |                |                |
| subjects affected / exposed                          | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 1 / 9 (11.11%) |
| occurrences (all)                                    | 0              | 0              | 1              |
| Non-cardiac chest pain                               |                |                |                |
| subjects affected / exposed                          | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                                    | 0              | 0              | 0              |
| Oedema peripheral                                    |                |                |                |
| subjects affected / exposed                          | 2 / 8 (25.00%) | 0 / 4 (0.00%)  | 2 / 9 (22.22%) |
| occurrences (all)                                    | 2              | 0              | 3              |
| Chest discomfort                                     |                |                |                |
| subjects affected / exposed                          | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                                    | 0              | 0              | 0              |
| Chest pain                                           |                |                |                |
| subjects affected / exposed                          | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 1 / 9 (11.11%) |
| occurrences (all)                                    | 0              | 0              | 1              |
| Chills                                               |                |                |                |
| subjects affected / exposed                          | 1 / 8 (12.50%) | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                                    | 1              | 0              | 0              |
| Early satiety                                        |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 1 / 8 (12.50%) | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                               | 2              | 0              | 0              |
| Infusion site extravasation                     |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Pain                                            |                |                |                |
| subjects affected / exposed                     | 1 / 8 (12.50%) | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                               | 1              | 0              | 0              |
| Performance status decreased                    |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Physical deconditioning                         |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Peripheral swelling                             |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Immune system disorders                         |                |                |                |
| Contrast media reaction                         |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 1 / 9 (11.11%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Reproductive system and breast disorders        |                |                |                |
| Erectile dysfunction                            |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Vaginal haemorrhage                             |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Respiratory, thoracic and mediastinal disorders |                |                |                |
| Cough                                           |                |                |                |
| subjects affected / exposed                     | 2 / 8 (25.00%) | 1 / 4 (25.00%) | 2 / 9 (22.22%) |
| occurrences (all)                               | 2              | 2              | 2              |
| Dyspnoea                                        |                |                |                |
| subjects affected / exposed                     | 1 / 8 (12.50%) | 1 / 4 (25.00%) | 2 / 9 (22.22%) |
| occurrences (all)                               | 2              | 1              | 5              |
| Oropharyngeal pain                              |                |                |                |

|                                                    |                |               |                |
|----------------------------------------------------|----------------|---------------|----------------|
| subjects affected / exposed                        | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                                  | 0              | 0             | 0              |
| Wheezing                                           |                |               |                |
| subjects affected / exposed                        | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                                  | 0              | 0             | 0              |
| Atelectasis                                        |                |               |                |
| subjects affected / exposed                        | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                                  | 0              | 0             | 0              |
| Pleural effusion                                   |                |               |                |
| subjects affected / exposed                        | 1 / 8 (12.50%) | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                                  | 1              | 0             | 0              |
| Acute respiratory distress syndrome                |                |               |                |
| subjects affected / exposed                        | 1 / 8 (12.50%) | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                                  | 1              | 0             | 0              |
| Nasal congestion                                   |                |               |                |
| subjects affected / exposed                        | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 2 / 9 (22.22%) |
| occurrences (all)                                  | 0              | 0             | 2              |
| Pulmonary embolism                                 |                |               |                |
| subjects affected / exposed                        | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)                                  | 0              | 0             | 1              |
| Rhinorrhoea                                        |                |               |                |
| subjects affected / exposed                        | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)                                  | 0              | 0             | 1              |
| Upper respiratory tract congestion                 |                |               |                |
| subjects affected / exposed                        | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)                                  | 0              | 0             | 2              |
| Increased viscosity of upper respiratory secretion |                |               |                |
| subjects affected / exposed                        | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                                  | 0              | 0             | 0              |
| Pneumothorax                                       |                |               |                |
| subjects affected / exposed                        | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                                  | 0              | 0             | 0              |
| Productive cough                                   |                |               |                |
| subjects affected / exposed                        | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                                  | 0              | 0             | 0              |

|                                      |                |               |                |
|--------------------------------------|----------------|---------------|----------------|
| Psychiatric disorders                |                |               |                |
| Depression                           |                |               |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Hallucination, auditory              |                |               |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Insomnia                             |                |               |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Anxiety                              |                |               |                |
| subjects affected / exposed          | 1 / 8 (12.50%) | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 1              | 0             | 0              |
| Confusional state                    |                |               |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Irritability                         |                |               |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Product issues                       |                |               |                |
| Device breakage                      |                |               |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Investigations                       |                |               |                |
| Blood alkaline phosphatase increased |                |               |                |
| subjects affected / exposed          | 1 / 8 (12.50%) | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 1              | 0             | 0              |
| Blood creatinine increased           |                |               |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)                    | 0              | 0             | 1              |
| Alanine aminotransferase increased   |                |               |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Aspartate aminotransferase increased |                |               |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |

|                                                                                            |                     |                     |                     |
|--------------------------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| Blood bilirubin increased<br>subjects affected / exposed<br>occurrences (all)              | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Blood cholesterol increased<br>subjects affected / exposed<br>occurrences (all)            | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Blood lactate dehydrogenase decreased<br>subjects affected / exposed<br>occurrences (all)  | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Blood phosphorus decreased<br>subjects affected / exposed<br>occurrences (all)             | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Electrocardiogram QT interval abnormal<br>subjects affected / exposed<br>occurrences (all) | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Electrocardiogram QT prolonged<br>subjects affected / exposed<br>occurrences (all)         | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Gamma-glutamyltransferase increased<br>subjects affected / exposed<br>occurrences (all)    | 1 / 8 (12.50%)<br>1 | 0 / 4 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Lymphocyte count decreased<br>subjects affected / exposed<br>occurrences (all)             | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Neutrophil count decreased<br>subjects affected / exposed<br>occurrences (all)             | 2 / 8 (25.00%)<br>4 | 1 / 4 (25.00%)<br>1 | 0 / 9 (0.00%)<br>0  |
| Weight decreased<br>subjects affected / exposed<br>occurrences (all)                       | 2 / 8 (25.00%)<br>2 | 0 / 4 (0.00%)<br>0  | 1 / 9 (11.11%)<br>1 |
| Weight increased<br>subjects affected / exposed<br>occurrences (all)                       | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  | 1 / 9 (11.11%)<br>1 |
| White blood cell count decreased                                                           |                     |                     |                     |

|                                                |                |               |                |
|------------------------------------------------|----------------|---------------|----------------|
| subjects affected / exposed                    | 1 / 8 (12.50%) | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                              | 1              | 0             | 0              |
| Blood creatine phosphokinase increased         |                |               |                |
| subjects affected / exposed                    | 1 / 8 (12.50%) | 0 / 4 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)                              | 1              | 0             | 1              |
| Blood creatinine decreased                     |                |               |                |
| subjects affected / exposed                    | 1 / 8 (12.50%) | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                              | 1              | 0             | 0              |
| Blood lactate dehydrogenase increased          |                |               |                |
| subjects affected / exposed                    | 1 / 8 (12.50%) | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                              | 1              | 0             | 0              |
| Blood sodium decreased                         |                |               |                |
| subjects affected / exposed                    | 1 / 8 (12.50%) | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                              | 1              | 0             | 0              |
| Eosinophil count decreased                     |                |               |                |
| subjects affected / exposed                    | 1 / 8 (12.50%) | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                              | 1              | 0             | 0              |
| Platelet count decreased                       |                |               |                |
| subjects affected / exposed                    | 1 / 8 (12.50%) | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                              | 5              | 0             | 0              |
| White blood cell count increased               |                |               |                |
| subjects affected / exposed                    | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)                              | 0              | 0             | 2              |
| Ejection fraction decreased                    |                |               |                |
| subjects affected / exposed                    | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                              | 0              | 0             | 0              |
| Blood albumin decreased                        |                |               |                |
| subjects affected / exposed                    | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                              | 0              | 0             | 0              |
| Carbon dioxide decreased                       |                |               |                |
| subjects affected / exposed                    | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                              | 0              | 0             | 0              |
| Injury, poisoning and procedural complications |                |               |                |

|                                                                                            |                     |                    |                     |
|--------------------------------------------------------------------------------------------|---------------------|--------------------|---------------------|
| Spinal compression fracture<br>subjects affected / exposed<br>occurrences (all)            | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Contusion<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Fall<br>subjects affected / exposed<br>occurrences (all)                                   | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 | 2 / 9 (22.22%)<br>2 |
| Stoma prolapse<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Skin laceration<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Pelvic fracture<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Procedural pain<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Rib fracture<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Ulna fracture<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Cardiac disorders<br>Sinus tachycardia<br>subjects affected / exposed<br>occurrences (all) | 1 / 8 (12.50%)<br>1 | 0 / 4 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Atrial fibrillation<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 | 1 / 9 (11.11%)<br>1 |
| Palpitations                                                                               |                     |                    |                     |

|                                     |                |                |                |
|-------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed         | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 1 / 9 (11.11%) |
| occurrences (all)                   | 0              | 0              | 1              |
| Pericardial effusion                |                |                |                |
| subjects affected / exposed         | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 1 / 9 (11.11%) |
| occurrences (all)                   | 0              | 0              | 1              |
| Sinus bradycardia                   |                |                |                |
| subjects affected / exposed         | 0 / 8 (0.00%)  | 1 / 4 (25.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                   | 0              | 1              | 0              |
| Atrial thrombosis                   |                |                |                |
| subjects affected / exposed         | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                   | 0              | 0              | 0              |
| Atrioventricular block first degree |                |                |                |
| subjects affected / exposed         | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                   | 0              | 0              | 0              |
| Tachycardia                         |                |                |                |
| subjects affected / exposed         | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                   | 0              | 0              | 0              |
| Nervous system disorders            |                |                |                |
| Dizziness                           |                |                |                |
| subjects affected / exposed         | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                   | 0              | 0              | 0              |
| Ageusia                             |                |                |                |
| subjects affected / exposed         | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                   | 0              | 0              | 0              |
| Anosmia                             |                |                |                |
| subjects affected / exposed         | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                   | 0              | 0              | 0              |
| Dysgeusia                           |                |                |                |
| subjects affected / exposed         | 0 / 8 (0.00%)  | 1 / 4 (25.00%) | 1 / 9 (11.11%) |
| occurrences (all)                   | 0              | 1              | 1              |
| Headache                            |                |                |                |
| subjects affected / exposed         | 2 / 8 (25.00%) | 0 / 4 (0.00%)  | 3 / 9 (33.33%) |
| occurrences (all)                   | 2              | 0              | 3              |
| Hypoaesthesia                       |                |                |                |
| subjects affected / exposed         | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                   | 0              | 0              | 0              |

|                             |                |               |                |
|-----------------------------|----------------|---------------|----------------|
| Sensory loss                |                |               |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Syncope                     |                |               |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Paraesthesia                |                |               |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Brain oedema                |                |               |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Neuropathy peripheral       |                |               |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)           | 0              | 0             | 1              |
| Post herpetic neuralgia     |                |               |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Taste disorder              |                |               |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Tremor                      |                |               |                |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 1              | 0             | 0              |
| Coordination abnormal       |                |               |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Cognitive disorder          |                |               |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Disturbance in attention    |                |               |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Parosmia                    |                |               |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |

