



## Clinical trial results:

### An Open-Label Phase Ib/II Study of Surufatinib in Combination with Tislelizumab in Subjects With Advanced Solid Tumors

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2020-004163-12 |
| Trial protocol           | ES FR          |
| Global end of trial date | 27 August 2024 |

#### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 18 July 2025 |
| First version publication date | 18 July 2025 |

#### Trial information

##### Trial identification

|                       |                |
|-----------------------|----------------|
| Sponsor protocol code | 2020-012-GLOB1 |
|-----------------------|----------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT04579757 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |                                                                                             |
|------------------------------|---------------------------------------------------------------------------------------------|
| Sponsor organisation name    | HUTCHMED Limited                                                                            |
| Sponsor organisation address | Building 4, 720 Cailun Road China (Shanghai) Pilot Free Trade Zone, Shanghai, China, 201203 |
| Public contact               | Nicky Murray, HUTCHMED Limited, +44 7738 881999, nicolam@hutch-med.com                      |
| Scientific contact           | William Schelman, HUTCHMED Limited, +1 9733064490, williams@hutch-med.com                   |

Notes:

#### Paediatric regulatory details

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

Notes:

## Results analysis stage

|                                                      |                |
|------------------------------------------------------|----------------|
| Analysis stage                                       | Final          |
| Date of interim/final analysis                       | 27 August 2024 |
| Is this the analysis of the primary completion data? | No             |
| Global end of trial reached?                         | Yes            |
| Global end of trial date                             | 27 August 2024 |
| Was the trial ended prematurely?                     | Yes            |

Notes:

## General information about the trial

Main objective of the trial:

Part 1: To evaluate the safety and tolerability of surufatinib, thereby determining the recommended phase 2 dose (RP2D) and/or the maximum tolerated dose (MTD) of surufatinib in combination with tislelizumab.

Part 2: To evaluate the objective response rate (ORR) as assessed by the investigator in patients with advanced solid tumors when treated with surufatinib in combination with tislelizumab according to Response Evaluation Criteria in Solid Tumors (RECIST) version (v) 1.1.

Protection of trial subjects:

The study was conducted in accordance with the protocol, consensus and ethical principles derived from international guidelines, including the Declaration of Helsinki and Council for International Organizations of Medical Sciences International Ethical Guidelines, applicable International Council for Harmonization Good Clinical Practice guidelines, and applicable regulations and guidelines governing clinical study conduct.

Background therapy: -

Evidence for comparator: -

|                                                           |               |
|-----------------------------------------------------------|---------------|
| Actual start date of recruitment                          | 05 March 2021 |
| Long term follow-up planned                               | No            |
| Independent data monitoring committee (IDMC) involvement? | No            |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                   |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Spain: 2          |
| Country: Number of subjects enrolled | United States: 85 |
| Worldwide total number of subjects   | 87                |
| EEA total number of subjects         | 2                 |

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)      | 47 |
| From 65 to 84 years       | 40 |
| 85 years and over         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

This phase 1b/2, 2-part, open-label study was conducted in patients with advanced solid tumors. The study consisted of a dose-escalation phase and a dose expansion phase. A total of 12 patients in dose-escalation phase and 75 patients in dose-expansion phase were enrolled in this study.

### Pre-assignment

Screening details:

The study was terminated early based on the strategic re-evaluation of clinical development of surufatinib in the United States and Europe with no safety concerns. No patients were enrolled in Cohort E1 (alveolar soft part sarcoma) in the dose-expansion phase, hence this cohort is not presented in results.

### Period 1

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

### Arms

|                              |                                                          |
|------------------------------|----------------------------------------------------------|
| Are arms mutually exclusive? | Yes                                                      |
| <b>Arm title</b>             | Dose Escalation Phase: Surufatinib 250 mg + Tislelizumab |

Arm description:

Patients with advanced or metastatic solid tumors of any kind who had progressed on or were intolerant of standard therapies received surufatinib 250 milligrams (mg) orally once daily (QD) in combination with tislelizumab 200 mg intravenous (IV) infusion every 3 weeks (Q3W) until progressive disease (PD), unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.

|                                        |              |
|----------------------------------------|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Surufatinib  |
| Investigational medicinal product code | HMPL-012     |
| Other name                             |              |
| Pharmaceutical forms                   | Capsule      |
| Routes of administration               | Oral use     |

Dosage and administration details:

Surufatinib 250 mg oral capsule was administered QD Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.

|                                        |                       |
|----------------------------------------|-----------------------|
| Investigational medicinal product name | Tislelizumab          |
| Investigational medicinal product code | BGB-A317              |
| Other name                             |                       |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Intravenous use       |

Dosage and administration details:

Tislelizumab 200 mg IV infusion was administered over 60 minutes in Cycles 1 and 2 and over at least 30 minutes in subsequent cycles (cycle duration: 3 weeks) until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.

|                  |                                                          |
|------------------|----------------------------------------------------------|
| <b>Arm title</b> | Dose Escalation Phase: Surufatinib 300 mg + Tislelizumab |
|------------------|----------------------------------------------------------|

Arm description:

Patients with advanced or metastatic solid tumors of any kind who had progressed on or were intolerant of standard therapies received surufatinib 300 mg orally QD in combination with tislelizumab 200 mg IV infusion Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.

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

|                                        |             |
|----------------------------------------|-------------|
| Investigational medicinal product name | Surufatinib |
| Investigational medicinal product code | HMPL-012    |
| Other name                             |             |
| Pharmaceutical forms                   | Capsule     |
| Routes of administration               | Oral use    |

**Dosage and administration details:**

Surufatinib 300 mg oral capsule was administered QD Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.

|                                        |                       |
|----------------------------------------|-----------------------|
| Investigational medicinal product name | Tislelizumab          |
| Investigational medicinal product code | BGB-A317              |
| Other name                             |                       |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Intravenous use       |

**Dosage and administration details:**

Tislelizumab 200 mg IV infusion was administered over 60 minutes in Cycles 1 and 2 and over at least 30 minutes in subsequent cycles (cycle duration: 3 weeks) until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.

|                  |                                     |
|------------------|-------------------------------------|
| <b>Arm title</b> | Dose Expansion Phase: Cohort A: CRC |
|------------------|-------------------------------------|

**Arm description:**

Patients with microsatellite stable, locally advanced or metastatic colorectal cancer (CRC) that was previously treated with at least 3 prior lines of therapy received surufatinib 300 mg orally QD in combination with tislelizumab 200 mg IV infusion Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.

|                                        |              |
|----------------------------------------|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Surufatinib  |
| Investigational medicinal product code | HMPL-012     |
| Other name                             |              |
| Pharmaceutical forms                   | Capsule      |
| Routes of administration               | Oral use     |

**Dosage and administration details:**

Surufatinib 300 mg oral capsule was administered QD Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.

|                                        |                       |
|----------------------------------------|-----------------------|
| Investigational medicinal product name | Tislelizumab          |
| Investigational medicinal product code | BGB-A317              |
| Other name                             |                       |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Intravenous use       |

**Dosage and administration details:**

Tislelizumab 200 mg IV infusion was administered over 60 minutes in Cycles 1 and 2 and over at least 30 minutes in subsequent cycles (cycle duration: 3 weeks) until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.

|                  |                                                |
|------------------|------------------------------------------------|
| <b>Arm title</b> | Dose Expansion Phase: Cohort B1: Thoracic NETs |
|------------------|------------------------------------------------|

**Arm description:**

Patients with thoracic neuroendocrine tumor (NET) who had progressive, locally advanced or metastatic, low-to-intermediate grade (Grade 1 or Grade 2), well-differentiated NETs that progressed on at least 1 line of standard therapy received surufatinib 300 mg orally QD in combination with tislelizumab 200 mg IV infusion Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.

|                                        |              |
|----------------------------------------|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Surufatinib  |
| Investigational medicinal product code | HMPL-012     |
| Other name                             |              |
| Pharmaceutical forms                   | Capsule      |
| Routes of administration               | Oral use     |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                           |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------|
| Dosage and administration details:                                                                                                                                                                                                                                                                                                                                                                                                             |                                           |
| Surufatinib 300 mg oral capsule was administered QD Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.                                                                                                                                                                                                                                                                           |                                           |
| Investigational medicinal product name                                                                                                                                                                                                                                                                                                                                                                                                         | Tislelizumab                              |
| Investigational medicinal product code                                                                                                                                                                                                                                                                                                                                                                                                         | BGB-A317                                  |
| Other name                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                           |
| Pharmaceutical forms                                                                                                                                                                                                                                                                                                                                                                                                                           | Solution for infusion                     |
| Routes of administration                                                                                                                                                                                                                                                                                                                                                                                                                       | Intravenous use                           |
| Dosage and administration details:                                                                                                                                                                                                                                                                                                                                                                                                             |                                           |
| Tislelizumab 200 mg IV infusion was administered over 60 minutes in Cycles 1 and 2 and over at least 30 minutes in subsequent cycles (cycle duration: 3 weeks) until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.                                                                                                                                                                    |                                           |
| <b>Arm title</b>                                                                                                                                                                                                                                                                                                                                                                                                                               | Dose Expansion Phase: Cohort B2: GEP NETs |
| Arm description:                                                                                                                                                                                                                                                                                                                                                                                                                               |                                           |
| Patients with gastroenteropancreatic (GEP) NET who had progressive, locally advanced or metastatic, low-to-intermediate grade (Grade 1 or Grade 2), well-differentiated NETs that progressed on at least 1 line of standard therapy received surufatinib 300 mg orally QD in combination with tislelizumab 200 mg IV infusion Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death. |                                           |
| Arm type                                                                                                                                                                                                                                                                                                                                                                                                                                       | Experimental                              |
| Investigational medicinal product name                                                                                                                                                                                                                                                                                                                                                                                                         | Surufatinib                               |
| Investigational medicinal product code                                                                                                                                                                                                                                                                                                                                                                                                         | HMPL-012                                  |
| Other name                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                           |
| Pharmaceutical forms                                                                                                                                                                                                                                                                                                                                                                                                                           | Capsule                                   |
| Routes of administration                                                                                                                                                                                                                                                                                                                                                                                                                       | Oral use                                  |
| Dosage and administration details:                                                                                                                                                                                                                                                                                                                                                                                                             |                                           |
| Surufatinib 300 mg oral capsule was administered QD Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.                                                                                                                                                                                                                                                                           |                                           |
| Investigational medicinal product name                                                                                                                                                                                                                                                                                                                                                                                                         | Tislelizumab                              |
| Investigational medicinal product code                                                                                                                                                                                                                                                                                                                                                                                                         | BGB-A317                                  |
| Other name                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                           |
| Pharmaceutical forms                                                                                                                                                                                                                                                                                                                                                                                                                           | Solution for infusion                     |
| Routes of administration                                                                                                                                                                                                                                                                                                                                                                                                                       | Intravenous use                           |
| Dosage and administration details:                                                                                                                                                                                                                                                                                                                                                                                                             |                                           |
| Tislelizumab 200 mg IV infusion was administered over 60 minutes in Cycles 1 and 2 and over at least 30 minutes in subsequent cycles (cycle duration: 3 weeks) until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.                                                                                                                                                                    |                                           |
| <b>Arm title</b>                                                                                                                                                                                                                                                                                                                                                                                                                               | Dose Expansion Phase: Cohort C: SCLC      |
| Arm description:                                                                                                                                                                                                                                                                                                                                                                                                                               |                                           |
| Patients with locally advanced or metastatic small-cell lung cancer (SCLC) that was previously progressed on first-line chemotherapy received surufatinib 300 mg orally QD in combination with tislelizumab 200 mg IV infusion Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.                                                                                                |                                           |
| Arm type                                                                                                                                                                                                                                                                                                                                                                                                                                       | Experimental                              |
| Investigational medicinal product name                                                                                                                                                                                                                                                                                                                                                                                                         | Surufatinib                               |
| Investigational medicinal product code                                                                                                                                                                                                                                                                                                                                                                                                         | HMPL-012                                  |
| Other name                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                           |
| Pharmaceutical forms                                                                                                                                                                                                                                                                                                                                                                                                                           | Capsule                                   |
| Routes of administration                                                                                                                                                                                                                                                                                                                                                                                                                       | Oral use                                  |
| Dosage and administration details:                                                                                                                                                                                                                                                                                                                                                                                                             |                                           |
| Surufatinib 300 mg oral capsule was administered QD Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.                                                                                                                                                                                                                                                                           |                                           |
| Investigational medicinal product name                                                                                                                                                                                                                                                                                                                                                                                                         | Tislelizumab                              |
| Investigational medicinal product code                                                                                                                                                                                                                                                                                                                                                                                                         | BGB-A317                                  |
| Other name                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                           |

|                          |                       |
|--------------------------|-----------------------|
| Pharmaceutical forms     | Solution for infusion |
| Routes of administration | Intravenous use       |