|                                      |                |               |                |
|--------------------------------------|----------------|---------------|----------------|
| Blood and lymphatic system disorders |                |               |                |
| Anaemia                              |                |               |                |
| subjects affected / exposed          | 1 / 8 (12.50%) | 0 / 4 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)                    | 8              | 0             | 3              |
| Leukocytosis                         |                |               |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)                    | 0              | 0             | 1              |
| Leukopenia                           |                |               |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)                    | 0              | 0             | 1              |
| Thrombocytopenia                     |                |               |                |
| subjects affected / exposed          | 1 / 8 (12.50%) | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 4              | 0             | 0              |
| Lymphopenia                          |                |               |                |
| subjects affected / exposed          | 1 / 8 (12.50%) | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 5              | 0             | 0              |
| Neutropenia                          |                |               |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)                    | 0              | 0             | 1              |
| Ear and labyrinth disorders          |                |               |                |
| Tinnitus                             |                |               |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)                    | 0              | 0             | 1              |
| Hyperacusis                          |                |               |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Eye disorders                        |                |               |                |
| Vision blurred                       |                |               |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Conjunctival haemorrhage             |                |               |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Eye pain                             |                |               |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Vitreous floaters                    |                |               |                |

|                             |                |                 |                |
|-----------------------------|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 4 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Diplopia                    |                |                 |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 4 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Gastrointestinal disorders  |                |                 |                |
| Nausea                      |                |                 |                |
| subjects affected / exposed | 7 / 8 (87.50%) | 4 / 4 (100.00%) | 7 / 9 (77.78%) |
| occurrences (all)           | 14             | 5               | 19             |
| Vomiting                    |                |                 |                |
| subjects affected / exposed | 6 / 8 (75.00%) | 1 / 4 (25.00%)  | 3 / 9 (33.33%) |
| occurrences (all)           | 7              | 2               | 6              |
| Abdominal pain              |                |                 |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 4 (0.00%)   | 1 / 9 (11.11%) |
| occurrences (all)           | 0              | 0               | 1              |
| Constipation                |                |                 |                |
| subjects affected / exposed | 2 / 8 (25.00%) | 1 / 4 (25.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)           | 3              | 1               | 0              |
| Diarrhoea                   |                |                 |                |
| subjects affected / exposed | 6 / 8 (75.00%) | 3 / 4 (75.00%)  | 6 / 9 (66.67%) |
| occurrences (all)           | 25             | 3               | 11             |
| Abdominal distension        |                |                 |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 4 (0.00%)   | 1 / 9 (11.11%) |
| occurrences (all)           | 0              | 0               | 1              |
| Dry mouth                   |                |                 |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 4 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Haematochezia               |                |                 |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 4 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Retching                    |                |                 |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 4 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Anal incontinence           |                |                 |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 4 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |

|                                  |                |                |               |
|----------------------------------|----------------|----------------|---------------|
| Dyspepsia                        |                |                |               |
| subjects affected / exposed      | 0 / 8 (0.00%)  | 1 / 4 (25.00%) | 0 / 9 (0.00%) |
| occurrences (all)                | 0              | 1              | 0             |
| Dysphagia                        |                |                |               |
| subjects affected / exposed      | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 0 / 9 (0.00%) |
| occurrences (all)                | 0              | 0              | 0             |
| Faeces soft                      |                |                |               |
| subjects affected / exposed      | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 0 / 9 (0.00%) |
| occurrences (all)                | 0              | 0              | 0             |
| Flatulence                       |                |                |               |
| subjects affected / exposed      | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 0 / 9 (0.00%) |
| occurrences (all)                | 0              | 0              | 0             |
| Gastrooesophageal reflux disease |                |                |               |
| subjects affected / exposed      | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 0 / 9 (0.00%) |
| occurrences (all)                | 0              | 0              | 0             |
| Salivary hypersecretion          |                |                |               |
| subjects affected / exposed      | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 0 / 9 (0.00%) |
| occurrences (all)                | 0              | 0              | 0             |
| Stomatitis                       |                |                |               |
| subjects affected / exposed      | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 0 / 9 (0.00%) |
| occurrences (all)                | 0              | 0              | 0             |
| Abdominal pain upper             |                |                |               |
| subjects affected / exposed      | 0 / 8 (0.00%)  | 1 / 4 (25.00%) | 0 / 9 (0.00%) |
| occurrences (all)                | 0              | 1              | 0             |
| Colitis                          |                |                |               |
| subjects affected / exposed      | 1 / 8 (12.50%) | 0 / 4 (0.00%)  | 0 / 9 (0.00%) |
| occurrences (all)                | 1              | 0              | 0             |
| Food poisoning                   |                |                |               |
| subjects affected / exposed      | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 0 / 9 (0.00%) |
| occurrences (all)                | 0              | 0              | 0             |
| Tooth discolouration             |                |                |               |
| subjects affected / exposed      | 0 / 8 (0.00%)  | 1 / 4 (25.00%) | 0 / 9 (0.00%) |
| occurrences (all)                | 0              | 1              | 0             |
| Ascites                          |                |                |               |
| subjects affected / exposed      | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 0 / 9 (0.00%) |
| occurrences (all)                | 0              | 0              | 0             |

|                                                                                                                    |                     |                    |                     |
|--------------------------------------------------------------------------------------------------------------------|---------------------|--------------------|---------------------|
| Parotid gland enlargement<br>subjects affected / exposed<br>occurrences (all)                                      | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Rectal haemorrhage<br>subjects affected / exposed<br>occurrences (all)                                             | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Tooth erosion<br>subjects affected / exposed<br>occurrences (all)                                                  | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Tooth loss<br>subjects affected / exposed<br>occurrences (all)                                                     | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Hepatobiliary disorders<br>Hyperbilirubinaemia<br>subjects affected / exposed<br>occurrences (all)                 | 1 / 8 (12.50%)<br>2 | 0 / 4 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Hepatitis acute<br>subjects affected / exposed<br>occurrences (all)                                                | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Biliary dilatation<br>subjects affected / exposed<br>occurrences (all)                                             | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Skin and subcutaneous tissue disorders<br>Dermatitis acneiform<br>subjects affected / exposed<br>occurrences (all) | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Pruritus<br>subjects affected / exposed<br>occurrences (all)                                                       | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 | 1 / 9 (11.11%)<br>1 |
| Rash maculo-papular<br>subjects affected / exposed<br>occurrences (all)                                            | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Dermatitis contact<br>subjects affected / exposed<br>occurrences (all)                                             | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 | 1 / 9 (11.11%)<br>1 |
| Night sweats                                                                                                       |                     |                    |                     |

|                                        |                |                |                |
|----------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed            | 1 / 8 (12.50%) | 1 / 4 (25.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                      | 1              | 1              | 0              |
| Rash                                   |                |                |                |
| subjects affected / exposed            | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 1 / 9 (11.11%) |
| occurrences (all)                      | 0              | 0              | 1              |
| Rash macular                           |                |                |                |
| subjects affected / exposed            | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Skin lesion                            |                |                |                |
| subjects affected / exposed            | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Hyperhidrosis                          |                |                |                |
| subjects affected / exposed            | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Renal and urinary disorders            |                |                |                |
| Ketonuria                              |                |                |                |
| subjects affected / exposed            | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Urinary incontinence                   |                |                |                |
| subjects affected / exposed            | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Haematuria                             |                |                |                |
| subjects affected / exposed            | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Proteinuria                            |                |                |                |
| subjects affected / exposed            | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 1 / 9 (11.11%) |
| occurrences (all)                      | 0              | 0              | 1              |
| Renal colic                            |                |                |                |
| subjects affected / exposed            | 0 / 8 (0.00%)  | 1 / 4 (25.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                      | 0              | 1              | 0              |
| Glycosuria                             |                |                |                |
| subjects affected / exposed            | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Endocrine disorders                    |                |                |                |
| Pituitary-dependent Cushing's syndrome |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Hypothyroidism                                  |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Musculoskeletal and connective tissue disorders |                |                |                |
| Back pain                                       |                |                |                |
| subjects affected / exposed                     | 1 / 8 (12.50%) | 1 / 4 (25.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                               | 1              | 1              | 0              |
| Myalgia                                         |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Arthralgia                                      |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 1 / 4 (25.00%) | 1 / 9 (11.11%) |
| occurrences (all)                               | 0              | 2              | 2              |
| Groin pain                                      |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Muscle spasms                                   |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Musculoskeletal pain                            |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Osteoarthritis                                  |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Fistula                                         |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  | 1 / 9 (11.11%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Musculoskeletal chest pain                      |                |                |                |
| subjects affected / exposed                     | 1 / 8 (12.50%) | 0 / 4 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                               | 2              | 0              | 0              |
| Osteoporosis                                    |                |                |                |

|                             |                |               |                |
|-----------------------------|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Pain in extremity           |                |               |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 2 / 9 (22.22%) |
| occurrences (all)           | 0              | 0             | 2              |
| Coccydynia                  |                |               |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Infections and infestations |                |               |                |
| COVID-19                    |                |               |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 3 / 9 (33.33%) |
| occurrences (all)           | 0              | 0             | 3              |
| Pneumonia                   |                |               |                |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 4 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)           | 1              | 0             | 1              |
| Urinary tract infection     |                |               |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Respiratory tract infection |                |               |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Cellulitis                  |                |               |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Onychomycosis               |                |               |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Oral candidiasis            |                |               |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Pneumonia aspiration        |                |               |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Skin infection              |                |               |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |

|                                                                                       |                     |                     |                     |
|---------------------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  | 1 / 9 (11.11%)<br>2 |
| Candida infection<br>subjects affected / exposed<br>occurrences (all)                 | 1 / 8 (12.50%)<br>1 | 0 / 4 (0.00%)<br>0  | 1 / 9 (11.11%)<br>1 |
| Herpes zoster<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  | 1 / 9 (11.11%)<br>1 |
| Vaginal infection<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Coronavirus infection<br>subjects affected / exposed<br>occurrences (all)             | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Influenza<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Metabolism and nutrition disorders                                                    |                     |                     |                     |
| Decreased appetite<br>subjects affected / exposed<br>occurrences (all)                | 3 / 8 (37.50%)<br>6 | 1 / 4 (25.00%)<br>1 | 2 / 9 (22.22%)<br>4 |
| Hypercalcaemia<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Hyperkalaemia<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Hypomagnesaemia<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Dehydration                                                                           |                     |                     |                     |

|                             |                |               |                |
|-----------------------------|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Gout                        |                |               |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Hyperglycaemia              |                |               |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)           | 0              | 0             | 2              |
| Hyperlipidaemia             |                |               |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Hypokalaemia                |                |               |                |
| subjects affected / exposed | 3 / 8 (37.50%) | 0 / 4 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)           | 3              | 0             | 3              |
| Hyponatraemia               |                |               |                |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 4 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)           | 1              | 0             | 3              |
| Hypophosphataemia           |                |               |                |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 4 (0.00%) | 4 / 9 (44.44%) |
| occurrences (all)           | 2              | 0             | 5              |
| Vitamin B12 deficiency      |                |               |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Vitamin D deficiency        |                |               |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Hypoalbuminaemia            |                |               |                |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 1              | 0             | 0              |
| Hypocalcaemia               |                |               |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Hypoglycaemia               |                |               |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 4 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Hyperuricaemia              |                |               |                |

|                             |               |               |               |
|-----------------------------|---------------|---------------|---------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 4 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Malnutrition                |               |               |               |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 4 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |

| <b>Non-serious adverse events</b>                                   | Dose Escalation:<br>Phase 1a: Cohort 13 | Dose Escalation:<br>Phase 1a: Cohort 14 | Dose Expansion:<br>Phase 1b: Cohort 1 |
|---------------------------------------------------------------------|-----------------------------------------|-----------------------------------------|---------------------------------------|
| Total subjects affected by non-serious adverse events               |                                         |                                         |                                       |
| subjects affected / exposed                                         | 8 / 8 (100.00%)                         | 6 / 6 (100.00%)                         | 12 / 12 (100.00%)                     |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                         |                                         |                                       |
| Cancer pain                                                         |                                         |                                         |                                       |
| subjects affected / exposed                                         | 0 / 8 (0.00%)                           | 0 / 6 (0.00%)                           | 0 / 12 (0.00%)                        |
| occurrences (all)                                                   | 0                                       | 0                                       | 0                                     |
| Tumour pain                                                         |                                         |                                         |                                       |
| subjects affected / exposed                                         | 0 / 8 (0.00%)                           | 1 / 6 (16.67%)                          | 0 / 12 (0.00%)                        |
| occurrences (all)                                                   | 0                                       | 1                                       | 0                                     |
| Vascular disorders                                                  |                                         |                                         |                                       |
| Hypotension                                                         |                                         |                                         |                                       |
| subjects affected / exposed                                         | 0 / 8 (0.00%)                           | 0 / 6 (0.00%)                           | 0 / 12 (0.00%)                        |
| occurrences (all)                                                   | 0                                       | 0                                       | 0                                     |
| Deep vein thrombosis                                                |                                         |                                         |                                       |
| subjects affected / exposed                                         | 0 / 8 (0.00%)                           | 1 / 6 (16.67%)                          | 1 / 12 (8.33%)                        |
| occurrences (all)                                                   | 0                                       | 1                                       | 2                                     |
| Hypertension                                                        |                                         |                                         |                                       |
| subjects affected / exposed                                         | 0 / 8 (0.00%)                           | 0 / 6 (0.00%)                           | 0 / 12 (0.00%)                        |
| occurrences (all)                                                   | 0                                       | 0                                       | 0                                     |
| Embolism                                                            |                                         |                                         |                                       |
| subjects affected / exposed                                         | 0 / 8 (0.00%)                           | 1 / 6 (16.67%)                          | 0 / 12 (0.00%)                        |
| occurrences (all)                                                   | 0                                       | 1                                       | 0                                     |
| Hot flush                                                           |                                         |                                         |                                       |
| subjects affected / exposed                                         | 0 / 8 (0.00%)                           | 0 / 6 (0.00%)                           | 0 / 12 (0.00%)                        |
| occurrences (all)                                                   | 0                                       | 0                                       | 0                                     |
| Pallor                                                              |                                         |                                         |                                       |
| subjects affected / exposed                                         | 0 / 8 (0.00%)                           | 0 / 6 (0.00%)                           | 0 / 12 (0.00%)                        |
| occurrences (all)                                                   | 0                                       | 0                                       | 0                                     |
| Peripheral embolism                                                 |                                         |                                         |                                       |

|                                                      |                |                |                 |
|------------------------------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed                          | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                                    | 0              | 0              | 0               |
| General disorders and administration site conditions |                |                |                 |
| Pyrexia                                              |                |                |                 |
| subjects affected / exposed                          | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 1 / 12 (8.33%)  |
| occurrences (all)                                    | 0              | 0              | 1               |
| Fatigue                                              |                |                |                 |
| subjects affected / exposed                          | 4 / 8 (50.00%) | 3 / 6 (50.00%) | 8 / 12 (66.67%) |
| occurrences (all)                                    | 4              | 3              | 12              |
| Asthenia                                             |                |                |                 |
| subjects affected / exposed                          | 0 / 8 (0.00%)  | 1 / 6 (16.67%) | 1 / 12 (8.33%)  |
| occurrences (all)                                    | 0              | 1              | 1               |
| Gait disturbance                                     |                |                |                 |
| subjects affected / exposed                          | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                                    | 0              | 0              | 0               |
| Influenza like illness                               |                |                |                 |
| subjects affected / exposed                          | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                                    | 0              | 0              | 0               |
| Non-cardiac chest pain                               |                |                |                 |
| subjects affected / exposed                          | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 1 / 12 (8.33%)  |
| occurrences (all)                                    | 0              | 0              | 1               |
| Oedema peripheral                                    |                |                |                 |
| subjects affected / exposed                          | 0 / 8 (0.00%)  | 1 / 6 (16.67%) | 2 / 12 (16.67%) |
| occurrences (all)                                    | 0              | 1              | 2               |
| Chest discomfort                                     |                |                |                 |
| subjects affected / exposed                          | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                                    | 0              | 0              | 0               |
| Chest pain                                           |                |                |                 |
| subjects affected / exposed                          | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                                    | 0              | 0              | 0               |
| Chills                                               |                |                |                 |
| subjects affected / exposed                          | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 1 / 12 (8.33%)  |
| occurrences (all)                                    | 0              | 0              | 1               |
| Early satiety                                        |                |                |                 |

|                                                 |                |                |                 |
|-------------------------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0               |
| Infusion site extravasation                     |                |                |                 |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0               |
| Pain                                            |                |                |                 |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0               |
| Performance status decreased                    |                |                |                 |
| subjects affected / exposed                     | 1 / 8 (12.50%) | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                               | 1              | 0              | 0               |
| Physical deconditioning                         |                |                |                 |
| subjects affected / exposed                     | 1 / 8 (12.50%) | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                               | 1              | 0              | 0               |
| Peripheral swelling                             |                |                |                 |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0               |
| Immune system disorders                         |                |                |                 |
| Contrast media reaction                         |                |                |                 |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0               |
| Reproductive system and breast disorders        |                |                |                 |
| Erectile dysfunction                            |                |                |                 |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0               |
| Vaginal haemorrhage                             |                |                |                 |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 1 / 12 (8.33%)  |
| occurrences (all)                               | 0              | 0              | 1               |
| Respiratory, thoracic and mediastinal disorders |                |                |                 |
| Cough                                           |                |                |                 |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 1 / 6 (16.67%) | 3 / 12 (25.00%) |
| occurrences (all)                               | 0              | 1              | 4               |
| Dyspnoea                                        |                |                |                 |
| subjects affected / exposed                     | 2 / 8 (25.00%) | 1 / 6 (16.67%) | 2 / 12 (16.67%) |
| occurrences (all)                               | 2              | 1              | 2               |
| Oropharyngeal pain                              |                |                |                 |

|                                                    |               |               |                |
|----------------------------------------------------|---------------|---------------|----------------|
| subjects affected / exposed                        | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all)                                  | 0             | 0             | 1              |
| Wheezing                                           |               |               |                |
| subjects affected / exposed                        | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all)                                  | 0             | 0             | 1              |
| Atelectasis                                        |               |               |                |
| subjects affected / exposed                        | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                                  | 0             | 0             | 0              |
| Pleural effusion                                   |               |               |                |
| subjects affected / exposed                        | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                                  | 0             | 0             | 0              |
| Acute respiratory distress syndrome                |               |               |                |
| subjects affected / exposed                        | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                                  | 0             | 0             | 0              |
| Nasal congestion                                   |               |               |                |
| subjects affected / exposed                        | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                                  | 0             | 0             | 0              |
| Pulmonary embolism                                 |               |               |                |
| subjects affected / exposed                        | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                                  | 0             | 0             | 0              |
| Rhinorrhoea                                        |               |               |                |
| subjects affected / exposed                        | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                                  | 0             | 0             | 0              |
| Upper respiratory tract congestion                 |               |               |                |
| subjects affected / exposed                        | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                                  | 0             | 0             | 0              |
| Increased viscosity of upper respiratory secretion |               |               |                |
| subjects affected / exposed                        | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all)                                  | 0             | 0             | 1              |
| Pneumothorax                                       |               |               |                |
| subjects affected / exposed                        | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                                  | 0             | 0             | 0              |
| Productive cough                                   |               |               |                |
| subjects affected / exposed                        | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all)                                  | 0             | 0             | 1              |

|                                      |                |                |                |
|--------------------------------------|----------------|----------------|----------------|
| Psychiatric disorders                |                |                |                |
| Depression                           |                |                |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 1 / 12 (8.33%) |
| occurrences (all)                    | 0              | 0              | 1              |
| Hallucination, auditory              |                |                |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0              |
| Insomnia                             |                |                |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 1 / 12 (8.33%) |
| occurrences (all)                    | 0              | 0              | 1              |
| Anxiety                              |                |                |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 1 / 6 (16.67%) | 1 / 12 (8.33%) |
| occurrences (all)                    | 0              | 1              | 1              |
| Confusional state                    |                |                |                |
| subjects affected / exposed          | 1 / 8 (12.50%) | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                    | 1              | 0              | 0              |
| Irritability                         |                |                |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 1 / 12 (8.33%) |
| occurrences (all)                    | 0              | 0              | 1              |
| Product issues                       |                |                |                |
| Device breakage                      |                |                |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 1 / 12 (8.33%) |
| occurrences (all)                    | 0              | 0              | 1              |
| Investigations                       |                |                |                |
| Blood alkaline phosphatase increased |                |                |                |
| subjects affected / exposed          | 1 / 8 (12.50%) | 0 / 6 (0.00%)  | 1 / 12 (8.33%) |
| occurrences (all)                    | 3              | 0              | 1              |
| Blood creatinine increased           |                |                |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 1 / 12 (8.33%) |
| occurrences (all)                    | 0              | 0              | 1              |
| Alanine aminotransferase increased   |                |                |                |
| subjects affected / exposed          | 1 / 8 (12.50%) | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                    | 2              | 0              | 0              |
| Aspartate aminotransferase increased |                |                |                |
| subjects affected / exposed          | 1 / 8 (12.50%) | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                    | 3              | 0              | 0              |

|                                        |                |                |                 |
|----------------------------------------|----------------|----------------|-----------------|
| Blood bilirubin increased              |                |                |                 |
| subjects affected / exposed            | 1 / 8 (12.50%) | 0 / 6 (0.00%)  | 1 / 12 (8.33%)  |
| occurrences (all)                      | 2              | 0              | 1               |
| Blood cholesterol increased            |                |                |                 |
| subjects affected / exposed            | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0               |
| Blood lactate dehydrogenase decreased  |                |                |                 |
| subjects affected / exposed            | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0               |
| Blood phosphorus decreased             |                |                |                 |
| subjects affected / exposed            | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0               |
| Electrocardiogram QT interval abnormal |                |                |                 |
| subjects affected / exposed            | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0               |
| Electrocardiogram QT prolonged         |                |                |                 |
| subjects affected / exposed            | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0               |
| Gamma-glutamyltransferase increased    |                |                |                 |
| subjects affected / exposed            | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0               |
| Lymphocyte count decreased             |                |                |                 |
| subjects affected / exposed            | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0               |
| Neutrophil count decreased             |                |                |                 |
| subjects affected / exposed            | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0               |
| Weight decreased                       |                |                |                 |
| subjects affected / exposed            | 1 / 8 (12.50%) | 1 / 6 (16.67%) | 2 / 12 (16.67%) |
| occurrences (all)                      | 1              | 1              | 2               |
| Weight increased                       |                |                |                 |
| subjects affected / exposed            | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0               |
| White blood cell count decreased       |                |                |                 |