**Dosage and administration details:**

Tislelizumab 200 mg IV infusion was administered over 60 minutes in Cycles 1 and 2 and over at least 30 minutes in subsequent cycles (cycle duration: 3 weeks) until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.

|                  |                                    |
|------------------|------------------------------------|
| <b>Arm title</b> | Dose Expansion Phase: Cohort D: GC |
|------------------|------------------------------------|

**Arm description:**

Patients with microsatellite stable, programmed death-ligand 1 (PD-L1)  $\geq 5\%$ , locally advanced or metastatic adenocarcinoma of the stomach or gastroesophageal junction (gastric cancer [GC]), and were previously treated with at least 2 lines of standard therapy received surufatinib 300 mg orally QD in combination with tislelizumab 200 mg IV infusion Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.

|                                        |              |
|----------------------------------------|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Surufatinib  |
| Investigational medicinal product code | HMPL-012     |
| Other name                             |              |
| Pharmaceutical forms                   | Capsule      |
| Routes of administration               | Oral use     |

**Dosage and administration details:**

Surufatinib 300 mg oral capsule was administered QD Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.

|                                        |                       |
|----------------------------------------|-----------------------|
| Investigational medicinal product name | Tislelizumab          |
| Investigational medicinal product code | BGB-A317              |
| Other name                             |                       |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Intravenous use       |

**Dosage and administration details:**

Tislelizumab 200 mg IV infusion was administered over 60 minutes in Cycles 1 and 2 and over at least 30 minutes in subsequent cycles (cycle duration: 3 weeks) until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.

|                  |                                      |
|------------------|--------------------------------------|
| <b>Arm title</b> | Dose Expansion Phase: Cohort E2: UPS |
|------------------|--------------------------------------|

**Arm description:**

Patients with undifferentiated pleomorphic sarcoma (UPS) who progressed on, or had discontinued due to intolerable toxicity to, at least 1 line of standard therapy or were unsuitable for standard frontline cytotoxic chemotherapy received surufatinib 300 mg orally QD in combination with tislelizumab 200 mg IV infusion Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.

|                                        |              |
|----------------------------------------|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Surufatinib  |
| Investigational medicinal product code | HMPL-012     |
| Other name                             |              |
| Pharmaceutical forms                   | Capsule      |
| Routes of administration               | Oral use     |

**Dosage and administration details:**

Surufatinib 300 mg oral capsule was administered QD Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.

|                                        |                       |
|----------------------------------------|-----------------------|
| Investigational medicinal product name | Tislelizumab          |
| Investigational medicinal product code | BGB-A317              |
| Other name                             |                       |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Intravenous use       |

**Dosage and administration details:**

Tislelizumab 200 mg IV infusion was administered over 60 minutes in Cycles 1 and 2 and over at least 30 minutes in subsequent cycles (cycle duration: 3 weeks) until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                     |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|
| <b>Arm title</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Dose Expansion Phase: Cohort F: ATC |
| Arm description:                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                     |
| Patients with locally advanced or metastatic anaplastic thyroid cancer (ATC) and who had a B-Raf kinase V600E (BRAFV600E) mutation were previously treated with 1 line of systemic therapy (not including radiation therapy) with a BRAF-targeted therapy received surufatinib 300 mg orally QD in combination with tislelizumab 200 mg IV infusion Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death. |                                     |
| Arm type                                                                                                                                                                                                                                                                                                                                                                                                                                                             | Experimental                        |
| Investigational medicinal product name                                                                                                                                                                                                                                                                                                                                                                                                                               | Surufatinib                         |
| Investigational medicinal product code                                                                                                                                                                                                                                                                                                                                                                                                                               | HMPL-012                            |
| Other name                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                     |
| Pharmaceutical forms                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Capsule                             |
| Routes of administration                                                                                                                                                                                                                                                                                                                                                                                                                                             | Oral use                            |
| Dosage and administration details:                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                     |
| Surufatinib 300 mg oral capsule was administered QD Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.                                                                                                                                                                                                                                                                                                 |                                     |
| Investigational medicinal product name                                                                                                                                                                                                                                                                                                                                                                                                                               | Tislelizumab                        |
| Investigational medicinal product code                                                                                                                                                                                                                                                                                                                                                                                                                               | BGB-A317                            |
| Other name                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                     |
| Pharmaceutical forms                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Solution for infusion               |
| Routes of administration                                                                                                                                                                                                                                                                                                                                                                                                                                             | Intravenous use                     |
| Dosage and administration details:                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                     |
| Tislelizumab 200 mg IV infusion was administered over 60 minutes in Cycles 1 and 2 and over at least 30 minutes in subsequent cycles (cycle duration: 3 weeks) until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.                                                                                                                                                                                          |                                     |

| <b>Number of subjects in period 1</b> | Dose Escalation Phase: Surufatinib 250 mg + Tislelizumab | Dose Escalation Phase: Surufatinib 300 mg + Tislelizumab | Dose Expansion Phase: Cohort A: CRC |
|---------------------------------------|----------------------------------------------------------|----------------------------------------------------------|-------------------------------------|
| Started                               | 6                                                        | 6                                                        | 15                                  |
| Completed                             | 0                                                        | 0                                                        | 0                                   |
| Not completed                         | 6                                                        | 6                                                        | 15                                  |
| Consent withdrawn by subject          | 1                                                        | 1                                                        | -                                   |
| Physician decision                    | -                                                        | -                                                        | -                                   |
| Start of new therapy                  | -                                                        | -                                                        | -                                   |
| Adverse event, non-fatal              | -                                                        | -                                                        | -                                   |
| Death                                 | 4                                                        | 1                                                        | 14                                  |
| Study terminated by sponsor           | -                                                        | -                                                        | -                                   |
| Radiological or clinical PD           | 1                                                        | 4                                                        | 1                                   |

| <b>Number of subjects in period 1</b> | Dose Expansion Phase: Cohort B1: Thoracic NETs | Dose Expansion Phase: Cohort B2: GEP NETs | Dose Expansion Phase: Cohort C: SCLC |
|---------------------------------------|------------------------------------------------|-------------------------------------------|--------------------------------------|
| Started                               | 10                                             | 20                                        | 15                                   |
| Completed                             | 0                                              | 1                                         | 0                                    |
| Not completed                         | 10                                             | 19                                        | 15                                   |
| Consent withdrawn by subject          | -                                              | 2                                         | 1                                    |
| Physician decision                    | 2                                              | 1                                         | 1                                    |

|                             |   |   |   |
|-----------------------------|---|---|---|
| Start of new therapy        | - | 2 | 1 |
| Adverse event, non-fatal    | 2 | 1 | 1 |
| Death                       | 3 | 2 | 7 |
| Study terminated by sponsor | - | 2 | - |
| Radiological or clinical PD | 3 | 9 | 4 |

| Number of subjects in period 1 | Dose Expansion<br>Phase: Cohort D: GC | Dose Expansion<br>Phase: Cohort E2:<br>UPS | Dose Expansion<br>Phase: Cohort F:<br>ATC |
|--------------------------------|---------------------------------------|--------------------------------------------|-------------------------------------------|
|                                |                                       |                                            |                                           |
| Started                        | 3                                     | 9                                          | 3                                         |
| Completed                      | 0                                     | 1                                          | 0                                         |
| Not completed                  | 3                                     | 8                                          | 3                                         |
| Consent withdrawn by subject   | -                                     | 3                                          | -                                         |
| Physician decision             | 1                                     | -                                          | -                                         |
| Start of new therapy           | -                                     | -                                          | -                                         |
| Adverse event, non-fatal       | -                                     | -                                          | -                                         |
| Death                          | -                                     | 1                                          | 3                                         |
| Study terminated by sponsor    | -                                     | 2                                          | -                                         |
| Radiological or clinical PD    | 2                                     | 2                                          | -                                         |

## Baseline characteristics

### Reporting groups

|                       |                                                          |
|-----------------------|----------------------------------------------------------|
| Reporting group title | Dose Escalation Phase: Surufatinib 250 mg + Tislelizumab |
|-----------------------|----------------------------------------------------------|

#### Reporting group description:

Patients with advanced or metastatic solid tumors of any kind who had progressed on or were intolerant of standard therapies received surufatinib 250 milligrams (mg) orally once daily (QD) in combination with tislelizumab 200 mg intravenous (IV) infusion every 3 weeks (Q3W) until progressive disease (PD), unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.

|                       |                                                          |
|-----------------------|----------------------------------------------------------|
| Reporting group title | Dose Escalation Phase: Surufatinib 300 mg + Tislelizumab |
|-----------------------|----------------------------------------------------------|

#### Reporting group description:

Patients with advanced or metastatic solid tumors of any kind who had progressed on or were intolerant of standard therapies received surufatinib 300 mg orally QD in combination with tislelizumab 200 mg IV infusion Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.

|                       |                                     |
|-----------------------|-------------------------------------|
| Reporting group title | Dose Expansion Phase: Cohort A: CRC |
|-----------------------|-------------------------------------|

#### Reporting group description:

Patients with microsatellite stable, locally advanced or metastatic colorectal cancer (CRC) that was previously treated with at least 3 prior lines of therapy received surufatinib 300 mg orally QD in combination with tislelizumab 200 mg IV infusion Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.

|                       |                                                |
|-----------------------|------------------------------------------------|
| Reporting group title | Dose Expansion Phase: Cohort B1: Thoracic NETs |
|-----------------------|------------------------------------------------|

#### Reporting group description:

Patients with thoracic neuroendocrine tumor (NET) who had progressive, locally advanced or metastatic, low-to-intermediate grade (Grade 1 or Grade 2), well-differentiated NETs that progressed on at least 1 line of standard therapy received surufatinib 300 mg orally QD in combination with tislelizumab 200 mg IV infusion Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.

|                       |                                           |
|-----------------------|-------------------------------------------|
| Reporting group title | Dose Expansion Phase: Cohort B2: GEP NETs |
|-----------------------|-------------------------------------------|

#### Reporting group description:

Patients with gastroenteropancreatic (GEP) NET who had progressive, locally advanced or metastatic, low-to-intermediate grade (Grade 1 or Grade 2), well-differentiated NETs that progressed on at least 1 line of standard therapy received surufatinib 300 mg orally QD in combination with tislelizumab 200 mg IV infusion Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.

|                       |                                      |
|-----------------------|--------------------------------------|
| Reporting group title | Dose Expansion Phase: Cohort C: SCLC |
|-----------------------|--------------------------------------|

#### Reporting group description:

Patients with locally advanced or metastatic small-cell lung cancer (SCLC) that was previously progressed on first-line chemotherapy received surufatinib 300 mg orally QD in combination with tislelizumab 200 mg IV infusion Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.

|                       |                                    |
|-----------------------|------------------------------------|
| Reporting group title | Dose Expansion Phase: Cohort D: GC |
|-----------------------|------------------------------------|

#### Reporting group description:

Patients with microsatellite stable, programmed death-ligand 1 (PD-L1)  $\geq 5\%$ , locally advanced or metastatic adenocarcinoma of the stomach or gastroesophageal junction (gastric cancer [GC]), and were previously treated with at least 2 lines of standard therapy received surufatinib 300 mg orally QD in combination with tislelizumab 200 mg IV infusion Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.

|                       |                                      |
|-----------------------|--------------------------------------|
| Reporting group title | Dose Expansion Phase: Cohort E2: UPS |
|-----------------------|--------------------------------------|

#### Reporting group description:

Patients with undifferentiated pleomorphic sarcoma (UPS) who progressed on, or had discontinued due to intolerable toxicity to, at least 1 line of standard therapy or were unsuitable for standard frontline cytotoxic chemotherapy received surufatinib 300 mg orally QD in combination with tislelizumab 200 mg IV infusion Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.

|                       |                                     |
|-----------------------|-------------------------------------|
| Reporting group title | Dose Expansion Phase: Cohort F: ATC |
|-----------------------|-------------------------------------|

#### Reporting group description:

Patients with locally advanced or metastatic anaplastic thyroid cancer (ATC) and who had a B-Raf kinase V600E (BRAFV600E) mutation were previously treated with 1 line of systemic therapy (not including

radiation therapy) with a BRAF-targeted therapy received surufatinib 300 mg orally QD in combination with tislelizumab 200 mg IV infusion Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.

| <b>Reporting group values</b>      | Dose Escalation Phase: Surufatinib 250 mg + Tislelizumab | Dose Escalation Phase: Surufatinib 300 mg + Tislelizumab | Dose Expansion Phase: Cohort A: CRC |
|------------------------------------|----------------------------------------------------------|----------------------------------------------------------|-------------------------------------|
| Number of subjects                 | 6                                                        | 6                                                        | 15                                  |
| Age categorical<br>Units: Subjects |                                                          |                                                          |                                     |

|                                                                         |                 |                |                 |
|-------------------------------------------------------------------------|-----------------|----------------|-----------------|
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | 62.5<br>± 14.69 | 68.2<br>± 9.83 | 53.5<br>± 11.99 |
| Gender categorical<br>Units: Subjects                                   |                 |                |                 |
| Female                                                                  | 1               | 2              | 8               |
| Male                                                                    | 5               | 4              | 7               |
| Ethnicity<br>Units: Subjects                                            |                 |                |                 |
| Hispanic or Latino                                                      | 0               | 0              | 0               |
| Not Hispanic or Latino                                                  | 5               | 6              | 15              |
| Unknown or Not Reported                                                 | 1               | 0              | 0               |
| Race<br>Units: Subjects                                                 |                 |                |                 |
| Asian                                                                   | 0               | 0              | 0               |
| Native Hawaiian or Other Pacific Islander                               | 1               | 0              | 0               |
| Black or African American                                               | 0               | 1              | 4               |
| White                                                                   | 3               | 3              | 10              |
| More than one race                                                      | 1               | 1              | 0               |
| Unknown or Not Reported                                                 | 1               | 1              | 1               |

| <b>Reporting group values</b>      | Dose Expansion Phase: Cohort B1: Thoracic NETs | Dose Expansion Phase: Cohort B2: GEP NETs | Dose Expansion Phase: Cohort C: SCLC |
|------------------------------------|------------------------------------------------|-------------------------------------------|--------------------------------------|
| Number of subjects                 | 10                                             | 20                                        | 15                                   |
| Age categorical<br>Units: Subjects |                                                |                                           |                                      |

|                                                                         |                |                |                 |
|-------------------------------------------------------------------------|----------------|----------------|-----------------|
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | 58.6<br>± 9.70 | 63.2<br>± 9.23 | 58.1<br>± 14.27 |
| Gender categorical<br>Units: Subjects                                   |                |                |                 |
| Female                                                                  | 4              | 10             | 8               |
| Male                                                                    | 6              | 10             | 7               |

|                                           |   |    |    |
|-------------------------------------------|---|----|----|
| Ethnicity                                 |   |    |    |
| Units: Subjects                           |   |    |    |
| Hispanic or Latino                        | 0 | 2  | 1  |
| Not Hispanic or Latino                    | 9 | 18 | 13 |
| Unknown or Not Reported                   | 1 | 0  | 1  |
| Race                                      |   |    |    |
| Units: Subjects                           |   |    |    |
| Asian                                     | 1 | 0  | 0  |
| Native Hawaiian or Other Pacific Islander | 0 | 0  | 0  |
| Black or African American                 | 0 | 3  | 1  |
| White                                     | 8 | 17 | 12 |
| More than one race                        | 0 | 0  | 1  |
| Unknown or Not Reported                   | 1 | 0  | 1  |

| Reporting group values | Dose Expansion Phase: Cohort D: GC | Dose Expansion Phase: Cohort E2: UPS | Dose Expansion Phase: Cohort F: ATC |
|------------------------|------------------------------------|--------------------------------------|-------------------------------------|
| Number of subjects     | 3                                  | 9                                    | 3                                   |
| Age categorical        |                                    |                                      |                                     |
| Units: Subjects        |                                    |                                      |                                     |

|                                           |        |         |         |
|-------------------------------------------|--------|---------|---------|
| Age continuous                            |        |         |         |
| Units: years                              |        |         |         |
| arithmetic mean                           | 60.7   | 59.9    | 63.0    |
| standard deviation                        | ± 5.86 | ± 13.94 | ± 19.05 |
| Gender categorical                        |        |         |         |
| Units: Subjects                           |        |         |         |
| Female                                    | 0      | 6       | 1       |
| Male                                      | 3      | 3       | 2       |
| Ethnicity                                 |        |         |         |
| Units: Subjects                           |        |         |         |
| Hispanic or Latino                        | 0      | 1       | 0       |
| Not Hispanic or Latino                    | 3      | 8       | 2       |
| Unknown or Not Reported                   | 0      | 0       | 1       |
| Race                                      |        |         |         |
| Units: Subjects                           |        |         |         |
| Asian                                     | 0      | 0       | 0       |
| Native Hawaiian or Other Pacific Islander | 0      | 0       | 0       |
| Black or African American                 | 0      | 0       | 0       |
| White                                     | 3      | 9       | 3       |
| More than one race                        | 0      | 0       | 0       |
| Unknown or Not Reported                   | 0      | 0       | 0       |

| Reporting group values | Total |  |  |
|------------------------|-------|--|--|
| Number of subjects     | 87    |  |  |
| Age categorical        |       |  |  |
| Units: Subjects        |       |  |  |

|                                                                         |    |  |  |
|-------------------------------------------------------------------------|----|--|--|
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | -  |  |  |
| Gender categorical<br>Units: Subjects                                   |    |  |  |
| Female                                                                  | 40 |  |  |
| Male                                                                    | 47 |  |  |
| Ethnicity<br>Units: Subjects                                            |    |  |  |
| Hispanic or Latino                                                      | 4  |  |  |
| Not Hispanic or Latino                                                  | 79 |  |  |
| Unknown or Not Reported                                                 | 4  |  |  |
| Race<br>Units: Subjects                                                 |    |  |  |
| Asian                                                                   | 1  |  |  |
| Native Hawaiian or Other Pacific<br>Islander                            | 1  |  |  |
| Black or African American                                               | 9  |  |  |
| White                                                                   | 68 |  |  |
| More than one race                                                      | 3  |  |  |
| Unknown or Not Reported                                                 | 5  |  |  |

## End points

### End points reporting groups

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                          |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------|
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Dose Escalation Phase: Surufatinib 250 mg + Tislelizumab |
| Reporting group description:<br>Patients with advanced or metastatic solid tumors of any kind who had progressed on or were intolerant of standard therapies received surufatinib 250 milligrams (mg) orally once daily (QD) in combination with tislelizumab 200 mg intravenous (IV) infusion every 3 weeks (Q3W) until progressive disease (PD), unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.                                                                 |                                                          |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Dose Escalation Phase: Surufatinib 300 mg + Tislelizumab |
| Reporting group description:<br>Patients with advanced or metastatic solid tumors of any kind who had progressed on or were intolerant of standard therapies received surufatinib 300 mg orally QD in combination with tislelizumab 200 mg IV infusion Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.                                                                                                                                               |                                                          |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Dose Expansion Phase: Cohort A: CRC                      |
| Reporting group description:<br>Patients with microsatellite stable, locally advanced or metastatic colorectal cancer (CRC) that was previously treated with at least 3 prior lines of therapy received surufatinib 300 mg orally QD in combination with tislelizumab 200 mg IV infusion Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.                                                                                                             |                                                          |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Dose Expansion Phase: Cohort B1: Thoracic NETs           |
| Reporting group description:<br>Patients with thoracic neuroendocrine tumor (NET) who had progressive, locally advanced or metastatic, low-to-intermediate grade (Grade 1 or Grade 2), well-differentiated NETs that progressed on at least 1 line of standard therapy received surufatinib 300 mg orally QD in combination with tislelizumab 200 mg IV infusion Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.                                     |                                                          |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Dose Expansion Phase: Cohort B2: GEP NETs                |
| Reporting group description:<br>Patients with gastroenteropancreatic (GEP) NET who had progressive, locally advanced or metastatic, low-to-intermediate grade (Grade 1 or Grade 2), well-differentiated NETs that progressed on at least 1 line of standard therapy received surufatinib 300 mg orally QD in combination with tislelizumab 200 mg IV infusion Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.                                        |                                                          |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Dose Expansion Phase: Cohort C: SCLC                     |
| Reporting group description:<br>Patients with locally advanced or metastatic small-cell lung cancer (SCLC) that was previously progressed on first-line chemotherapy received surufatinib 300 mg orally QD in combination with tislelizumab 200 mg IV infusion Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.                                                                                                                                       |                                                          |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Dose Expansion Phase: Cohort D: GC                       |
| Reporting group description:<br>Patients with microsatellite stable, programmed death-ligand 1 (PD-L1) $\geq 5\%$ , locally advanced or metastatic adenocarcinoma of the stomach or gastroesophageal junction (gastric cancer [GC]), and were previously treated with at least 2 lines of standard therapy received surufatinib 300 mg orally QD in combination with tislelizumab 200 mg IV infusion Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death. |                                                          |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Dose Expansion Phase: Cohort E2: UPS                     |
| Reporting group description:<br>Patients with undifferentiated pleomorphic sarcoma (UPS) who progressed on, or had discontinued due to intolerable toxicity to, at least 1 line of standard therapy or were unsuitable for standard frontline cytotoxic chemotherapy received surufatinib 300 mg orally QD in combination with tislelizumab 200 mg IV infusion Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.                                       |                                                          |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Dose Expansion Phase: Cohort F: ATC                      |
| Reporting group description:<br>Patients with locally advanced or metastatic anaplastic thyroid cancer (ATC) and who had a B-Raf kinase V600E (BRAFV600E) mutation were previously treated with 1 line of systemic therapy (not including                                                                                                                                                                                                                                                                             |                                                          |

radiation therapy) with a BRAF-targeted therapy received surufatinib 300 mg orally QD in combination with tislelizumab 200 mg IV infusion Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.

### Primary: Dose Escalation Phase: Number of Patients With Dose-Limiting Toxicities (DLTs)

|                 |                                                                                                  |
|-----------------|--------------------------------------------------------------------------------------------------|
| End point title | Dose Escalation Phase: Number of Patients With Dose-Limiting Toxicities (DLTs) <sup>[1][2]</sup> |
|-----------------|--------------------------------------------------------------------------------------------------|

End point description:

Per National Cancer Institute Common Terminology Criteria for Adverse Events (AEs) v5.0, DLT=any following AE: Nonhematologic toxicity:  $\geq$  grade (G) 3 nonhematologic toxicity, except: G3 fatigue lasting  $<7$  days, G3 rash returning to baseline or  $\leq$  G1 within 7 days with treatment, G3 hypertension downgraded to  $\leq$  G1 within 7 days with therapy, G3 endocrinopathy controlled by hormonal replacement with no hospitalization and resolving to  $\leq$  G1 within 7 days,  $\geq$  G3 amylase/lipase elevation without symptoms of pancreatitis, G3 nausea/vomiting or diarrhea for  $<72$  hours with care,  $\geq$  G3 electrolyte abnormality lasting up to 72 hours and resolving with treatment. Hematologic toxicity:  $\geq$  G3 febrile neutropenia, G4 neutropenia; G4 thrombocytopenia lasting  $>7$  days, G3 thrombocytopenia with severe bleeding, G4 anemia. DLT-evaluable analysis set=all patients enrolled in dose escalation phase, evaluable for DLT assessment; received  $\geq 85\%$  of surufatinib and  $\geq 67\%$  of tislelizumab administration during DLT assessment or had a DLT.

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

End point timeframe:

From the first dose of study drug (Day 1) up to Day 21 of Cycle 1 (cycle duration: 3 weeks)

Notes:

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

Justification: As the endpoint is descriptive in nature, no statistical analysis is provided.

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

Justification: Only dose escalation phase arms were analyzed for this endpoint.

| End point values            | Dose Escalation Phase: Surufatinib 250 mg + Tislelizumab | Dose Escalation Phase: Surufatinib 300 mg + Tislelizumab |  |  |
|-----------------------------|----------------------------------------------------------|----------------------------------------------------------|--|--|
| Subject group type          | Reporting group                                          | Reporting group                                          |  |  |
| Number of subjects analysed | 6                                                        | 6                                                        |  |  |
| Units: patients             | 1                                                        | 1                                                        |  |  |

### Statistical analyses

No statistical analyses for this end point

### Primary: Dose Escalation Phase: Number of Patients With Treatment-Emergent Adverse Events (TEAEs), Treatment-Emergent Serious Adverse Events (TESAEs) and TEAEs Leading to Treatment Discontinuation

|                 |                                                                                                                                                                                                               |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Dose Escalation Phase: Number of Patients With Treatment-Emergent Adverse Events (TEAEs), Treatment-Emergent Serious Adverse Events (TESAEs) and TEAEs Leading to Treatment Discontinuation <sup>[3][4]</sup> |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

An AE was any untoward medical occurrence in a clinical study patient temporally associated with the use of a study treatment in humans, whether or not considered related to the treatment. An AE was

considered "serious" if, in the view of either the investigator or sponsor, it resulted in death, was life-threatening, required inpatient hospitalization or prolongation of existing hospitalization, was a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, was a congenital anomaly/birth defect or was an important medical event. TEAEs were defined as AEs that started or worsened in severity on or after the first dose of study treatment and up to 30 days after the date of last study treatment administration. The safety analysis set (SAS) included all enrolled patients who received at least 1 dose of surufatinib or tislelizumab.

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

End point timeframe:

From the first dose of study treatment (Day 1) up to 30 days after the last dose of study treatment, approximately 9 months

Notes:

[3] - 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: As the endpoint is descriptive in nature, no statistical analysis is provided.