|                                                |                |                |                |
|------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                    | 1 / 8 (12.50%) | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                              | 1              | 0              | 0              |
| Blood creatine phosphokinase increased         |                |                |                |
| subjects affected / exposed                    | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0              |
| Blood creatinine decreased                     |                |                |                |
| subjects affected / exposed                    | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0              |
| Blood lactate dehydrogenase increased          |                |                |                |
| subjects affected / exposed                    | 1 / 8 (12.50%) | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                              | 1              | 0              | 0              |
| Blood sodium decreased                         |                |                |                |
| subjects affected / exposed                    | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0              |
| Eosinophil count decreased                     |                |                |                |
| subjects affected / exposed                    | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0              |
| Platelet count decreased                       |                |                |                |
| subjects affected / exposed                    | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0              |
| White blood cell count increased               |                |                |                |
| subjects affected / exposed                    | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0              |
| Ejection fraction decreased                    |                |                |                |
| subjects affected / exposed                    | 0 / 8 (0.00%)  | 1 / 6 (16.67%) | 0 / 12 (0.00%) |
| occurrences (all)                              | 0              | 1              | 0              |
| Blood albumin decreased                        |                |                |                |
| subjects affected / exposed                    | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0              |
| Carbon dioxide decreased                       |                |                |                |
| subjects affected / exposed                    | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 1 / 12 (8.33%) |
| occurrences (all)                              | 0              | 0              | 1              |
| Injury, poisoning and procedural complications |                |                |                |

|                                                                                 |                     |                     |                     |
|---------------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| Spinal compression fracture<br>subjects affected / exposed<br>occurrences (all) | 0 / 8 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0 |
| Contusion<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 8 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0 |
| Fall<br>subjects affected / exposed<br>occurrences (all)                        | 1 / 8 (12.50%)<br>2 | 1 / 6 (16.67%)<br>1 | 0 / 12 (0.00%)<br>0 |
| Stoma prolapse<br>subjects affected / exposed<br>occurrences (all)              | 0 / 8 (0.00%)<br>0  | 1 / 6 (16.67%)<br>1 | 0 / 12 (0.00%)<br>0 |
| Skin laceration<br>subjects affected / exposed<br>occurrences (all)             | 1 / 8 (12.50%)<br>1 | 0 / 6 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0 |
| Pelvic fracture<br>subjects affected / exposed<br>occurrences (all)             | 0 / 8 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 1 / 12 (8.33%)<br>1 |
| Procedural pain<br>subjects affected / exposed<br>occurrences (all)             | 0 / 8 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0 |
| Rib fracture<br>subjects affected / exposed<br>occurrences (all)                | 0 / 8 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0 |
| Ulna fracture<br>subjects affected / exposed<br>occurrences (all)               | 0 / 8 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 1 / 12 (8.33%)<br>1 |
| Cardiac disorders                                                               |                     |                     |                     |
| Sinus tachycardia<br>subjects affected / exposed<br>occurrences (all)           | 0 / 8 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0 |
| Atrial fibrillation<br>subjects affected / exposed<br>occurrences (all)         | 0 / 8 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0 |
| Palpitations                                                                    |                     |                     |                     |

|                                     |                |                |                 |
|-------------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed         | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                   | 0              | 0              | 0               |
| Pericardial effusion                |                |                |                 |
| subjects affected / exposed         | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                   | 0              | 0              | 0               |
| Sinus bradycardia                   |                |                |                 |
| subjects affected / exposed         | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                   | 0              | 0              | 0               |
| Atrial thrombosis                   |                |                |                 |
| subjects affected / exposed         | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 1 / 12 (8.33%)  |
| occurrences (all)                   | 0              | 0              | 1               |
| Atrioventricular block first degree |                |                |                 |
| subjects affected / exposed         | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 1 / 12 (8.33%)  |
| occurrences (all)                   | 0              | 0              | 1               |
| Tachycardia                         |                |                |                 |
| subjects affected / exposed         | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 1 / 12 (8.33%)  |
| occurrences (all)                   | 0              | 0              | 1               |
| Nervous system disorders            |                |                |                 |
| Dizziness                           |                |                |                 |
| subjects affected / exposed         | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 2 / 12 (16.67%) |
| occurrences (all)                   | 0              | 0              | 2               |
| Ageusia                             |                |                |                 |
| subjects affected / exposed         | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                   | 0              | 0              | 0               |
| Anosmia                             |                |                |                 |
| subjects affected / exposed         | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                   | 0              | 0              | 0               |
| Dysgeusia                           |                |                |                 |
| subjects affected / exposed         | 1 / 8 (12.50%) | 0 / 6 (0.00%)  | 4 / 12 (33.33%) |
| occurrences (all)                   | 1              | 0              | 4               |
| Headache                            |                |                |                 |
| subjects affected / exposed         | 1 / 8 (12.50%) | 1 / 6 (16.67%) | 0 / 12 (0.00%)  |
| occurrences (all)                   | 1              | 1              | 0               |
| Hypoaesthesia                       |                |                |                 |
| subjects affected / exposed         | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                   | 0              | 0              | 0               |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| Sensory loss                |                |                |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Syncope                     |                |                |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Paraesthesia                |                |                |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 1 / 6 (16.67%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Brain oedema                |                |                |                |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Neuropathy peripheral       |                |                |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Post herpetic neuralgia     |                |                |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Taste disorder              |                |                |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Tremor                      |                |                |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Coordination abnormal       |                |                |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 1 / 6 (16.67%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 2              | 0              |
| Cognitive disorder          |                |                |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 1 / 12 (8.33%) |
| occurrences (all)           | 0              | 0              | 1              |
| Disturbance in attention    |                |                |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Parosmia                    |                |                |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 1 / 12 (8.33%) |
| occurrences (all)           | 0              | 0              | 1              |

|                                      |                |                |                |
|--------------------------------------|----------------|----------------|----------------|
| Blood and lymphatic system disorders |                |                |                |
| Anaemia                              |                |                |                |
| subjects affected / exposed          | 1 / 8 (12.50%) | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                    | 1              | 0              | 0              |
| Leukocytosis                         |                |                |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0              |
| Leukopenia                           |                |                |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0              |
| Thrombocytopenia                     |                |                |                |
| subjects affected / exposed          | 2 / 8 (25.00%) | 1 / 6 (16.67%) | 0 / 12 (0.00%) |
| occurrences (all)                    | 3              | 1              | 0              |
| Lymphopenia                          |                |                |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0              |
| Neutropenia                          |                |                |                |
| subjects affected / exposed          | 1 / 8 (12.50%) | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                    | 2              | 0              | 0              |
| Ear and labyrinth disorders          |                |                |                |
| Tinnitus                             |                |                |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0              |
| Hyperacusis                          |                |                |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0              |
| Eye disorders                        |                |                |                |
| Vision blurred                       |                |                |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0              |
| Conjunctival haemorrhage             |                |                |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0              |
| Eye pain                             |                |                |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0              |
| Vitreous floaters                    |                |                |                |

|                             |                |                |                  |
|-----------------------------|----------------|----------------|------------------|
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%)   |
| occurrences (all)           | 0              | 0              | 0                |
| Diplopia                    |                |                |                  |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%)   |
| occurrences (all)           | 0              | 0              | 0                |
| Gastrointestinal disorders  |                |                |                  |
| Nausea                      |                |                |                  |
| subjects affected / exposed | 5 / 8 (62.50%) | 4 / 6 (66.67%) | 10 / 12 (83.33%) |
| occurrences (all)           | 10             | 8              | 14               |
| Vomiting                    |                |                |                  |
| subjects affected / exposed | 5 / 8 (62.50%) | 3 / 6 (50.00%) | 5 / 12 (41.67%)  |
| occurrences (all)           | 8              | 5              | 11               |
| Abdominal pain              |                |                |                  |
| subjects affected / exposed | 1 / 8 (12.50%) | 1 / 6 (16.67%) | 3 / 12 (25.00%)  |
| occurrences (all)           | 1              | 1              | 3                |
| Constipation                |                |                |                  |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 1 / 12 (8.33%)   |
| occurrences (all)           | 0              | 0              | 1                |
| Diarrhoea                   |                |                |                  |
| subjects affected / exposed | 7 / 8 (87.50%) | 3 / 6 (50.00%) | 9 / 12 (75.00%)  |
| occurrences (all)           | 12             | 6              | 22               |
| Abdominal distension        |                |                |                  |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%)   |
| occurrences (all)           | 0              | 0              | 0                |
| Dry mouth                   |                |                |                  |
| subjects affected / exposed | 0 / 8 (0.00%)  | 1 / 6 (16.67%) | 1 / 12 (8.33%)   |
| occurrences (all)           | 0              | 1              | 1                |
| Haematochezia               |                |                |                  |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%)   |
| occurrences (all)           | 0              | 0              | 0                |
| Retching                    |                |                |                  |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 1 / 12 (8.33%)   |
| occurrences (all)           | 0              | 0              | 1                |
| Anal incontinence           |                |                |                  |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 1 / 12 (8.33%)   |
| occurrences (all)           | 0              | 0              | 1                |

|                                  |                |               |                 |
|----------------------------------|----------------|---------------|-----------------|
| Dyspepsia                        |                |               |                 |
| subjects affected / exposed      | 0 / 8 (0.00%)  | 0 / 6 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)                | 0              | 0             | 0               |
| Dysphagia                        |                |               |                 |
| subjects affected / exposed      | 0 / 8 (0.00%)  | 0 / 6 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)                | 0              | 0             | 0               |
| Faeces soft                      |                |               |                 |
| subjects affected / exposed      | 0 / 8 (0.00%)  | 0 / 6 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)                | 0              | 0             | 0               |
| Flatulence                       |                |               |                 |
| subjects affected / exposed      | 0 / 8 (0.00%)  | 0 / 6 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)                | 0              | 0             | 0               |
| Gastrooesophageal reflux disease |                |               |                 |
| subjects affected / exposed      | 0 / 8 (0.00%)  | 0 / 6 (0.00%) | 1 / 12 (8.33%)  |
| occurrences (all)                | 0              | 0             | 1               |
| Salivary hypersecretion          |                |               |                 |
| subjects affected / exposed      | 0 / 8 (0.00%)  | 0 / 6 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)                | 0              | 0             | 0               |
| Stomatitis                       |                |               |                 |
| subjects affected / exposed      | 0 / 8 (0.00%)  | 0 / 6 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)                | 0              | 0             | 0               |
| Abdominal pain upper             |                |               |                 |
| subjects affected / exposed      | 0 / 8 (0.00%)  | 0 / 6 (0.00%) | 2 / 12 (16.67%) |
| occurrences (all)                | 0              | 0             | 2               |
| Colitis                          |                |               |                 |
| subjects affected / exposed      | 0 / 8 (0.00%)  | 0 / 6 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)                | 0              | 0             | 0               |
| Food poisoning                   |                |               |                 |
| subjects affected / exposed      | 1 / 8 (12.50%) | 0 / 6 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)                | 1              | 0             | 0               |
| Tooth discolouration             |                |               |                 |
| subjects affected / exposed      | 0 / 8 (0.00%)  | 0 / 6 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)                | 0              | 0             | 0               |
| Ascites                          |                |               |                 |
| subjects affected / exposed      | 0 / 8 (0.00%)  | 0 / 6 (0.00%) | 1 / 12 (8.33%)  |
| occurrences (all)                | 0              | 0             | 1               |