[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: Only dose escalation phase arms were analyzed for this endpoint.

| End point values                                  | Dose Escalation Phase:<br>Surufatinib 250 mg +<br>Tislelizumab | Dose Escalation Phase:<br>Surufatinib 300 mg +<br>Tislelizumab |  |  |
|---------------------------------------------------|----------------------------------------------------------------|----------------------------------------------------------------|--|--|
| Subject group type                                | Reporting group                                                | Reporting group                                                |  |  |
| Number of subjects analysed                       | 6                                                              | 6                                                              |  |  |
| Units: patients                                   |                                                                |                                                                |  |  |
| Any TEAEs                                         | 6                                                              | 6                                                              |  |  |
| Any TSEAEs                                        | 5                                                              | 3                                                              |  |  |
| Any TEAEs leading to surufatinib discontinuation  | 3                                                              | 0                                                              |  |  |
| Any TEAEs leading to tislelizumab discontinuation | 3                                                              | 0                                                              |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Dose Expansion Phase: Objective Response Rate

|                 |                                                                 |
|-----------------|-----------------------------------------------------------------|
| End point title | Dose Expansion Phase: Objective Response Rate <sup>[5][6]</sup> |
|-----------------|-----------------------------------------------------------------|

End point description:

ORR was defined as the percentage of patients with a confirmed best overall response (BOR) of complete response (CR) or partial response (PR) as determined by the investigator using RECIST v1.1. BOR was defined as the best response recorded from the start of study treatment until documented RECIST v1.1 progression or the start date of new anticancer therapy, whichever came first. CR was defined as disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) had a reduction in short axis to <10 millimeters (mm). PR was defined as at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum of diameters. The SAS included all enrolled patients who received at least 1 dose of surufatinib or tislelizumab. Here, +/- 9999 = values were not estimable as there were no patients with CR or PR in that disease cohort.

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

End point timeframe:

Tumor assessments performed every 6 weeks (+/-1 week) for the first 24 weeks and every 9 weeks (+/-1 week) thereafter, up to a maximum of approximately 37 months

Notes:

[5] - 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: As the endpoint is descriptive in nature, no statistical analysis is provided.

[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: Only dose expansion phase arms were analyzed for this endpoint.

| End point values                 | Dose Expansion Phase: Cohort A: CRC | Dose Expansion Phase: Cohort B1: Thoracic NETs | Dose Expansion Phase: Cohort B2: GEP NETs | Dose Expansion Phase: Cohort C: SCLC |
|----------------------------------|-------------------------------------|------------------------------------------------|-------------------------------------------|--------------------------------------|
| Subject group type               | Reporting group                     | Reporting group                                | Reporting group                           | Reporting group                      |
| Number of subjects analysed      | 15                                  | 10                                             | 20                                        | 15                                   |
| Units: percentage of patients    |                                     |                                                |                                           |                                      |
| number (confidence interval 95%) | 6.7 (0.2 to 31.9)                   | 0 (-9999 to 9999)                              | 15.0 (3.2 to 37.9)                        | 13.3 (1.7 to 40.5)                   |

| End point values                 | Dose Expansion Phase: Cohort D: GC | Dose Expansion Phase: Cohort E2: UPS | Dose Expansion Phase: Cohort F: ATC |  |
|----------------------------------|------------------------------------|--------------------------------------|-------------------------------------|--|
| Subject group type               | Reporting group                    | Reporting group                      | Reporting group                     |  |
| Number of subjects analysed      | 3                                  | 9                                    | 3                                   |  |
| Units: percentage of patients    |                                    |                                      |                                     |  |
| number (confidence interval 95%) | 33.3 (0.8 to 90.6)                 | 44.4 (13.7 to 78.8)                  | 0 (-9999 to 9999)                   |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Dose Escalation Phase: Objective Response Rate

|                 |                                                               |
|-----------------|---------------------------------------------------------------|
| End point title | Dose Escalation Phase: Objective Response Rate <sup>[7]</sup> |
|-----------------|---------------------------------------------------------------|

End point description:

ORR was defined as the percentage of patients with a confirmed BOR of CR or PR as determined by the investigator using RECIST v1.1. BOR was defined as the best response recorded from the start of study treatment until documented RECIST v1.1 progression or the start date of new anticancer therapy, whichever came first. CR was defined as disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) had a reduction in short axis to <10 mm. PR was defined as at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum of diameters. The SAS included all enrolled patients who received at least 1 dose of surufatinib or tislelizumab. Here, +/- 9999 = values were not estimable as there were no patients with CR or PR in that disease cohort.

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

End point timeframe:

Tumor assessments performed every 6 weeks (+/-1 week) for the first 24 weeks and every 9 weeks (+/-1 week) thereafter, up to a maximum of approximately 42 months

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: Only dose escalation phase arms were analyzed for this endpoint.

| End point values                 | Dose Escalation Phase: Surufatinib 250 mg + Tislelizumab | Dose Escalation Phase: Surufatinib 300 mg + Tislelizumab |  |  |
|----------------------------------|----------------------------------------------------------|----------------------------------------------------------|--|--|
| Subject group type               | Reporting group                                          | Reporting group                                          |  |  |
| Number of subjects analysed      | 6                                                        | 6                                                        |  |  |
| Units: percentage of patients    |                                                          |                                                          |  |  |
| number (confidence interval 95%) | 0 (-9999 to 9999)                                        | 0 (-9999 to 9999)                                        |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Dose Escalation and Dose Expansion Phases: Progression-free Survival (PFS)

|                 |                                                                            |
|-----------------|----------------------------------------------------------------------------|
| End point title | Dose Escalation and Dose Expansion Phases: Progression-free Survival (PFS) |
|-----------------|----------------------------------------------------------------------------|

End point description:

PFS was defined as the time from the start of study treatment until the first radiographic documentation of objective progression as assessed by the investigator using RECIST v1.1, or death from any cause. PD was defined as at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study (nadir), including baseline. In addition to the relative increase of 20%, the sum also demonstrated an absolute increase of at least 5 mm. The appearance of one or more new lesions was also considered progression. The SAS included all enrolled patients who received at least 1 dose of surufatinib or tislelizumab. Here, 9999 = values were not estimable due to insufficient number of patients with events at study closure.

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

End point timeframe:

Tumor assessments performed every 6 weeks (+/-1 week) for the first 24 weeks and every 9 weeks (+/-1 week) thereafter, up to a maximum of approximately 42 months

| End point values                 | Dose Escalation Phase: Surufatinib 250 mg + Tislelizumab | Dose Escalation Phase: Surufatinib 300 mg + Tislelizumab | Dose Expansion Phase: Cohort A: CRC | Dose Expansion Phase: Cohort B1: Thoracic NETs |
|----------------------------------|----------------------------------------------------------|----------------------------------------------------------|-------------------------------------|------------------------------------------------|
| Subject group type               | Reporting group                                          | Reporting group                                          | Reporting group                     | Reporting group                                |
| Number of subjects analysed      | 6                                                        | 6                                                        | 15                                  | 10                                             |
| Units: months                    |                                                          |                                                          |                                     |                                                |
| median (confidence interval 95%) | 1.5 (1.2 to 9999)                                        | 6.0 (1.8 to 9999)                                        | 4.7 (2.7 to 5.4)                    | 4.5 (0.3 to 9999)                              |

| End point values | Dose Expansion Phase: Cohort B2: GEP NETs | Dose Expansion Phase: Cohort C: SCLC | Dose Expansion Phase: Cohort D: GC | Dose Expansion Phase: Cohort E2: UPS |
|------------------|-------------------------------------------|--------------------------------------|------------------------------------|--------------------------------------|
|------------------|-------------------------------------------|--------------------------------------|------------------------------------|--------------------------------------|

| Subject group type               | Reporting group   | Reporting group  | Reporting group   | Reporting group    |
|----------------------------------|-------------------|------------------|-------------------|--------------------|
| Number of subjects analysed      | 20                | 15               | 3                 | 9                  |
| Units: months                    |                   |                  |                   |                    |
| median (confidence interval 95%) | 7.4 (3.1 to 20.0) | 1.4 (1.0 to 4.0) | 9.6 (5.6 to 9999) | 9999 (1.3 to 9999) |

|                                  |                                     |  |  |  |
|----------------------------------|-------------------------------------|--|--|--|
| <b>End point values</b>          | Dose Expansion Phase: Cohort F: ATC |  |  |  |
| Subject group type               | Reporting group                     |  |  |  |
| Number of subjects analysed      | 3                                   |  |  |  |
| Units: months                    |                                     |  |  |  |
| median (confidence interval 95%) | 2.8 (1.2 to 9999)                   |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Dose Escalation and Dose Expansion Phases: Disease Control Rate (DCR)

|                 |                                                                       |
|-----------------|-----------------------------------------------------------------------|
| End point title | Dose Escalation and Dose Expansion Phases: Disease Control Rate (DCR) |
|-----------------|-----------------------------------------------------------------------|

End point description:

DCR was defined as percentage of patients with a BOR of CR, PR, or stable disease (SD) lasting for at least 7 weeks as determined by the investigator using RECIST v1.1. BOR was defined as best response recorded from start of study treatment until documented RECIST v1.1 progression or start date of new anticancer therapy, whichever came first. CR was defined as disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) had a reduction in short axis to <10 mm. PR was defined as at least a 30% decrease in sum of diameters of target lesions, taking as reference baseline sum of diameters. SD was defined as neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference smallest sum on study. SAS included all enrolled patients who received at least 1 dose of surufatinib or tislelizumab. Here, +/- 9999 = values were not estimable due to no patients with CR, PR, or SD for at least 7 weeks.

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

End point timeframe:

Tumor assessments performed every 6 weeks (+/-1 week) for the first 24 weeks and every 9 weeks (+/-1 week) thereafter, up to a maximum of approximately 42 months

|                                  |                                                          |                                                          |                                     |                                                |
|----------------------------------|----------------------------------------------------------|----------------------------------------------------------|-------------------------------------|------------------------------------------------|
| <b>End point values</b>          | Dose Escalation Phase: Surufatinib 250 mg + Tislelizumab | Dose Escalation Phase: Surufatinib 300 mg + Tislelizumab | Dose Expansion Phase: Cohort A: CRC | Dose Expansion Phase: Cohort B1: Thoracic NETs |
| Subject group type               | Reporting group                                          | Reporting group                                          | Reporting group                     | Reporting group                                |
| Number of subjects analysed      | 6                                                        | 6                                                        | 15                                  | 10                                             |
| Units: percentage of patients    |                                                          |                                                          |                                     |                                                |
| number (confidence interval 95%) | 0 (-9999 to 9999)                                        | 66.7 (22.3 to 95.7)                                      | 66.7 (38.4 to 88.2)                 | 50.0 (18.7 to 81.3)                            |

| End point values                 | Dose Expansion Phase: Cohort B2: GEP NETs | Dose Expansion Phase: Cohort C: SCLC | Dose Expansion Phase: Cohort D: GC | Dose Expansion Phase: Cohort E2: UPS |
|----------------------------------|-------------------------------------------|--------------------------------------|------------------------------------|--------------------------------------|
| Subject group type               | Reporting group                           | Reporting group                      | Reporting group                    | Reporting group                      |
| Number of subjects analysed      | 20                                        | 15                                   | 3                                  | 9                                    |
| Units: percentage of patients    |                                           |                                      |                                    |                                      |
| number (confidence interval 95%) | 70.0 (45.7 to 88.1)                       | 26.7 (7.8 to 55.1)                   | 66.7 (9.4 to 99.2)                 | 55.6 (21.2 to 86.3)                  |

| End point values                 | Dose Expansion Phase: Cohort F: ATC |  |  |  |
|----------------------------------|-------------------------------------|--|--|--|
| Subject group type               | Reporting group                     |  |  |  |
| Number of subjects analysed      | 3                                   |  |  |  |
| Units: percentage of patients    |                                     |  |  |  |
| number (confidence interval 95%) | 33.3 (0.8 to 90.6)                  |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Dose Escalation and Dose Expansion Phases: Clinical Benefit Rate (CBR)

|                 |                                                                        |
|-----------------|------------------------------------------------------------------------|
| End point title | Dose Escalation and Dose Expansion Phases: Clinical Benefit Rate (CBR) |
|-----------------|------------------------------------------------------------------------|

End point description:

CBR was defined as percentage of patients with BOR of CR, PR, or durable SD as determined by investigator using RECIST v1.1. Durable SD was SD for at least 6 months. BOR was defined as best response recorded from start of study treatment until documented RECIST v1.1 progression or start date of new anticancer therapy, whichever came first. CR was defined as disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) had reduction in short axis to <10 mm. PR was defined as at least 30% decrease in sum of diameters of target lesions, taking as reference baseline sum of diameters. SD was defined as neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference smallest sum on study. SAS included all enrolled patients who received at least 1 dose of surufatinib or tislelizumab. Here, +/- 9999 = values were not estimable due to no patients with CR, PR, or SD lasting for at least 6 months.

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

End point timeframe:

Tumor assessments performed every 6 weeks (+/-1 week) for the first 24 weeks and every 9 weeks (+/-1 week) thereafter, up to a maximum of approximately 42 months

| End point values                 | Dose Escalation Phase: Surufatinib 250 mg + Tislelizumab | Dose Escalation Phase: Surufatinib 300 mg + Tislelizumab | Dose Expansion Phase: Cohort A: CRC | Dose Expansion Phase: Cohort B1: Thoracic NETs |
|----------------------------------|----------------------------------------------------------|----------------------------------------------------------|-------------------------------------|------------------------------------------------|
| Subject group type               | Reporting group                                          | Reporting group                                          | Reporting group                     | Reporting group                                |
| Number of subjects analysed      | 6                                                        | 6                                                        | 15                                  | 10                                             |
| Units: percentage of patients    |                                                          |                                                          |                                     |                                                |
| number (confidence interval 95%) | 0 (-9999 to 9999)                                        | 50.0 (11.8 to 88.2)                                      | 20.0 (4.3 to 48.1)                  | 20.0 (2.5 to 55.6)                             |

| End point values                 | Dose Expansion Phase: Cohort B2: GEP NETs | Dose Expansion Phase: Cohort C: SCLC | Dose Expansion Phase: Cohort D: GC | Dose Expansion Phase: Cohort E2: UPS |
|----------------------------------|-------------------------------------------|--------------------------------------|------------------------------------|--------------------------------------|
| Subject group type               | Reporting group                           | Reporting group                      | Reporting group                    | Reporting group                      |
| Number of subjects analysed      | 20                                        | 15                                   | 3                                  | 9                                    |
| Units: percentage of patients    |                                           |                                      |                                    |                                      |
| number (confidence interval 95%) | 40.0 (19.1 to 63.9)                       | 13.3 (1.7 to 40.5)                   | 33.3 (0.8 to 90.6)                 | 44.4 (13.7 to 78.8)                  |

| End point values                 | Dose Expansion Phase: Cohort F: ATC |  |  |  |
|----------------------------------|-------------------------------------|--|--|--|
| Subject group type               | Reporting group                     |  |  |  |
| Number of subjects analysed      | 3                                   |  |  |  |
| Units: percentage of patients    |                                     |  |  |  |
| number (confidence interval 95%) | 0 (-9999 to 9999)                   |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Dose Escalation and Dose Expansion Phases: Duration of Response (DoR)

|                 |                                                                       |
|-----------------|-----------------------------------------------------------------------|
| End point title | Dose Escalation and Dose Expansion Phases: Duration of Response (DoR) |
|-----------------|-----------------------------------------------------------------------|

End point description:

DoR was defined as the time from the first occurrence of PR or CR by RECIST v1.1, until PD or death, whichever came first. CR was defined as disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) had a reduction in short axis to <10 mm. PR was defined as at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum of diameters. The SAS included all enrolled patients who received at least 1 dose of surufatinib or tislelizumab. Only those patients with PR or CR (responders) were included in the analysis. Here, +/- 9999 = values were not estimable due to insufficient number of patients with events at study closure.

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

End point timeframe:

Tumor assessments performed every 6 weeks (+/-1 week) for the first 24 weeks and every 9 weeks (+/-1 week) thereafter, up to a maximum of approximately 42 months

| End point values                 | Dose Escalation Phase: Surufatinib 250 mg + Tislelizumab | Dose Escalation Phase: Surufatinib 300 mg + Tislelizumab | Dose Expansion Phase: Cohort A: CRC | Dose Expansion Phase: Cohort B1: Thoracic NETs |
|----------------------------------|----------------------------------------------------------|----------------------------------------------------------|-------------------------------------|------------------------------------------------|
| Subject group type               | Reporting group                                          | Reporting group                                          | Reporting group                     | Reporting group                                |
| Number of subjects analysed      | 0 <sup>[8]</sup>                                         | 0 <sup>[9]</sup>                                         | 1                                   | 0 <sup>[10]</sup>                              |
| Units: months                    |                                                          |                                                          |                                     |                                                |
| median (confidence interval 95%) | ( to )                                                   | ( to )                                                   | 9999 (9999 to 9999)                 | ( to )                                         |

Notes:

[8] - There were no patients with PR or CR (responders) in this cohort.

[9] - There were no patients with PR or CR (responders) in this cohort.

[10] - There were no patients with PR or CR (responders) in this cohort.

| End point values                 | Dose Expansion Phase: Cohort B2: GEP NETs | Dose Expansion Phase: Cohort C: SCLC | Dose Expansion Phase: Cohort D: GC | Dose Expansion Phase: Cohort E2: UPS |
|----------------------------------|-------------------------------------------|--------------------------------------|------------------------------------|--------------------------------------|
| Subject group type               | Reporting group                           | Reporting group                      | Reporting group                    | Reporting group                      |
| Number of subjects analysed      | 3                                         | 2                                    | 1                                  | 4                                    |
| Units: months                    |                                           |                                      |                                    |                                      |
| median (confidence interval 95%) | 9999 (15.0 to 9999)                       | 8.3 (5.8 to 9999)                    | 11.0 (-9999 to 9999)               | 9999 (9999 to 9999)                  |

| End point values                 | Dose Expansion Phase: Cohort F: ATC |  |  |  |
|----------------------------------|-------------------------------------|--|--|--|
| Subject group type               | Reporting group                     |  |  |  |
| Number of subjects analysed      | 0 <sup>[11]</sup>                   |  |  |  |
| Units: months                    |                                     |  |  |  |
| median (confidence interval 95%) | ( to )                              |  |  |  |

Notes:

[11] - There were no patients with PR or CR (responders) in this cohort.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Dose Escalation and Dose Expansion Phases: Time to Response (TTR)

|                 |                                                                   |
|-----------------|-------------------------------------------------------------------|
| End point title | Dose Escalation and Dose Expansion Phases: Time to Response (TTR) |
|-----------------|-------------------------------------------------------------------|

End point description:

TTR was defined as the time from start of study treatment until the date of first documented objective response, either CR or PR (whichever status was recorded first), according to RECIST v1.1. CR was

defined as disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) had a reduction in short axis to <10 mm. PR was defined as at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum of diameters. The SAS included all enrolled patients who received at least 1 dose of surufatinib or tislelizumab. Only those patients with PR or CR (responders) were included in the analysis. Here, +/- 9999 = values were not estimable due to insufficient number of patients with events at study closure.

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

End point timeframe:

Tumor assessments performed every 6 weeks (+/-1 week) for the first 24 weeks and every 9 weeks (+/-1 week) thereafter, up to a maximum of approximately 42 months

| End point values                 | Dose Escalation Phase: Surufatinib 250 mg + Tislelizumab | Dose Escalation Phase: Surufatinib 300 mg + Tislelizumab | Dose Expansion Phase: Cohort A: CRC | Dose Expansion Phase: Cohort B1: Thoracic NETs |
|----------------------------------|----------------------------------------------------------|----------------------------------------------------------|-------------------------------------|------------------------------------------------|
| Subject group type               | Reporting group                                          | Reporting group                                          | Reporting group                     | Reporting group                                |
| Number of subjects analysed      | 0 <sup>[12]</sup>                                        | 0 <sup>[13]</sup>                                        | 1                                   | 0 <sup>[14]</sup>                              |
| Units: months                    |                                                          |                                                          |                                     |                                                |
| median (confidence interval 95%) | ( to )                                                   | ( to )                                                   | 2.7 (-9999 to 9999)                 | ( to )                                         |

Notes:

[12] - There were no patients with PR or CR (responders) in this cohort.

[13] - There were no patients with PR or CR (responders) in this cohort.

[14] - There were no patients with PR or CR (responders) in this cohort.

| End point values                 | Dose Expansion Phase: Cohort B2: GEP NETs | Dose Expansion Phase: Cohort C: SCLC | Dose Expansion Phase: Cohort D: GC | Dose Expansion Phase: Cohort E2: UPS |
|----------------------------------|-------------------------------------------|--------------------------------------|------------------------------------|--------------------------------------|
| Subject group type               | Reporting group                           | Reporting group                      | Reporting group                    | Reporting group                      |
| Number of subjects analysed      | 3                                         | 2                                    | 1                                  | 4                                    |
| Units: months                    |                                           |                                      |                                    |                                      |
| median (confidence interval 95%) | 3.9 (2.7 to 9999)                         | 3.5 (1.3 to 9999)                    | 2.7 (-9999 to 9999)                | 1.4 (1.2 to 9999)                    |

| End point values                 | Dose Expansion Phase: Cohort F: ATC |  |  |  |
|----------------------------------|-------------------------------------|--|--|--|
| Subject group type               | Reporting group                     |  |  |  |
| Number of subjects analysed      | 0 <sup>[15]</sup>                   |  |  |  |
| Units: months                    |                                     |  |  |  |
| median (confidence interval 95%) | ( to )                              |  |  |  |

Notes:

[15] - There were no patients with PR or CR (responders) in this cohort.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Dose Escalation and Dose Expansion Phases: Plasma Concentration of Surufatinib

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Dose Escalation and Dose Expansion Phases: Plasma Concentration of Surufatinib |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                |
| Blood samples were collected at the specified timepoints to determine plasma concentration of surufatinib. The pharmacokinetic (PK) analysis set included all patients with at least 1 quantifiable concentration of surufatinib or tislelizumab. Here, n = number of patients with data collected at specified timepoints. 9999 = values were not estimable as they were below the lower limit of quantification (LLOQ) of 1.00 nanograms per milliliter (ng/mL). 99999 = standard deviation (SD) was not estimable for 1 patient. 55555 = no patients were analyzed. C = Cycle and D = Day. |                                                                                |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Secondary                                                                      |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                |
| Pre-dose on Day 1 of Cycles 1, 2, 5, 9, 17 and on Days 8 and 15 of Cycle 1; 2 to 4 hours (h) post-dose on Days 1 and 15 of Cycle 1 (cycle duration: 3 weeks)                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                |

| End point values                                   | Dose Escalation Phase: Surufatinib 250 mg + Tislelizumab | Dose Escalation Phase: Surufatinib 300 mg + Tislelizumab | Dose Expansion Phase: Cohort A: CRC | Dose Expansion Phase: Cohort B1: Thoracic NETs |
|----------------------------------------------------|----------------------------------------------------------|----------------------------------------------------------|-------------------------------------|------------------------------------------------|
| Subject group type                                 | Reporting group                                          | Reporting group                                          | Reporting group                     | Reporting group                                |
| Number of subjects analysed                        | 6                                                        | 6                                                        | 15                                  | 10                                             |
| Units: ng/mL                                       |                                                          |                                                          |                                     |                                                |
| arithmetic mean (standard deviation)               |                                                          |                                                          |                                     |                                                |
| C1D1: Pre-dose (n=5,6,15,10,19,15,3,9,2)           | 9999 (± 9999)                                            | 9999 (± 9999)                                            | 9999 (± 9999)                       | 9999 (± 9999)                                  |
| C1D1: 2 to 4 h post-dose (n=6,6,15,10,19,15,3,9,2) | 293.03 (± 244.593)                                       | 576.00 (± 415.108)                                       | 426.62 (± 312.209)                  | 276.36 (± 243.080)                             |
| C1D8: Pre-dose (n=4,6,12,5,14,9,2,6,1)             | 77.00 (± 44.023)                                         | 189.93 (± 113.750)                                       | 170.33 (± 131.533)                  | 100.12 (± 71.600)                              |
| C1D15: Pre-dose (n=5,5,11,4,15,10,2,6,0)           | 64.36 (± 15.246)                                         | 181.56 (± 125.156)                                       | 135.96 (± 83.673)                   | 159.00 (± 139.802)                             |
| C1D15: 2 to 4 h post-dose (n=3,3,13,4,12,11,2,7,0) | 318.67 (± 146.770)                                       | 757.33 (± 498.399)                                       | 657.54 (± 369.146)                  | 354.25 (± 52.519)                              |
| C2D1: Pre-dose (n=5,4,10,3,9,11,2,2,1)             | 45.82 (± 27.567)                                         | 96.80 (± 38.895)                                         | 151.44 (± 99.521)                   | 89.37 (± 53.475)                               |
| C5D1: Pre-dose (n=0,2,3,1,4,2,0,0,0)               | 55555 (± 55555)                                          | 55.25 (± 8.132)                                          | 141.20 (± 117.885)                  | 41.00 (± 99999)                                |
| C9D1: Pre-dose (n=0,1,0,0,3,1,0,0,0)               | 55555 (± 55555)                                          | 65.90 (± 99999)                                          | 55555 (± 55555)                     | 55555 (± 55555)                                |
| C17D1: Pre-dose (n=0,0,0,0,1,0,0,0,0)              | 55555 (± 55555)                                          | 55555 (± 55555)                                          | 55555 (± 55555)                     | 55555 (± 55555)                                |