|                                                                               |                    |                    |                     |
|-------------------------------------------------------------------------------|--------------------|--------------------|---------------------|
| Parotid gland enlargement<br>subjects affected / exposed<br>occurrences (all) | 0 / 8 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 | 1 / 12 (8.33%)<br>1 |
| Rectal haemorrhage<br>subjects affected / exposed<br>occurrences (all)        | 0 / 8 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 | 1 / 12 (8.33%)<br>1 |
| Tooth erosion<br>subjects affected / exposed<br>occurrences (all)             | 0 / 8 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 | 1 / 12 (8.33%)<br>1 |
| Tooth loss<br>subjects affected / exposed<br>occurrences (all)                | 0 / 8 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 | 1 / 12 (8.33%)<br>2 |
| Hepatobiliary disorders                                                       |                    |                    |                     |
| Hyperbilirubinaemia<br>subjects affected / exposed<br>occurrences (all)       | 0 / 8 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 | 1 / 12 (8.33%)<br>1 |
| Hepatitis acute<br>subjects affected / exposed<br>occurrences (all)           | 0 / 8 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |
| Biliary dilatation<br>subjects affected / exposed<br>occurrences (all)        | 0 / 8 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |
| Skin and subcutaneous tissue disorders                                        |                    |                    |                     |
| Dermatitis acneiform<br>subjects affected / exposed<br>occurrences (all)      | 0 / 8 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |
| Pruritus<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 8 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 | 1 / 12 (8.33%)<br>1 |
| Rash maculo-papular<br>subjects affected / exposed<br>occurrences (all)       | 0 / 8 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |
| Dermatitis contact<br>subjects affected / exposed<br>occurrences (all)        | 0 / 8 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |
| Night sweats                                                                  |                    |                    |                     |

|                                        |               |                |                |
|----------------------------------------|---------------|----------------|----------------|
| subjects affected / exposed            | 0 / 8 (0.00%) | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                      | 0             | 0              | 0              |
| Rash                                   |               |                |                |
| subjects affected / exposed            | 0 / 8 (0.00%) | 0 / 6 (0.00%)  | 1 / 12 (8.33%) |
| occurrences (all)                      | 0             | 0              | 1              |
| Rash macular                           |               |                |                |
| subjects affected / exposed            | 0 / 8 (0.00%) | 0 / 6 (0.00%)  | 1 / 12 (8.33%) |
| occurrences (all)                      | 0             | 0              | 1              |
| Skin lesion                            |               |                |                |
| subjects affected / exposed            | 0 / 8 (0.00%) | 0 / 6 (0.00%)  | 1 / 12 (8.33%) |
| occurrences (all)                      | 0             | 0              | 1              |
| Hyperhidrosis                          |               |                |                |
| subjects affected / exposed            | 0 / 8 (0.00%) | 0 / 6 (0.00%)  | 1 / 12 (8.33%) |
| occurrences (all)                      | 0             | 0              | 1              |
| Renal and urinary disorders            |               |                |                |
| Ketonuria                              |               |                |                |
| subjects affected / exposed            | 0 / 8 (0.00%) | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                      | 0             | 0              | 0              |
| Urinary incontinence                   |               |                |                |
| subjects affected / exposed            | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 0 / 12 (0.00%) |
| occurrences (all)                      | 0             | 1              | 0              |
| Haematuria                             |               |                |                |
| subjects affected / exposed            | 0 / 8 (0.00%) | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                      | 0             | 0              | 0              |
| Proteinuria                            |               |                |                |
| subjects affected / exposed            | 0 / 8 (0.00%) | 0 / 6 (0.00%)  | 1 / 12 (8.33%) |
| occurrences (all)                      | 0             | 0              | 1              |
| Renal colic                            |               |                |                |
| subjects affected / exposed            | 0 / 8 (0.00%) | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                      | 0             | 0              | 0              |
| Glycosuria                             |               |                |                |
| subjects affected / exposed            | 0 / 8 (0.00%) | 0 / 6 (0.00%)  | 1 / 12 (8.33%) |
| occurrences (all)                      | 0             | 0              | 1              |
| Endocrine disorders                    |               |                |                |
| Pituitary-dependent Cushing's syndrome |               |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Hypothyroidism                                  |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Musculoskeletal and connective tissue disorders |                |                |                |
| Back pain                                       |                |                |                |
| subjects affected / exposed                     | 1 / 8 (12.50%) | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                               | 1              | 0              | 0              |
| Myalgia                                         |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 1 / 6 (16.67%) | 0 / 12 (0.00%) |
| occurrences (all)                               | 0              | 1              | 0              |
| Arthralgia                                      |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Groin pain                                      |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Muscle spasms                                   |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Musculoskeletal pain                            |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Osteoarthritis                                  |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Fistula                                         |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Musculoskeletal chest pain                      |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Osteoporosis                                    |                |                |                |

|                             |               |                |                 |
|-----------------------------|---------------|----------------|-----------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0               |
| Pain in extremity           |               |                |                 |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0               |
| Coccydynia                  |               |                |                 |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%)  | 1 / 12 (8.33%)  |
| occurrences (all)           | 0             | 0              | 1               |
| Infections and infestations |               |                |                 |
| COVID-19                    |               |                |                 |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 6 (33.33%) | 0 / 12 (0.00%)  |
| occurrences (all)           | 0             | 2              | 0               |
| Pneumonia                   |               |                |                 |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0               |
| Urinary tract infection     |               |                |                 |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%)  | 3 / 12 (25.00%) |
| occurrences (all)           | 0             | 0              | 4               |
| Respiratory tract infection |               |                |                 |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0               |
| Cellulitis                  |               |                |                 |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0               |
| Onychomycosis               |               |                |                 |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0               |
| Oral candidiasis            |               |                |                 |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 0 / 12 (0.00%)  |
| occurrences (all)           | 0             | 1              | 0               |
| Pneumonia aspiration        |               |                |                 |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0               |
| Skin infection              |               |                |                 |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0               |

|                                                                                       |                     |                     |                       |
|---------------------------------------------------------------------------------------|---------------------|---------------------|-----------------------|
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 0 / 8 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 2 / 12 (16.67%)<br>2  |
| Candida infection<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 8 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0   |
| Herpes zoster<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 8 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0   |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 8 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0   |
| Vaginal infection<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 8 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0   |
| Coronavirus infection<br>subjects affected / exposed<br>occurrences (all)             | 0 / 8 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0   |
| Influenza<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 8 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0   |
| Metabolism and nutrition disorders                                                    |                     |                     |                       |
| Decreased appetite<br>subjects affected / exposed<br>occurrences (all)                | 1 / 8 (12.50%)<br>2 | 1 / 6 (16.67%)<br>2 | 6 / 12 (50.00%)<br>10 |
| Hypercalcaemia<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 8 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0   |
| Hyperkalaemia<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 8 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0   |
| Hypomagnesaemia<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 8 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0   |
| Dehydration                                                                           |                     |                     |                       |

|                             |                |                |                 |
|-----------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 4 / 12 (33.33%) |
| occurrences (all)           | 0              | 0              | 5               |
| Gout                        |                |                |                 |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Hyperglycaemia              |                |                |                 |
| subjects affected / exposed | 0 / 8 (0.00%)  | 1 / 6 (16.67%) | 0 / 12 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0               |
| Hyperlipidaemia             |                |                |                 |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Hypokalaemia                |                |                |                 |
| subjects affected / exposed | 2 / 8 (25.00%) | 2 / 6 (33.33%) | 0 / 12 (0.00%)  |
| occurrences (all)           | 2              | 2              | 0               |
| Hyponatraemia               |                |                |                 |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Hypophosphataemia           |                |                |                 |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 2 / 12 (16.67%) |
| occurrences (all)           | 0              | 0              | 2               |
| Vitamin B12 deficiency      |                |                |                 |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Vitamin D deficiency        |                |                |                 |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Hypoalbuminaemia            |                |                |                 |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0               |
| Hypocalcaemia               |                |                |                 |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0               |
| Hypoglycaemia               |                |                |                 |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 6 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0               |
| Hyperuricaemia              |                |                |                 |

|                             |               |               |                |
|-----------------------------|---------------|---------------|----------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all)           | 0             | 0             | 1              |
| Malnutrition                |               |               |                |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all)           | 0             | 0             | 1              |

| <b>Non-serious adverse events</b>                                   | Dose Expansion:<br>Phase 1b: Cohort 2 |  |  |
|---------------------------------------------------------------------|---------------------------------------|--|--|
| Total subjects affected by non-serious adverse events               |                                       |  |  |
| subjects affected / exposed                                         | 12 / 12 (100.00%)                     |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                       |  |  |
| Cancer pain                                                         |                                       |  |  |
| subjects affected / exposed                                         | 0 / 12 (0.00%)                        |  |  |
| occurrences (all)                                                   | 0                                     |  |  |
| Tumour pain                                                         |                                       |  |  |
| subjects affected / exposed                                         | 0 / 12 (0.00%)                        |  |  |
| occurrences (all)                                                   | 0                                     |  |  |
| Vascular disorders                                                  |                                       |  |  |
| Hypotension                                                         |                                       |  |  |
| subjects affected / exposed                                         | 0 / 12 (0.00%)                        |  |  |
| occurrences (all)                                                   | 0                                     |  |  |
| Deep vein thrombosis                                                |                                       |  |  |
| subjects affected / exposed                                         | 0 / 12 (0.00%)                        |  |  |
| occurrences (all)                                                   | 0                                     |  |  |
| Hypertension                                                        |                                       |  |  |
| subjects affected / exposed                                         | 0 / 12 (0.00%)                        |  |  |
| occurrences (all)                                                   | 0                                     |  |  |
| Embolism                                                            |                                       |  |  |
| subjects affected / exposed                                         | 0 / 12 (0.00%)                        |  |  |
| occurrences (all)                                                   | 0                                     |  |  |
| Hot flush                                                           |                                       |  |  |
| subjects affected / exposed                                         | 0 / 12 (0.00%)                        |  |  |
| occurrences (all)                                                   | 0                                     |  |  |
| Pallor                                                              |                                       |  |  |
| subjects affected / exposed                                         | 0 / 12 (0.00%)                        |  |  |
| occurrences (all)                                                   | 0                                     |  |  |
| Peripheral embolism                                                 |                                       |  |  |

|                                                      |                 |  |  |
|------------------------------------------------------|-----------------|--|--|
| subjects affected / exposed                          | 1 / 12 (8.33%)  |  |  |
| occurrences (all)                                    | 1               |  |  |
| General disorders and administration site conditions |                 |  |  |
| Pyrexia                                              |                 |  |  |
| subjects affected / exposed                          | 1 / 12 (8.33%)  |  |  |
| occurrences (all)                                    | 1               |  |  |
| Fatigue                                              |                 |  |  |
| subjects affected / exposed                          | 7 / 12 (58.33%) |  |  |
| occurrences (all)                                    | 11              |  |  |
| Asthenia                                             |                 |  |  |
| subjects affected / exposed                          | 0 / 12 (0.00%)  |  |  |
| occurrences (all)                                    | 0               |  |  |
| Gait disturbance                                     |                 |  |  |
| subjects affected / exposed                          | 0 / 12 (0.00%)  |  |  |
| occurrences (all)                                    | 0               |  |  |
| Influenza like illness                               |                 |  |  |
| subjects affected / exposed                          | 0 / 12 (0.00%)  |  |  |
| occurrences (all)                                    | 0               |  |  |
| Non-cardiac chest pain                               |                 |  |  |
| subjects affected / exposed                          | 1 / 12 (8.33%)  |  |  |
| occurrences (all)                                    | 1               |  |  |
| Oedema peripheral                                    |                 |  |  |
| subjects affected / exposed                          | 2 / 12 (16.67%) |  |  |
| occurrences (all)                                    | 2               |  |  |
| Chest discomfort                                     |                 |  |  |
| subjects affected / exposed                          | 1 / 12 (8.33%)  |  |  |
| occurrences (all)                                    | 1               |  |  |
| Chest pain                                           |                 |  |  |
| subjects affected / exposed                          | 1 / 12 (8.33%)  |  |  |
| occurrences (all)                                    | 1               |  |  |
| Chills                                               |                 |  |  |
| subjects affected / exposed                          | 1 / 12 (8.33%)  |  |  |
| occurrences (all)                                    | 1               |  |  |
| Early satiety                                        |                 |  |  |