| End point values                     | Dose Expansion Phase: Cohort B2: GEP NETs | Dose Expansion Phase: Cohort C: SCLC | Dose Expansion Phase: Cohort D: GC | Dose Expansion Phase: Cohort E2: UPS |
|--------------------------------------|-------------------------------------------|--------------------------------------|------------------------------------|--------------------------------------|
| Subject group type                   | Reporting group                           | Reporting group                      | Reporting group                    | Reporting group                      |
| Number of subjects analysed          | 19                                        | 15                                   | 3                                  | 9                                    |
| Units: ng/mL                         |                                           |                                      |                                    |                                      |
| arithmetic mean (standard deviation) |                                           |                                      |                                    |                                      |

|                                                       |                    |                    |                    |                    |
|-------------------------------------------------------|--------------------|--------------------|--------------------|--------------------|
| C1D1: Pre-dose<br>(n=5,6,15,10,19,15,3,9,2)           | 9999 (± 9999)      | 9999 (± 9999)      | 9999 (± 9999)      | 9999 (± 9999)      |
| C1D1: 2 to 4 h post-dose<br>(n=6,6,15,10,19,15,3,9,2) | 294.13 (± 292.335) | 406.97 (± 212.791) | 506.27 (± 653.616) | 275.64 (± 165.937) |
| C1D8: Pre-dose<br>(n=4,6,12,5,14,9,2,6,1)             | 92.26 (± 63.901)   | 122.80 (± 70.875)  | 109.10 (± 18.243)  | 97.70 (± 40.471)   |
| C1D15: Pre-dose<br>(n=5,5,11,4,15,10,2,6,0)           | 84.95 (± 70.121)   | 96.79 (± 43.933)   | 111.05 (± 19.728)  | 118.92 (± 75.457)  |
| C1D15: 2 to 4 h post-dose<br>(n=3,3,13,4,12,11,2,7,0) | 471.78 (± 330.598) | 425.75 (± 235.698) | 188.00 (± 41.012)  | 518.00 (± 302.182) |
| C2D1: Pre-dose<br>(n=5,4,10,3,9,11,2,2,1)             | 75.94 (± 53.028)   | 117.68 (± 79.721)  | 146.50 (± 26.163)  | 71.95 (± 9.405)    |
| C5D1: Pre-dose (n=0,2,3,1,4,2,0,0,0)                  | 61.08 (± 22.279)   | 105.70 (± 54.164)  | 55555 (± 55555)    | 55555 (± 55555)    |
| C9D1: Pre-dose (n=0,1,0,0,3,1,0,0,0)                  | 87.20 (± 14.964)   | 41.70 (± 99999)    | 55555 (± 55555)    | 55555 (± 55555)    |
| C17D1: Pre-dose (n=0,0,0,0,1,0,0,0,0)                 | 85.10 (± 99999)    | 55555 (± 55555)    | 55555 (± 55555)    | 55555 (± 55555)    |

| End point values                                      | Dose Expansion<br>Phase: Cohort<br>F: ATC |  |  |  |
|-------------------------------------------------------|-------------------------------------------|--|--|--|
| Subject group type                                    | Reporting group                           |  |  |  |
| Number of subjects analysed                           | 2                                         |  |  |  |
| Units: ng/mL                                          |                                           |  |  |  |
| arithmetic mean (standard deviation)                  |                                           |  |  |  |
| C1D1: Pre-dose<br>(n=5,6,15,10,19,15,3,9,2)           | 9999 (± 9999)                             |  |  |  |
| C1D1: 2 to 4 h post-dose<br>(n=6,6,15,10,19,15,3,9,2) | 782.50 (± 463.155)                        |  |  |  |
| C1D8: Pre-dose<br>(n=4,6,12,5,14,9,2,6,1)             | 709.00 (± 99999)                          |  |  |  |
| C1D15: Pre-dose<br>(n=5,5,11,4,15,10,2,6,0)           | 55555 (± 55555)                           |  |  |  |
| C1D15: 2 to 4 h post-dose<br>(n=3,3,13,4,12,11,2,7,0) | 55555 (± 55555)                           |  |  |  |
| C2D1: Pre-dose<br>(n=5,4,10,3,9,11,2,2,1)             | 147.00 (± 99999)                          |  |  |  |
| C5D1: Pre-dose (n=0,2,3,1,4,2,0,0,0)                  | 55555 (± 55555)                           |  |  |  |
| C9D1: Pre-dose (n=0,1,0,0,3,1,0,0,0)                  | 55555 (± 55555)                           |  |  |  |
| C17D1: Pre-dose (n=0,0,0,0,1,0,0,0,0)                 | 55555 (± 55555)                           |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Dose Escalation and Dose Expansion Phases: Serum Concentration of Tislelizumab

|                 |                                                                                |
|-----------------|--------------------------------------------------------------------------------|
| End point title | Dose Escalation and Dose Expansion Phases: Serum Concentration of Tislelizumab |
|-----------------|--------------------------------------------------------------------------------|

End point description:

Blood samples were collected at the specified timepoints to determine serum concentration of tislelizumab. The PK analysis set included all patients with at least 1 quantifiable concentration of surufatinib or tislelizumab. Here, n = number of patients with data collected at specified timepoints. 9999 = values were not estimable as they were below the LLOQ of 400 ng/mL. 99999 = SD was not estimable for 1 patient. 55555 = no patients were analyzed. C = Cycle and D = Day.

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

End point timeframe:

Pre-infusion on Day 1 of Cycles 1, 2, 5, 9, 17; end of infusion on Day 1 of Cycles 1 and 5; on Days 8 and 15 of Cycle 1 (cycle duration: 3 weeks)

| End point values                                | Dose Escalation Phase: Surufatinib 250 mg + Tislelizumab | Dose Escalation Phase: Surufatinib 300 mg + Tislelizumab | Dose Expansion Phase: Cohort A: CRC | Dose Expansion Phase: Cohort B1: Thoracic NETs |
|-------------------------------------------------|----------------------------------------------------------|----------------------------------------------------------|-------------------------------------|------------------------------------------------|
| Subject group type                              | Reporting group                                          | Reporting group                                          | Reporting group                     | Reporting group                                |
| Number of subjects analysed                     | 6                                                        | 6                                                        | 15                                  | 10                                             |
| Units: ng/mL                                    |                                                          |                                                          |                                     |                                                |
| arithmetic mean (standard deviation)            |                                                          |                                                          |                                     |                                                |
| C1D1: Pre-infusion (n=6,6,15,9,19,15,3,9,2)     | 9999 (± 9999)                                            | 9999 (± 9999)                                            | 9999 (± 9999)                       | 9999 (± 9999)                                  |
| C1D1: End of infusion (n=6,6,15,10,19,15,3,9,2) | 44550.0 (± 7420.98)                                      | 62750.0 (± 17420.53)                                     | 57233.3 (± 8846.28)                 | 70990.0 (± 41600.73)                           |
| C1D8 (n=6,6,13,8,18,12,3,8,2)                   | 16980.0 (± 6850.75)                                      | 26216.7 (± 7702.32)                                      | 26446.2 (± 6387.83)                 | 29575.0 (± 5751.46)                            |
| C1D15 (n=6,6,12,7,16,12,2,8,2)                  | 14296.7 (± 5945.36)                                      | 17900.0 (± 5297.55)                                      | 17414.2 (± 4199.94)                 | 20571.4 (± 2817.63)                            |
| C2D1: Pre-infusion (n=5,5,14,6,15,12,2,8,2)     | 9564.0 (± 7871.14)                                       | 13804.0 (± 4782.16)                                      | 13858.6 (± 4730.49)                 | 14033.3 (± 2436.12)                            |
| C5D1: Pre-infusion (n=0,3,8,1,8,4,1,3,1)        | 55555 (± 55555)                                          | 24400.0 (± 14028.90)                                     | 36412.5 (± 34947.57)                | 46400.0 (± 99999)                              |
| C5D1: End of infusion (n=0,3,7,2,8,4,1,3,1)     | 55555 (± 55555)                                          | 87166.7 (± 34425.04)                                     | 102500.0 (± 26662.02)               | 117500.0 (± 6363.96)                           |
| C9D1: Pre-infusion (n=0,2,1,1,5,2,0,2,0)        | 55555 (± 55555)                                          | 22700.0 (± 4101.22)                                      | 44800.0 (± 99999)                   | 50000.0 (± 99999)                              |
| C17D1: Pre-infusion (n=0,0,0,1,3,1,0,1,0)       | 55555 (± 55555)                                          | 55555 (± 55555)                                          | 55555 (± 55555)                     | 55555 (± 55555)                                |

| End point values                                | Dose Expansion Phase: Cohort B2: GEP NETs | Dose Expansion Phase: Cohort C: SCLC | Dose Expansion Phase: Cohort D: GC | Dose Expansion Phase: Cohort E2: UPS |
|-------------------------------------------------|-------------------------------------------|--------------------------------------|------------------------------------|--------------------------------------|
| Subject group type                              | Reporting group                           | Reporting group                      | Reporting group                    | Reporting group                      |
| Number of subjects analysed                     | 19                                        | 15                                   | 3                                  | 9                                    |
| Units: ng/mL                                    |                                           |                                      |                                    |                                      |
| arithmetic mean (standard deviation)            |                                           |                                      |                                    |                                      |
| C1D1: Pre-infusion (n=6,6,15,9,19,15,3,9,2)     | 9999 (± 9999)                             | 9999 (± 9999)                        | 9999 (± 9999)                      | 9999 (± 9999)                        |
| C1D1: End of infusion (n=6,6,15,10,19,15,3,9,2) | 61136.8 (± 15927.90)                      | 66220.0 (± 17336.43)                 | 67966.7 (± 45015.59)               | 55955.6 (± 15499.61)                 |
| C1D8 (n=6,6,13,8,18,12,3,8,2)                   | 32244.4 (± 7253.58)                       | 35450.0 (± 8899.39)                  | 38233.3 (± 35800.33)               | 25475.0 (± 6549.10)                  |

|                                             |                       |                       |                      |                       |
|---------------------------------------------|-----------------------|-----------------------|----------------------|-----------------------|
| C1D15 (n=6,6,12,7,16,12,2,8,2)              | 24506.3 (± 6403.07)   | 23783.3 (± 4274.20)   | 43950.0 (± 40658.64) | 19300.0 (± 4755.45)   |
| C2D1: Pre-infusion (n=5,5,14,6,15,12,2,8,2) | 18020.0 (± 5688.23)   | 17725.0 (± 3860.55)   | 38000.0 (± 36910.97) | 12161.3 (± 4443.93)   |
| C5D1: Pre-infusion (n=0,3,8,1,8,4,1,3,1)    | 41575.0 (± 10065.32)  | 31225.0 (± 12388.81)  | 20100.0 (± 99999)    | 19200.0 (± 3143.25)   |
| C5D1: End of infusion (n=0,3,7,2,8,4,1,3,1) | 113475.0 (± 16286.34) | 117550.0 (± 43800.65) | 80800.0 (± 99999)    | 103033.3 (± 17737.06) |
| C9D1: Pre-infusion (n=0,2,1,1,5,2,0,2,0)    | 45500.0 (± 5384.24)   | 41200.0 (± 24607.32)  | 55555 (± 55555)      | 41100.0 (± 16970.56)  |
| C17D1: Pre-infusion (n=0,0,0,1,3,1,0,1,0)   | 44766.7 (± 12196.86)  | 51900.0 (± 99999)     | 55555 (± 55555)      | 47300.0 (± 99999)     |

| End point values                                | Dose Expansion Phase: Cohort F: ATC |  |  |  |
|-------------------------------------------------|-------------------------------------|--|--|--|
| Subject group type                              | Reporting group                     |  |  |  |
| Number of subjects analysed                     | 2                                   |  |  |  |
| Units: ng/mL                                    |                                     |  |  |  |
| arithmetic mean (standard deviation)            |                                     |  |  |  |
| C1D1: Pre-infusion (n=6,6,15,9,19,15,3,9,2)     | 9999 (± 9999)                       |  |  |  |
| C1D1: End of infusion (n=6,6,15,10,19,15,3,9,2) | 42200.0 (± 12727.92)                |  |  |  |
| C1D8 (n=6,6,13,8,18,12,3,8,2)                   | 16050.0 (± 1767.77)                 |  |  |  |
| C1D15 (n=6,6,12,7,16,12,2,8,2)                  | 10940.0 (± 2489.02)                 |  |  |  |
| C2D1: Pre-infusion (n=5,5,14,6,15,12,2,8,2)     | 7640.0 (± 2729.43)                  |  |  |  |
| C5D1: Pre-infusion (n=0,3,8,1,8,4,1,3,1)        | 22700.0 (± 99999)                   |  |  |  |
| C5D1: End of infusion (n=0,3,7,2,8,4,1,3,1)     | 69000.0 (± 99999)                   |  |  |  |
| C9D1: Pre-infusion (n=0,2,1,1,5,2,0,2,0)        | 55555 (± 55555)                     |  |  |  |
| C17D1: Pre-infusion (n=0,0,0,1,3,1,0,1,0)       | 55555 (± 55555)                     |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Dose Escalation and Dose Expansion Phases: Number of Patients With Antidrug Antibodies (ADA) to Tislelizumab

|                 |                                                                                                              |
|-----------------|--------------------------------------------------------------------------------------------------------------|
| End point title | Dose Escalation and Dose Expansion Phases: Number of Patients With Antidrug Antibodies (ADA) to Tislelizumab |
|-----------------|--------------------------------------------------------------------------------------------------------------|

End point description:

Blood samples were collected at the specified timepoints to detect ADAs to tislelizumab. Treatment-boosted ADA was defined as ADA positive at baseline that was boosted to a 4-fold or higher-level following treatment administration. Treatment-induced ADA was defined as ADA negative at baseline and ADA positive post-baseline. The ADA analysis set included all patients who received at least 1 dose of tislelizumab and had a baseline and at least 1 post-baseline ADA result.

|                                                                                                                                                                                                            |           |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|
| End point type                                                                                                                                                                                             | Secondary |
| End point timeframe:                                                                                                                                                                                       |           |
| From the first dose of study treatment (Day 1) up to 30 days after the last dose of study treatment, approximately 9 months for dose escalation phase and approximately 33 months for dose expansion phase |           |

| End point values            | Dose Escalation Phase: Surufatinib 250 mg + Tislelizumab | Dose Escalation Phase: Surufatinib 300 mg + Tislelizumab | Dose Expansion Phase: Cohort A: CRC | Dose Expansion Phase: Cohort B1: Thoracic NETs |
|-----------------------------|----------------------------------------------------------|----------------------------------------------------------|-------------------------------------|------------------------------------------------|
| Subject group type          | Reporting group                                          | Reporting group                                          | Reporting group                     | Reporting group                                |
| Number of subjects analysed | 6                                                        | 5                                                        | 14                                  | 8                                              |
| Units: patients             |                                                          |                                                          |                                     |                                                |
| Treatment-Boosted ADA       | 0                                                        | 0                                                        | 2                                   | 0                                              |
| Treatment-Induced ADA       | 2                                                        | 2                                                        | 5                                   | 3                                              |

| End point values            | Dose Expansion Phase: Cohort B2: GEP NETs | Dose Expansion Phase: Cohort C: SCLC | Dose Expansion Phase: Cohort D: GC | Dose Expansion Phase: Cohort E2: UPS |
|-----------------------------|-------------------------------------------|--------------------------------------|------------------------------------|--------------------------------------|
| Subject group type          | Reporting group                           | Reporting group                      | Reporting group                    | Reporting group                      |
| Number of subjects analysed | 16                                        | 13                                   | 2                                  | 9                                    |
| Units: patients             |                                           |                                      |                                    |                                      |
| Treatment-Boosted ADA       | 0                                         | 0                                    | 0                                  | 0                                    |
| Treatment-Induced ADA       | 5                                         | 1                                    | 0                                  | 5                                    |

| End point values            | Dose Expansion Phase: Cohort F: ATC |  |  |  |
|-----------------------------|-------------------------------------|--|--|--|
| Subject group type          | Reporting group                     |  |  |  |
| Number of subjects analysed | 2                                   |  |  |  |
| Units: patients             |                                     |  |  |  |
| Treatment-Boosted ADA       | 0                                   |  |  |  |
| Treatment-Induced ADA       | 1                                   |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Dose Expansion Phase (Cohorts A and F): Overall Survival (OS)

|                 |                                                          |
|-----------------|----------------------------------------------------------|
| End point title | Dose Expansion Phase (Cohorts A and F): Overall Survival |
|-----------------|----------------------------------------------------------|

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**End point description:**

OS was defined as the time from the start of study treatment until the date of death due to any cause. The SAS included all enrolled patients who received at least 1 dose of surufatinib or tislelizumab. As pre-specified in the protocol and statistical analysis plan (SAP), OS was assessed only in Cohort A (CRC) and Cohort F (ATC) of the dose expansion phase. Here, 9999 = value was not estimable due to insufficient number of patients with events at study closure.

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

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**End point timeframe:**

From the first dose of study treatment (Day 1) up to date of death due to any cause, up to approximately 42 months

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**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: As pre-specified in the protocol and statistical analysis plan (SAP), this endpoint was analyzed only in Cohort A (CRC) and Cohort F (ATC) of the dose expansion phase.

| End point values                 | Dose Expansion Phase: Cohort A: CRC | Dose Expansion Phase: Cohort F: ATC |  |  |
|----------------------------------|-------------------------------------|-------------------------------------|--|--|
| Subject group type               | Reporting group                     | Reporting group                     |  |  |
| Number of subjects analysed      | 15                                  | 3                                   |  |  |
| Units: months                    |                                     |                                     |  |  |
| median (confidence interval 95%) | 7.1 (4.8 to 11.8)                   | 5.3 (2.8 to 9999)                   |  |  |

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**Statistical analyses**

No statistical analyses for this end point

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**Secondary: Dose Expansion Phase: Number of Patients With Treatment-Emergent Adverse Events, Treatment-Emergent Serious Adverse Events and TEAEs Leading to Treatment Discontinuation**

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|                 |                                                                                                                                                                                           |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Dose Expansion Phase: Number of Patients With Treatment-Emergent Adverse Events, Treatment-Emergent Serious Adverse Events and TEAEs Leading to Treatment Discontinuation <sup>[17]</sup> |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

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**End point description:**

An AE was any untoward medical occurrence in a clinical study patient temporally associated with the use of a study treatment in humans, whether or not considered related to the treatment. An AE was considered "serious" if, in the view of either the investigator or sponsor, it resulted in death, was life-threatening, required inpatient hospitalization or prolongation of existing hospitalization, was a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, was a congenital anomaly/birth defect or was an important medical event. TEAEs were defined as AEs that started or worsened in severity on or after the first dose of study treatment and up to 30 days after the date of last study treatment administration. The SAS included all enrolled patients who received at least 1 dose of surufatinib or tislelizumab.

---

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

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**End point timeframe:**

From the first dose of study treatment (Day 1) up to 30 days after the last dose of study treatment, approximately 33 months

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**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: Only dose expansion phase arms were analyzed for this endpoint.

| <b>End point values</b>                              | Dose Expansion<br>Phase: Cohort<br>A: CRC | Dose Expansion<br>Phase: Cohort<br>B1: Thoracic<br>NETs | Dose Expansion<br>Phase: Cohort<br>B2: GEP NETs | Dose Expansion<br>Phase: Cohort<br>C: SCLC |
|------------------------------------------------------|-------------------------------------------|---------------------------------------------------------|-------------------------------------------------|--------------------------------------------|
| Subject group type                                   | Reporting group                           | Reporting group                                         | Reporting group                                 | Reporting group                            |
| Number of subjects analysed                          | 15                                        | 10                                                      | 20                                              | 15                                         |
| Units: patients                                      |                                           |                                                         |                                                 |                                            |
| Any TEAEs                                            | 14                                        | 10                                                      | 20                                              | 15                                         |
| Any TSEAEs                                           | 9                                         | 5                                                       | 9                                               | 8                                          |
| Any TEAEs leading to surufatinib<br>discontinuation  | 3                                         | 2                                                       | 5                                               | 5                                          |
| Any TEAEs leading to tislelizumab<br>discontinuation | 6                                         | 2                                                       | 6                                               | 5                                          |

| <b>End point values</b>                              | Dose Expansion<br>Phase: Cohort<br>D: GC | Dose Expansion<br>Phase: Cohort<br>E2: UPS | Dose Expansion<br>Phase: Cohort<br>F: ATC |  |
|------------------------------------------------------|------------------------------------------|--------------------------------------------|-------------------------------------------|--|
| Subject group type                                   | Reporting group                          | Reporting group                            | Reporting group                           |  |
| Number of subjects analysed                          | 3                                        | 9                                          | 3                                         |  |
| Units: patients                                      |                                          |                                            |                                           |  |
| Any TEAEs                                            | 3                                        | 9                                          | 3                                         |  |
| Any TSEAEs                                           | 0                                        | 4                                          | 1                                         |  |
| Any TEAEs leading to surufatinib<br>discontinuation  | 0                                        | 2                                          | 0                                         |  |
| Any TEAEs leading to tislelizumab<br>discontinuation | 0                                        | 2                                          | 0                                         |  |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

AEs: From first dose(Day 1) up to 30 days after last dose of study treatment, approximately 9 months for dose escalation and 33 months for dose expansion phase. Deaths: From signing of informed consent form up to end of follow up, approximately 42 months.

Adverse event reporting additional description:

The SAS included all enrolled patients who received at least 1 dose of surufatinib or tislelizumab.

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

### Dictionary used

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

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

### Reporting groups

|                       |                                                          |
|-----------------------|----------------------------------------------------------|
| Reporting group title | Dose Escalation Phase: Surufatinib 250 mg + Tislelizumab |
|-----------------------|----------------------------------------------------------|

Reporting group description:

Patients with advanced or metastatic solid tumors of any kind who had progressed on or were intolerant of standard therapies received surufatinib 250 mg orally QD in combination with tislelizumab 200 mg IV infusion Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.

|                       |                                                          |
|-----------------------|----------------------------------------------------------|
| Reporting group title | Dose Escalation Phase: Surufatinib 300 mg + Tislelizumab |
|-----------------------|----------------------------------------------------------|

Reporting group description:

Patients with advanced or metastatic solid tumors of any kind who had progressed on or were intolerant of standard therapies received surufatinib 300 mg orally QD in combination with tislelizumab 200 mg IV infusion Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.

|                       |                                     |
|-----------------------|-------------------------------------|
| Reporting group title | Dose Expansion Phase: Cohort A: CRC |
|-----------------------|-------------------------------------|

Reporting group description:

Patients with microsatellite stable, locally advanced or metastatic CRC that was previously treated with at least 3 prior lines of therapy received surufatinib 300 mg orally QD in combination with tislelizumab 200 mg IV infusion Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.

|                       |                                                |
|-----------------------|------------------------------------------------|
| Reporting group title | Dose Expansion Phase: Cohort B1: Thoracic NETs |
|-----------------------|------------------------------------------------|

Reporting group description:

Patients with thoracic NET who had progressive, locally advanced or metastatic, low-to-intermediate grade (Grade 1 or Grade 2), well-differentiated NETs that progressed on at least 1 line of standard therapy received surufatinib 300 mg orally QD in combination with tislelizumab 200 mg IV infusion Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.

|                       |                                           |
|-----------------------|-------------------------------------------|
| Reporting group title | Dose Expansion Phase: Cohort B2: GEP NETs |
|-----------------------|-------------------------------------------|

Reporting group description:

Patients with GEP NET who had progressive, locally advanced or metastatic, low-to-intermediate grade (Grade 1 or Grade 2), well-differentiated NETs that progressed on at least 1 line of standard therapy received surufatinib 300 mg orally QD in combination with tislelizumab 200 mg IV infusion Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.

|                       |                                      |
|-----------------------|--------------------------------------|
| Reporting group title | Dose Expansion Phase: Cohort C: SCLC |
|-----------------------|--------------------------------------|

Reporting group description:

Patients with locally advanced or metastatic SCLC that was previously progressed on first-line chemotherapy received surufatinib 300 mg orally QD in combination with tislelizumab 200 mg IV infusion Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.

|                       |                                    |
|-----------------------|------------------------------------|
| Reporting group title | Dose Expansion Phase: Cohort D: GC |
|-----------------------|------------------------------------|

Reporting group description:

Patients with microsatellite stable, PD-L1  $\geq 5\%$ , locally advanced or metastatic adenocarcinoma of the stomach or gastroesophageal junction (GC), and were previously treated with at least 2 lines of standard therapy received surufatinib 300 mg orally QD in combination with tislelizumab 200 mg IV infusion Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to

follow-up, or death.

|                       |                                      |
|-----------------------|--------------------------------------|
| Reporting group title | Dose Expansion Phase: Cohort E2: UPS |
|-----------------------|--------------------------------------|

Reporting group description:

Patients with UPS who progressed on, or had discontinued due to intolerable toxicity to, at least 1 line of standard therapy or were unsuitable for standard frontline cytotoxic chemotherapy received surufatinib 300 mg orally QD in combination with tislelizumab 200 mg IV infusion Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.

|                       |                                     |
|-----------------------|-------------------------------------|
| Reporting group title | Dose Expansion Phase: Cohort F: ATC |
|-----------------------|-------------------------------------|

Reporting group description:

Patients with locally advanced or metastatic ATC and who had a BRAFV600E mutation were previously treated with 1 line of systemic therapy (not including radiation therapy) with a BRAF-targeted therapy received surufatinib 300 mg orally QD in combination with tislelizumab 200 mg IV infusion Q3W until PD, unacceptable toxicity, withdrawal of consent, new anticancer therapy, lost to follow-up, or death.