|                                                 |                 |  |  |
|-------------------------------------------------|-----------------|--|--|
| subjects affected / exposed                     | 0 / 12 (0.00%)  |  |  |
| occurrences (all)                               | 0               |  |  |
| Infusion site extravasation                     |                 |  |  |
| subjects affected / exposed                     | 0 / 12 (0.00%)  |  |  |
| occurrences (all)                               | 0               |  |  |
| Pain                                            |                 |  |  |
| subjects affected / exposed                     | 0 / 12 (0.00%)  |  |  |
| occurrences (all)                               | 0               |  |  |
| Performance status decreased                    |                 |  |  |
| subjects affected / exposed                     | 0 / 12 (0.00%)  |  |  |
| occurrences (all)                               | 0               |  |  |
| Physical deconditioning                         |                 |  |  |
| subjects affected / exposed                     | 0 / 12 (0.00%)  |  |  |
| occurrences (all)                               | 0               |  |  |
| Peripheral swelling                             |                 |  |  |
| subjects affected / exposed                     | 1 / 12 (8.33%)  |  |  |
| occurrences (all)                               | 1               |  |  |
| Immune system disorders                         |                 |  |  |
| Contrast media reaction                         |                 |  |  |
| subjects affected / exposed                     | 0 / 12 (0.00%)  |  |  |
| occurrences (all)                               | 0               |  |  |
| Reproductive system and breast disorders        |                 |  |  |
| Erectile dysfunction                            |                 |  |  |
| subjects affected / exposed                     | 0 / 12 (0.00%)  |  |  |
| occurrences (all)                               | 0               |  |  |
| Vaginal haemorrhage                             |                 |  |  |
| subjects affected / exposed                     | 0 / 12 (0.00%)  |  |  |
| occurrences (all)                               | 0               |  |  |
| Respiratory, thoracic and mediastinal disorders |                 |  |  |
| Cough                                           |                 |  |  |
| subjects affected / exposed                     | 3 / 12 (25.00%) |  |  |
| occurrences (all)                               | 4               |  |  |
| Dyspnoea                                        |                 |  |  |
| subjects affected / exposed                     | 2 / 12 (16.67%) |  |  |
| occurrences (all)                               | 2               |  |  |
| Oropharyngeal pain                              |                 |  |  |

|                                                    |                |  |  |
|----------------------------------------------------|----------------|--|--|
| subjects affected / exposed                        | 0 / 12 (0.00%) |  |  |
| occurrences (all)                                  | 0              |  |  |
| Wheezing                                           |                |  |  |
| subjects affected / exposed                        | 1 / 12 (8.33%) |  |  |
| occurrences (all)                                  | 1              |  |  |
| Atelectasis                                        |                |  |  |
| subjects affected / exposed                        | 0 / 12 (0.00%) |  |  |
| occurrences (all)                                  | 0              |  |  |
| Pleural effusion                                   |                |  |  |
| subjects affected / exposed                        | 0 / 12 (0.00%) |  |  |
| occurrences (all)                                  | 0              |  |  |
| Acute respiratory distress syndrome                |                |  |  |
| subjects affected / exposed                        | 0 / 12 (0.00%) |  |  |
| occurrences (all)                                  | 0              |  |  |
| Nasal congestion                                   |                |  |  |
| subjects affected / exposed                        | 1 / 12 (8.33%) |  |  |
| occurrences (all)                                  | 1              |  |  |
| Pulmonary embolism                                 |                |  |  |
| subjects affected / exposed                        | 0 / 12 (0.00%) |  |  |
| occurrences (all)                                  | 0              |  |  |
| Rhinorrhoea                                        |                |  |  |
| subjects affected / exposed                        | 0 / 12 (0.00%) |  |  |
| occurrences (all)                                  | 0              |  |  |
| Upper respiratory tract congestion                 |                |  |  |
| subjects affected / exposed                        | 0 / 12 (0.00%) |  |  |
| occurrences (all)                                  | 0              |  |  |
| Increased viscosity of upper respiratory secretion |                |  |  |
| subjects affected / exposed                        | 0 / 12 (0.00%) |  |  |
| occurrences (all)                                  | 0              |  |  |
| Pneumothorax                                       |                |  |  |
| subjects affected / exposed                        | 1 / 12 (8.33%) |  |  |
| occurrences (all)                                  | 1              |  |  |
| Productive cough                                   |                |  |  |
| subjects affected / exposed                        | 0 / 12 (0.00%) |  |  |
| occurrences (all)                                  | 0              |  |  |

|                                      |                |  |  |
|--------------------------------------|----------------|--|--|
| Psychiatric disorders                |                |  |  |
| Depression                           |                |  |  |
| subjects affected / exposed          | 0 / 12 (0.00%) |  |  |
| occurrences (all)                    | 0              |  |  |
| Hallucination, auditory              |                |  |  |
| subjects affected / exposed          | 0 / 12 (0.00%) |  |  |
| occurrences (all)                    | 0              |  |  |
| Insomnia                             |                |  |  |
| subjects affected / exposed          | 1 / 12 (8.33%) |  |  |
| occurrences (all)                    | 1              |  |  |
| Anxiety                              |                |  |  |
| subjects affected / exposed          | 0 / 12 (0.00%) |  |  |
| occurrences (all)                    | 0              |  |  |
| Confusional state                    |                |  |  |
| subjects affected / exposed          | 0 / 12 (0.00%) |  |  |
| occurrences (all)                    | 0              |  |  |
| Irritability                         |                |  |  |
| subjects affected / exposed          | 0 / 12 (0.00%) |  |  |
| occurrences (all)                    | 0              |  |  |
| Product issues                       |                |  |  |
| Device breakage                      |                |  |  |
| subjects affected / exposed          | 0 / 12 (0.00%) |  |  |
| occurrences (all)                    | 0              |  |  |
| Investigations                       |                |  |  |
| Blood alkaline phosphatase increased |                |  |  |
| subjects affected / exposed          | 0 / 12 (0.00%) |  |  |
| occurrences (all)                    | 0              |  |  |
| Blood creatinine increased           |                |  |  |
| subjects affected / exposed          | 1 / 12 (8.33%) |  |  |
| occurrences (all)                    | 2              |  |  |
| Alanine aminotransferase increased   |                |  |  |
| subjects affected / exposed          | 0 / 12 (0.00%) |  |  |
| occurrences (all)                    | 0              |  |  |
| Aspartate aminotransferase increased |                |  |  |
| subjects affected / exposed          | 0 / 12 (0.00%) |  |  |
| occurrences (all)                    | 0              |  |  |

|                                        |                |  |  |
|----------------------------------------|----------------|--|--|
| Blood bilirubin increased              |                |  |  |
| subjects affected / exposed            | 1 / 12 (8.33%) |  |  |
| occurrences (all)                      | 1              |  |  |
| Blood cholesterol increased            |                |  |  |
| subjects affected / exposed            | 0 / 12 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Blood lactate dehydrogenase decreased  |                |  |  |
| subjects affected / exposed            | 0 / 12 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Blood phosphorus decreased             |                |  |  |
| subjects affected / exposed            | 0 / 12 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Electrocardiogram QT interval abnormal |                |  |  |
| subjects affected / exposed            | 0 / 12 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Electrocardiogram QT prolonged         |                |  |  |
| subjects affected / exposed            | 0 / 12 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Gamma-glutamyltransferase increased    |                |  |  |
| subjects affected / exposed            | 0 / 12 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Lymphocyte count decreased             |                |  |  |
| subjects affected / exposed            | 0 / 12 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Neutrophil count decreased             |                |  |  |
| subjects affected / exposed            | 0 / 12 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Weight decreased                       |                |  |  |
| subjects affected / exposed            | 0 / 12 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Weight increased                       |                |  |  |
| subjects affected / exposed            | 0 / 12 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| White blood cell count decreased       |                |  |  |

|                                                |                |  |  |
|------------------------------------------------|----------------|--|--|
| subjects affected / exposed                    | 1 / 12 (8.33%) |  |  |
| occurrences (all)                              | 7              |  |  |
| Blood creatine phosphokinase increased         |                |  |  |
| subjects affected / exposed                    | 0 / 12 (0.00%) |  |  |
| occurrences (all)                              | 0              |  |  |
| Blood creatinine decreased                     |                |  |  |
| subjects affected / exposed                    | 0 / 12 (0.00%) |  |  |
| occurrences (all)                              | 0              |  |  |
| Blood lactate dehydrogenase increased          |                |  |  |
| subjects affected / exposed                    | 0 / 12 (0.00%) |  |  |
| occurrences (all)                              | 0              |  |  |
| Blood sodium decreased                         |                |  |  |
| subjects affected / exposed                    | 0 / 12 (0.00%) |  |  |
| occurrences (all)                              | 0              |  |  |
| Eosinophil count decreased                     |                |  |  |
| subjects affected / exposed                    | 0 / 12 (0.00%) |  |  |
| occurrences (all)                              | 0              |  |  |
| Platelet count decreased                       |                |  |  |
| subjects affected / exposed                    | 1 / 12 (8.33%) |  |  |
| occurrences (all)                              | 2              |  |  |
| White blood cell count increased               |                |  |  |
| subjects affected / exposed                    | 0 / 12 (0.00%) |  |  |
| occurrences (all)                              | 0              |  |  |
| Ejection fraction decreased                    |                |  |  |
| subjects affected / exposed                    | 0 / 12 (0.00%) |  |  |
| occurrences (all)                              | 0              |  |  |
| Blood albumin decreased                        |                |  |  |
| subjects affected / exposed                    | 0 / 12 (0.00%) |  |  |
| occurrences (all)                              | 0              |  |  |
| Carbon dioxide decreased                       |                |  |  |
| subjects affected / exposed                    | 0 / 12 (0.00%) |  |  |
| occurrences (all)                              | 0              |  |  |
| Injury, poisoning and procedural complications |                |  |  |

|                                                                                 |                     |  |  |
|---------------------------------------------------------------------------------|---------------------|--|--|
| Spinal compression fracture<br>subjects affected / exposed<br>occurrences (all) | 0 / 12 (0.00%)<br>0 |  |  |
| Contusion<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 12 (0.00%)<br>0 |  |  |
| Fall<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 12 (0.00%)<br>0 |  |  |
| Stoma prolapse<br>subjects affected / exposed<br>occurrences (all)              | 0 / 12 (0.00%)<br>0 |  |  |
| Skin laceration<br>subjects affected / exposed<br>occurrences (all)             | 0 / 12 (0.00%)<br>0 |  |  |
| Pelvic fracture<br>subjects affected / exposed<br>occurrences (all)             | 0 / 12 (0.00%)<br>0 |  |  |
| Procedural pain<br>subjects affected / exposed<br>occurrences (all)             | 1 / 12 (8.33%)<br>1 |  |  |
| Rib fracture<br>subjects affected / exposed<br>occurrences (all)                | 1 / 12 (8.33%)<br>1 |  |  |
| Ulna fracture<br>subjects affected / exposed<br>occurrences (all)               | 0 / 12 (0.00%)<br>0 |  |  |
| Cardiac disorders                                                               |                     |  |  |
| Sinus tachycardia<br>subjects affected / exposed<br>occurrences (all)           | 0 / 12 (0.00%)<br>0 |  |  |
| Atrial fibrillation<br>subjects affected / exposed<br>occurrences (all)         | 1 / 12 (8.33%)<br>1 |  |  |
| Palpitations                                                                    |                     |  |  |

|                                     |                 |  |  |
|-------------------------------------|-----------------|--|--|
| subjects affected / exposed         | 0 / 12 (0.00%)  |  |  |
| occurrences (all)                   | 0               |  |  |
| Pericardial effusion                |                 |  |  |
| subjects affected / exposed         | 0 / 12 (0.00%)  |  |  |
| occurrences (all)                   | 0               |  |  |
| Sinus bradycardia                   |                 |  |  |
| subjects affected / exposed         | 0 / 12 (0.00%)  |  |  |
| occurrences (all)                   | 0               |  |  |
| Atrial thrombosis                   |                 |  |  |
| subjects affected / exposed         | 0 / 12 (0.00%)  |  |  |
| occurrences (all)                   | 0               |  |  |
| Atrioventricular block first degree |                 |  |  |
| subjects affected / exposed         | 0 / 12 (0.00%)  |  |  |
| occurrences (all)                   | 0               |  |  |
| Tachycardia                         |                 |  |  |
| subjects affected / exposed         | 0 / 12 (0.00%)  |  |  |
| occurrences (all)                   | 0               |  |  |
| Nervous system disorders            |                 |  |  |
| Dizziness                           |                 |  |  |
| subjects affected / exposed         | 1 / 12 (8.33%)  |  |  |
| occurrences (all)                   | 1               |  |  |
| Ageusia                             |                 |  |  |
| subjects affected / exposed         | 0 / 12 (0.00%)  |  |  |
| occurrences (all)                   | 0               |  |  |
| Anosmia                             |                 |  |  |
| subjects affected / exposed         | 0 / 12 (0.00%)  |  |  |
| occurrences (all)                   | 0               |  |  |
| Dysgeusia                           |                 |  |  |
| subjects affected / exposed         | 1 / 12 (8.33%)  |  |  |
| occurrences (all)                   | 1               |  |  |
| Headache                            |                 |  |  |
| subjects affected / exposed         | 2 / 12 (16.67%) |  |  |
| occurrences (all)                   | 2               |  |  |
| Hypoaesthesia                       |                 |  |  |
| subjects affected / exposed         | 0 / 12 (0.00%)  |  |  |
| occurrences (all)                   | 0               |  |  |

|                             |                |  |  |
|-----------------------------|----------------|--|--|
| Sensory loss                |                |  |  |
| subjects affected / exposed | 0 / 12 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
|                             |                |  |  |
| Syncope                     |                |  |  |
| subjects affected / exposed | 1 / 12 (8.33%) |  |  |
| occurrences (all)           | 2              |  |  |
|                             |                |  |  |
| Paraesthesia                |                |  |  |
| subjects affected / exposed | 0 / 12 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
|                             |                |  |  |
| Brain oedema                |                |  |  |
| subjects affected / exposed | 0 / 12 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
|                             |                |  |  |
| Neuropathy peripheral       |                |  |  |
| subjects affected / exposed | 0 / 12 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
|                             |                |  |  |
| Post herpetic neuralgia     |                |  |  |
| subjects affected / exposed | 0 / 12 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
|                             |                |  |  |
| Taste disorder              |                |  |  |
| subjects affected / exposed | 0 / 12 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
|                             |                |  |  |
| Tremor                      |                |  |  |
| subjects affected / exposed | 0 / 12 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
|                             |                |  |  |
| Coordination abnormal       |                |  |  |
| subjects affected / exposed | 0 / 12 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
|                             |                |  |  |
| Cognitive disorder          |                |  |  |
| subjects affected / exposed | 0 / 12 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
|                             |                |  |  |
| Disturbance in attention    |                |  |  |
| subjects affected / exposed | 1 / 12 (8.33%) |  |  |
| occurrences (all)           | 1              |  |  |
|                             |                |  |  |
| Parosmia                    |                |  |  |
| subjects affected / exposed | 0 / 12 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |

|                                      |                 |  |  |
|--------------------------------------|-----------------|--|--|
| Blood and lymphatic system disorders |                 |  |  |
| Anaemia                              |                 |  |  |
| subjects affected / exposed          | 2 / 12 (16.67%) |  |  |
| occurrences (all)                    | 2               |  |  |
| Leukocytosis                         |                 |  |  |
| subjects affected / exposed          | 0 / 12 (0.00%)  |  |  |
| occurrences (all)                    | 0               |  |  |
| Leukopenia                           |                 |  |  |
| subjects affected / exposed          | 0 / 12 (0.00%)  |  |  |
| occurrences (all)                    | 0               |  |  |
| Thrombocytopenia                     |                 |  |  |
| subjects affected / exposed          | 1 / 12 (8.33%)  |  |  |
| occurrences (all)                    | 5               |  |  |
| Lymphopenia                          |                 |  |  |
| subjects affected / exposed          | 0 / 12 (0.00%)  |  |  |
| occurrences (all)                    | 0               |  |  |
| Neutropenia                          |                 |  |  |
| subjects affected / exposed          | 2 / 12 (16.67%) |  |  |
| occurrences (all)                    | 5               |  |  |
| Ear and labyrinth disorders          |                 |  |  |
| Tinnitus                             |                 |  |  |
| subjects affected / exposed          | 0 / 12 (0.00%)  |  |  |
| occurrences (all)                    | 0               |  |  |
| Hyperacusis                          |                 |  |  |
| subjects affected / exposed          | 1 / 12 (8.33%)  |  |  |
| occurrences (all)                    | 1               |  |  |
| Eye disorders                        |                 |  |  |
| Vision blurred                       |                 |  |  |
| subjects affected / exposed          | 0 / 12 (0.00%)  |  |  |
| occurrences (all)                    | 0               |  |  |
| Conjunctival haemorrhage             |                 |  |  |
| subjects affected / exposed          | 0 / 12 (0.00%)  |  |  |
| occurrences (all)                    | 0               |  |  |
| Eye pain                             |                 |  |  |
| subjects affected / exposed          | 0 / 12 (0.00%)  |  |  |
| occurrences (all)                    | 0               |  |  |
| Vitreous floaters                    |                 |  |  |

|                             |                 |  |  |
|-----------------------------|-----------------|--|--|
| subjects affected / exposed | 0 / 12 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Diplopia                    |                 |  |  |
| subjects affected / exposed | 1 / 12 (8.33%)  |  |  |
| occurrences (all)           | 1               |  |  |
| Gastrointestinal disorders  |                 |  |  |
| Nausea                      |                 |  |  |
| subjects affected / exposed | 7 / 12 (58.33%) |  |  |
| occurrences (all)           | 13              |  |  |
| Vomiting                    |                 |  |  |
| subjects affected / exposed | 5 / 12 (41.67%) |  |  |
| occurrences (all)           | 7               |  |  |
| Abdominal pain              |                 |  |  |
| subjects affected / exposed | 1 / 12 (8.33%)  |  |  |
| occurrences (all)           | 1               |  |  |
| Constipation                |                 |  |  |
| subjects affected / exposed | 3 / 12 (25.00%) |  |  |
| occurrences (all)           | 3               |  |  |
| Diarrhoea                   |                 |  |  |
| subjects affected / exposed | 6 / 12 (50.00%) |  |  |
| occurrences (all)           | 15              |  |  |
| Abdominal distension        |                 |  |  |
| subjects affected / exposed | 0 / 12 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Dry mouth                   |                 |  |  |
| subjects affected / exposed | 0 / 12 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Haematochezia               |                 |  |  |
| subjects affected / exposed | 0 / 12 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Retching                    |                 |  |  |
| subjects affected / exposed | 1 / 12 (8.33%)  |  |  |
| occurrences (all)           | 2               |  |  |
| Anal incontinence           |                 |  |  |
| subjects affected / exposed | 0 / 12 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |

|                                  |                |  |  |
|----------------------------------|----------------|--|--|
| Dyspepsia                        |                |  |  |
| subjects affected / exposed      | 1 / 12 (8.33%) |  |  |
| occurrences (all)                | 1              |  |  |
| Dysphagia                        |                |  |  |
| subjects affected / exposed      | 0 / 12 (0.00%) |  |  |
| occurrences (all)                | 0              |  |  |
| Faeces soft                      |                |  |  |
| subjects affected / exposed      | 0 / 12 (0.00%) |  |  |
| occurrences (all)                | 0              |  |  |
| Flatulence                       |                |  |  |
| subjects affected / exposed      | 0 / 12 (0.00%) |  |  |
| occurrences (all)                | 0              |  |  |
| Gastrooesophageal reflux disease |                |  |  |
| subjects affected / exposed      | 1 / 12 (8.33%) |  |  |
| occurrences (all)                | 1              |  |  |
| Salivary hypersecretion          |                |  |  |
| subjects affected / exposed      | 0 / 12 (0.00%) |  |  |
| occurrences (all)                | 0              |  |  |
| Stomatitis                       |                |  |  |
| subjects affected / exposed      | 0 / 12 (0.00%) |  |  |
| occurrences (all)                | 0              |  |  |
| Abdominal pain upper             |                |  |  |
| subjects affected / exposed      | 1 / 12 (8.33%) |  |  |
| occurrences (all)                | 1              |  |  |
| Colitis                          |                |  |  |
| subjects affected / exposed      | 0 / 12 (0.00%) |  |  |
| occurrences (all)                | 0              |  |  |
| Food poisoning                   |                |  |  |
| subjects affected / exposed      | 0 / 12 (0.00%) |  |  |
| occurrences (all)                | 0              |  |  |
| Tooth discolouration             |                |  |  |
| subjects affected / exposed      | 0 / 12 (0.00%) |  |  |
| occurrences (all)                | 0              |  |  |
| Ascites                          |                |  |  |
| subjects affected / exposed      | 0 / 12 (0.00%) |  |  |
| occurrences (all)                | 0              |  |  |

|                                                                                                                    |                     |  |  |
|--------------------------------------------------------------------------------------------------------------------|---------------------|--|--|
| Parotid gland enlargement<br>subjects affected / exposed<br>occurrences (all)                                      | 0 / 12 (0.00%)<br>0 |  |  |
| Rectal haemorrhage<br>subjects affected / exposed<br>occurrences (all)                                             | 0 / 12 (0.00%)<br>0 |  |  |
| Tooth erosion<br>subjects affected / exposed<br>occurrences (all)                                                  | 0 / 12 (0.00%)<br>0 |  |  |
| Tooth loss<br>subjects affected / exposed<br>occurrences (all)                                                     | 0 / 12 (0.00%)<br>0 |  |  |
| Hepatobiliary disorders<br>Hyperbilirubinaemia<br>subjects affected / exposed<br>occurrences (all)                 | 1 / 12 (8.33%)<br>2 |  |  |
| Hepatitis acute<br>subjects affected / exposed<br>occurrences (all)                                                | 0 / 12 (0.00%)<br>0 |  |  |
| Biliary dilatation<br>subjects affected / exposed<br>occurrences (all)                                             | 0 / 12 (0.00%)<br>0 |  |  |
| Skin and subcutaneous tissue disorders<br>Dermatitis acneiform<br>subjects affected / exposed<br>occurrences (all) | 0 / 12 (0.00%)<br>0 |  |  |
| Pruritus<br>subjects affected / exposed<br>occurrences (all)                                                       | 0 / 12 (0.00%)<br>0 |  |  |
| Rash maculo-papular<br>subjects affected / exposed<br>occurrences (all)                                            | 0 / 12 (0.00%)<br>0 |  |  |
| Dermatitis contact<br>subjects affected / exposed<br>occurrences (all)                                             | 0 / 12 (0.00%)<br>0 |  |  |
| Night sweats                                                                                                       |                     |  |  |