| <b>Serious adverse events</b>                                       | Dose Escalation Phase: Surufatinib 250 mg + Tislelizumab | Dose Escalation Phase: Surufatinib 300 mg + Tislelizumab | Dose Expansion Phase: Cohort A: CRC |
|---------------------------------------------------------------------|----------------------------------------------------------|----------------------------------------------------------|-------------------------------------|
| Total subjects affected by serious adverse events                   |                                                          |                                                          |                                     |
| subjects affected / exposed                                         | 5 / 6 (83.33%)                                           | 3 / 6 (50.00%)                                           | 9 / 15 (60.00%)                     |
| number of deaths (all causes)                                       | 4                                                        | 1                                                        | 14                                  |
| number of deaths resulting from adverse events                      | 2                                                        | 0                                                        | 1                                   |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                                          |                                                          |                                     |
| Malignant neoplasm progression                                      |                                                          |                                                          |                                     |
| subjects affected / exposed                                         | 1 / 6 (16.67%)                                           | 0 / 6 (0.00%)                                            | 0 / 15 (0.00%)                      |
| occurrences causally related to treatment / all                     | 0 / 1                                                    | 0 / 0                                                    | 0 / 0                               |
| deaths causally related to treatment / all                          | 0 / 1                                                    | 0 / 0                                                    | 0 / 0                               |
| Basal cell carcinoma                                                |                                                          |                                                          |                                     |
| subjects affected / exposed                                         | 0 / 6 (0.00%)                                            | 0 / 6 (0.00%)                                            | 0 / 15 (0.00%)                      |
| occurrences causally related to treatment / all                     | 0 / 0                                                    | 0 / 0                                                    | 0 / 0                               |
| deaths causally related to treatment / all                          | 0 / 0                                                    | 0 / 0                                                    | 0 / 0                               |
| Vascular disorders                                                  |                                                          |                                                          |                                     |
| Deep vein thrombosis                                                |                                                          |                                                          |                                     |
| subjects affected / exposed                                         | 0 / 6 (0.00%)                                            | 0 / 6 (0.00%)                                            | 0 / 15 (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                               |
| Haematoma                                                           |                                                          |                                                          |                                     |
| subjects affected / exposed                                         | 0 / 6 (0.00%)                                            | 0 / 6 (0.00%)                                            | 0 / 15 (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                               |
| Hypertension                                                        |                                                          |                                                          |                                     |

|                                                      |                |               |                |
|------------------------------------------------------|----------------|---------------|----------------|
| subjects affected / exposed                          | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 0 / 15 (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 |                |               |                |
| Disease progression                                  |                |               |                |
| subjects affected / exposed                          | 1 / 6 (16.67%) | 0 / 6 (0.00%) | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 1          | 0 / 0         | 0 / 1          |
| Pyrexia                                              |                |               |                |
| subjects affected / exposed                          | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 0 / 15 (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          |
| Asthenia                                             |                |               |                |
| subjects affected / exposed                          | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         | 0 / 0          |
| Chills                                               |                |               |                |
| subjects affected / exposed                          | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 0 / 15 (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          |
| Fatigue                                              |                |               |                |
| subjects affected / exposed                          | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 0 / 15 (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          |
| Gait disturbance                                     |                |               |                |
| subjects affected / exposed                          | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 0 / 15 (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      |                |               |                |
| Hypoxia                                              |                |               |                |
| subjects affected / exposed                          | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 0 / 15 (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          |

|                                                 |                |               |                |
|-------------------------------------------------|----------------|---------------|----------------|
| Acute respiratory failure                       |                |               |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 0 / 15 (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                     | 1 / 6 (16.67%) | 0 / 6 (0.00%) | 0 / 15 (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          |
| Psychiatric disorders                           |                |               |                |
| Delirium                                        |                |               |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 0 / 15 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Investigations                                  |                |               |                |
| Liver function test increased                   |                |               |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 0 / 15 (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 / 6 (0.00%)  | 0 / 6 (0.00%) | 0 / 15 (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          |
| Hand fracture                                   |                |               |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 0 / 15 (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          |
| Splenic rupture                                 |                |               |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 0 / 15 (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          |
| Subdural haematoma                              |                |               |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (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 flutter                                  |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 6 (16.67%) | 0 / 15 (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          |
| Cardiac arrest                                  |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (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          |
| Myocarditis                                     |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (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 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (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          |
| Ventricular fibrillation                        |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (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                        |                |                |                |
| Cerebrovascular accident                        |                |                |                |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 6 (0.00%)  | 0 / 15 (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          |
| Dysarthria                                      |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hypertensive encephalopathy                     |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Neuropathy peripheral                           |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (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 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (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          |
| Syncope                                         |                |                |                |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 6 (0.00%)  | 0 / 15 (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          |
| Blood and lymphatic system disorders            |                |                |                |
| Anaemia                                         |                |                |                |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 6 (0.00%)  | 0 / 15 (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          |
| Ear and labyrinth disorders                     |                |                |                |
| Vertigo                                         |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 6 (16.67%) | 0 / 15 (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          |
| Gastrointestinal disorders                      |                |                |                |
| Abdominal pain                                  |                |                |                |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 6 (0.00%)  | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Diarrhoea                                       |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

|                                                 |                |               |                 |
|-------------------------------------------------|----------------|---------------|-----------------|
| Nausea                                          |                |               |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 2 / 15 (13.33%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 2 / 2           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0           |
| Vomiting                                        |                |               |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 1 / 15 (6.67%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0           |
| Enteritis                                       |                |               |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 0 / 15 (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 haemorrhage                    |                |               |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 0 / 15 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0           |
| Intestinal obstruction                          |                |               |                 |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 6 (0.00%) | 0 / 15 (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           |
| Intestinal perforation                          |                |               |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 0 / 15 (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           |
| Large intestinal obstruction                    |                |               |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 1 / 15 (6.67%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0           |
| Obstruction gastric                             |                |               |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 1 / 15 (6.67%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0           |
| Pancreatic fistula                              |                |               |                 |

|                                                 |                |               |                |
|-------------------------------------------------|----------------|---------------|----------------|
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 0 / 15 (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 / 6 (0.00%)  | 0 / 6 (0.00%) | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Hepatobiliary disorders                         |                |               |                |
| Biliary dyskinesia                              |                |               |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 0 / 15 (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          |
| Biliary obstruction                             |                |               |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 2          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Cholecystitis acute                             |                |               |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 0 / 15 (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          |
| Hepatic failure                                 |                |               |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 0 / 15 (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 and subcutaneous tissue disorders          |                |               |                |
| Angioedema                                      |                |               |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 0 / 15 (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          |
| Hyperhidrosis                                   |                |               |                |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 6 (0.00%) | 0 / 15 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1          | 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 / 6 (0.00%)  | 0 / 6 (0.00%) | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Musculoskeletal and connective tissue disorders |                |               |                |
| Back pain                                       |                |               |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 0 / 15 (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          |
| Fistula                                         |                |               |                |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 6 (0.00%) | 0 / 15 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Pain in extremity                               |                |               |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 0 / 15 (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          |
| Rhabdomyolysis                                  |                |               |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 0 / 15 (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                     |                |               |                |
| Sepsis                                          |                |               |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 1 / 15 (6.67%) |
| 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 infection                             |                |               |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 0 / 15 (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          |
| Cellulitis                                      |                |               |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 0 / 15 (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          |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| Clostridium difficile infection                 |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 2          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Sinusitis                                       |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 6 (16.67%) | 0 / 15 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Urinary tract infection                         |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Metabolism and nutrition disorders              |                |                |                |
| Dehydration                                     |                |                |                |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 1 / 6 (16.67%) | 0 / 15 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 1 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hyponatraemia                                   |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (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          |
| Decreased appetite                              |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hyperglycaemia                                  |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (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          |
| Hyperkalaemia                                   |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (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 Expansion<br>Phase: Cohort B1:<br>Thoracic NETs | Dose Expansion<br>Phase: Cohort B2:<br>GEP NETs | Dose Expansion<br>Phase: Cohort C:<br>SCLC |
|---------------------------------------------------------------------|------------------------------------------------------|-------------------------------------------------|--------------------------------------------|
| Total subjects affected by serious adverse events                   |                                                      |                                                 |                                            |
| subjects affected / exposed                                         | 5 / 10 (50.00%)                                      | 9 / 20 (45.00%)                                 | 8 / 15 (53.33%)                            |
| number of deaths (all causes)                                       | 4                                                    | 2                                               | 8                                          |
| number of deaths resulting from adverse events                      | 1                                                    | 1                                               | 5                                          |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                                      |                                                 |                                            |
| Malignant neoplasm progression                                      |                                                      |                                                 |                                            |
| subjects affected / exposed                                         | 0 / 10 (0.00%)                                       | 0 / 20 (0.00%)                                  | 1 / 15 (6.67%)                             |
| occurrences causally related to treatment / all                     | 0 / 0                                                | 0 / 0                                           | 0 / 1                                      |
| deaths causally related to treatment / all                          | 0 / 0                                                | 0 / 0                                           | 0 / 1                                      |
| Basal cell carcinoma                                                |                                                      |                                                 |                                            |
| subjects affected / exposed                                         | 0 / 10 (0.00%)                                       | 1 / 20 (5.00%)                                  | 0 / 15 (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                                      |
| Vascular disorders                                                  |                                                      |                                                 |                                            |
| Deep vein thrombosis                                                |                                                      |                                                 |                                            |
| subjects affected / exposed                                         | 0 / 10 (0.00%)                                       | 0 / 20 (0.00%)                                  | 0 / 15 (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                                      |
| Haematoma                                                           |                                                      |                                                 |                                            |
| subjects affected / exposed                                         | 0 / 10 (0.00%)                                       | 0 / 20 (0.00%)                                  | 0 / 15 (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                                      |
| Hypertension                                                        |                                                      |                                                 |                                            |
| subjects affected / exposed                                         | 1 / 10 (10.00%)                                      | 0 / 20 (0.00%)                                  | 0 / 15 (0.00%)                             |
| occurrences causally related to treatment / all                     | 1 / 1                                                | 0 / 0                                           | 0 / 0                                      |
| deaths causally related to treatment / all                          | 0 / 0                                                | 0 / 0                                           | 0 / 0                                      |
| General disorders and administration site conditions                |                                                      |                                                 |                                            |
| Disease progression                                                 |                                                      |                                                 |                                            |
| subjects affected / exposed                                         | 0 / 10 (0.00%)                                       | 0 / 20 (0.00%)                                  | 1 / 15 (6.67%)                             |
| occurrences causally related to treatment / all                     | 0 / 0                                                | 0 / 0                                           | 0 / 1                                      |
| deaths causally related to treatment / all                          | 0 / 0                                                | 0 / 0                                           | 0 / 1                                      |
| Pyrexia                                                             |                                                      |                                                 |                                            |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 10 (0.00%) | 1 / 20 (5.00%) | 0 / 15 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 2          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Asthenia                                        |                |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 20 (0.00%) | 0 / 15 (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          |
| Chills                                          |                |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 20 (0.00%) | 0 / 15 (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          |
| Fatigue                                         |                |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 1 / 20 (5.00%) | 0 / 15 (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          |
| Gait disturbance                                |                |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 20 (0.00%) | 0 / 15 (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 |                |                |                |
| Hypoxia                                         |                |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 20 (0.00%) | 0 / 15 (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          |
| Acute respiratory failure                       |                |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 1 / 20 (5.00%) | 0 / 15 (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 / 10 (0.00%) | 0 / 20 (0.00%) | 0 / 15 (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          |
| Psychiatric disorders                           |                |                |                |

|                                                 |                 |                |                |
|-------------------------------------------------|-----------------|----------------|----------------|
| Delirium                                        |                 |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Investigations                                  |                 |                |                |
| Liver function test increased                   |                 |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 1 / 15 (6.67%) |
| 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 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (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          |
| Hand fracture                                   |                 |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (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          |
| Splenic rupture                                 |                 |                |                |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 20 (0.00%) | 0 / 15 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Subdural haematoma                              |                 |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 2          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 1          |
| Cardiac disorders                               |                 |                |                |
| Atrial flutter                                  |                 |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (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 arrest                                  |                 |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 10 (0.00%) | 1 / 20 (5.00%) | 0 / 15 (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          |
| Myocarditis                                     |                |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 1 / 20 (5.00%) | 0 / 15 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pericardial effusion                            |                |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 20 (0.00%) | 0 / 15 (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          |
| Ventricular fibrillation                        |                |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 1 / 20 (5.00%) | 0 / 15 (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          |
| Nervous system disorders                        |                |                |                |
| Cerebrovascular accident                        |                |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 20 (0.00%) | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Dysarthria                                      |                |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 20 (0.00%) | 0 / 15 (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          |
| Hypertensive encephalopathy                     |                |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 20 (0.00%) | 0 / 15 (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          |
| Neuropathy peripheral                           |                |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 20 (0.00%) | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