|                                        |                |  |  |
|----------------------------------------|----------------|--|--|
| subjects affected / exposed            | 0 / 12 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Rash                                   |                |  |  |
| subjects affected / exposed            | 0 / 12 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Rash macular                           |                |  |  |
| subjects affected / exposed            | 1 / 12 (8.33%) |  |  |
| occurrences (all)                      | 1              |  |  |
| Skin lesion                            |                |  |  |
| subjects affected / exposed            | 1 / 12 (8.33%) |  |  |
| occurrences (all)                      | 1              |  |  |
| Hyperhidrosis                          |                |  |  |
| subjects affected / exposed            | 0 / 12 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Renal and urinary disorders            |                |  |  |
| Ketonuria                              |                |  |  |
| subjects affected / exposed            | 0 / 12 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Urinary incontinence                   |                |  |  |
| subjects affected / exposed            | 0 / 12 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Haematuria                             |                |  |  |
| subjects affected / exposed            | 0 / 12 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Proteinuria                            |                |  |  |
| subjects affected / exposed            | 0 / 12 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Renal colic                            |                |  |  |
| subjects affected / exposed            | 0 / 12 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Glycosuria                             |                |  |  |
| subjects affected / exposed            | 0 / 12 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Endocrine disorders                    |                |  |  |
| Pituitary-dependent Cushing's syndrome |                |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed                     | 0 / 12 (0.00%) |  |  |
| occurrences (all)                               | 0              |  |  |
| Hypothyroidism                                  |                |  |  |
| subjects affected / exposed                     | 0 / 12 (0.00%) |  |  |
| occurrences (all)                               | 0              |  |  |
| Musculoskeletal and connective tissue disorders |                |  |  |
| Back pain                                       |                |  |  |
| subjects affected / exposed                     | 0 / 12 (0.00%) |  |  |
| occurrences (all)                               | 0              |  |  |
| Myalgia                                         |                |  |  |
| subjects affected / exposed                     | 1 / 12 (8.33%) |  |  |
| occurrences (all)                               | 1              |  |  |
| Arthralgia                                      |                |  |  |
| subjects affected / exposed                     | 0 / 12 (0.00%) |  |  |
| occurrences (all)                               | 0              |  |  |
| Groin pain                                      |                |  |  |
| subjects affected / exposed                     | 0 / 12 (0.00%) |  |  |
| occurrences (all)                               | 0              |  |  |
| Muscle spasms                                   |                |  |  |
| subjects affected / exposed                     | 0 / 12 (0.00%) |  |  |
| occurrences (all)                               | 0              |  |  |
| Musculoskeletal pain                            |                |  |  |
| subjects affected / exposed                     | 0 / 12 (0.00%) |  |  |
| occurrences (all)                               | 0              |  |  |
| Osteoarthritis                                  |                |  |  |
| subjects affected / exposed                     | 0 / 12 (0.00%) |  |  |
| occurrences (all)                               | 0              |  |  |
| Fistula                                         |                |  |  |
| subjects affected / exposed                     | 0 / 12 (0.00%) |  |  |
| occurrences (all)                               | 0              |  |  |
| Musculoskeletal chest pain                      |                |  |  |
| subjects affected / exposed                     | 0 / 12 (0.00%) |  |  |
| occurrences (all)                               | 0              |  |  |
| Osteoporosis                                    |                |  |  |

|                             |                |  |  |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 12 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Pain in extremity           |                |  |  |
| subjects affected / exposed | 0 / 12 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Coccydynia                  |                |  |  |
| subjects affected / exposed | 0 / 12 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Infections and infestations |                |  |  |
| COVID-19                    |                |  |  |
| subjects affected / exposed | 0 / 12 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Pneumonia                   |                |  |  |
| subjects affected / exposed | 0 / 12 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Urinary tract infection     |                |  |  |
| subjects affected / exposed | 1 / 12 (8.33%) |  |  |
| occurrences (all)           | 1              |  |  |
| Respiratory tract infection |                |  |  |
| subjects affected / exposed | 0 / 12 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Cellulitis                  |                |  |  |
| subjects affected / exposed | 0 / 12 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Onychomycosis               |                |  |  |
| subjects affected / exposed | 0 / 12 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Oral candidiasis            |                |  |  |
| subjects affected / exposed | 0 / 12 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Pneumonia aspiration        |                |  |  |
| subjects affected / exposed | 0 / 12 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Skin infection              |                |  |  |
| subjects affected / exposed | 0 / 12 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |

|                                                                                       |                     |  |  |
|---------------------------------------------------------------------------------------|---------------------|--|--|
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 0 / 12 (0.00%)<br>0 |  |  |
| Candida infection<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 12 (0.00%)<br>0 |  |  |
| Herpes zoster<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 12 (0.00%)<br>0 |  |  |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 12 (0.00%)<br>0 |  |  |
| Vaginal infection<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 12 (0.00%)<br>0 |  |  |
| Coronavirus infection<br>subjects affected / exposed<br>occurrences (all)             | 1 / 12 (8.33%)<br>1 |  |  |
| Influenza<br>subjects affected / exposed<br>occurrences (all)                         | 1 / 12 (8.33%)<br>1 |  |  |
| Metabolism and nutrition disorders                                                    |                     |  |  |
| Decreased appetite<br>subjects affected / exposed<br>occurrences (all)                | 1 / 12 (8.33%)<br>1 |  |  |
| Hypercalcaemia<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 12 (0.00%)<br>0 |  |  |
| Hyperkalaemia<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 12 (0.00%)<br>0 |  |  |
| Hypomagnesaemia<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 12 (0.00%)<br>0 |  |  |
| Dehydration                                                                           |                     |  |  |

|                             |                |  |  |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 12 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Gout                        |                |  |  |
| subjects affected / exposed | 0 / 12 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Hyperglycaemia              |                |  |  |
| subjects affected / exposed | 0 / 12 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Hyperlipidaemia             |                |  |  |
| subjects affected / exposed | 0 / 12 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Hypokalaemia                |                |  |  |
| subjects affected / exposed | 0 / 12 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Hyponatraemia               |                |  |  |
| subjects affected / exposed | 1 / 12 (8.33%) |  |  |
| occurrences (all)           | 1              |  |  |
| Hypophosphataemia           |                |  |  |
| subjects affected / exposed | 0 / 12 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Vitamin B12 deficiency      |                |  |  |
| subjects affected / exposed | 0 / 12 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Vitamin D deficiency        |                |  |  |
| subjects affected / exposed | 0 / 12 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Hypoalbuminaemia            |                |  |  |
| subjects affected / exposed | 0 / 12 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Hypocalcaemia               |                |  |  |
| subjects affected / exposed | 1 / 12 (8.33%) |  |  |
| occurrences (all)           | 1              |  |  |
| Hypoglycaemia               |                |  |  |
| subjects affected / exposed | 0 / 12 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Hyperuricaemia              |                |  |  |

|                             |                |  |  |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 12 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Malnutrition                |                |  |  |
| subjects affected / exposed | 0 / 12 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date            | Amendment                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 01 May 2020     | The following changes were made as per Amendment 1: 1. A nonclinical rationale for each new Phase 2 cohort (sarcoma with murine Double minute 2 [MDM2] amplification [Cohort 2], CDKN2A loss [Cohort 3], and molecular features that may confer sensitivity to ASTX295 [Cohort 4]) was provided in addition to the previously defined malignant pleural mesothelioma (MPM) cohort [Cohort 1]. 2. The number of overall subjects and the duration of study was updated based on the additional Phase 2 cohorts. 3. The Phase 2 study design description was updated to define the new cohorts, Cohorts 2-4. 4. Scientific rationale for study design was updated to reflect the new cohorts added for Phase 2. 5. The inclusion and exclusion criteria were updated. 6. In the statistical hypotheses section for Phase 2, hypotheses were included for the new Phase 2 cohorts. 7. The sample size was calculated for new Cohorts 2, 3, and 4.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| 21 October 2020 | The following changes were made as per Amendment 2: 1. A secondary objective was added regarding PK parameters of ASTX295 after administration with food. 2. A concomitant change was made regarding the ASTX295 plasma concentration profiles and PK parameters in the fed state. 3. Figure was updated to add a food-effect cohort. 4. The addition of a window to activities occurring beyond Cycle 6. 5. Study rationale section was updated to add the rationale for a food bridging cohort. 6. Background section was updated to include information from a nonclinical PK food-effect study. 7. Objectives and endpoints were updated to include the determination of PK parameters of ASTX295 when administered with food. 8. Overall design section was updated to add the rationale for a food bridging cohort. This section was updated with language to address the impact and changes resulting from the coronavirus disease of 2019 (COVID-19) health emergency. 9. Scientific rationale for study design was updated to add the rationale for a food bridging cohort. 10. The "drug administration under fed state" section was added to provide meal requirements and procedures for subjects enrolled into the food-bridging cohort. 11. Study treatments administered section updated to provide information on alternative dispensing of study drug under extenuating circumstances, such as the COVID-19 health emergency. 12. Appendix was added to provide information and guidance to continue study during the COVID-19 emergency. |
| 15 June 2021    | The following changes were made as per Amendment 3: 1. Allowed an alternate dosing regimen (i.e., BID administration) to enhance exposure and based on the latest research findings. These include BID dosing or administration with food based on results from a food-bridging cohort (Amendment #2). 2. The study numbers were corrected (255 should have read 239) and increased from 28 to 60 for Phase 1a and up to an additional 15 to 20 subjects for Phase 1b. 3. For BID cohorts under fasting conditions, meals and dietary restrictions were updated. 4. Details of alternate dose regimen was updated in drug administration under fed conditions section.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |

|               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
|---------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 21 March 2022 | The following changes were made as per Amendment 4: 1. The duration of the study was increased. 2. Intermittent dosing was added to the possible dosing schedule modifications for Phase 1a. 3. The expected total numbers of screened and treated subjects in all phases were increased, and all numbers by phase were specified as approximate. 4. Up to an additional 14 days (up to 35 total screening days) was specified as being allowed for acquisition of archived tissue slides or a fresh biopsy for prospective eligibility confirmation in Phase 2. 5. "Fasting conditions" was deleted from the description of the last safe dose as determined by the DSRC for the description of Amendment 2, Phase 1, Cohort 7. 6. Consideration of twice daily dosing or intermittent dose schedules or meal options for improvement of tolerability while allowing for additional dose escalation was added. 7. The location of Phase 1b was changed from "North America" to "United States; same centers initiated in Phase 1a." 8. The expected total numbers of screened and treated subjects in all phases were increased, and all numbers by phase were specified as approximate. 9. Inclusion and exclusion criteria were modified. |
|---------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Phase 2 was not conducted due to Sponsor's strategic decision.

Notes: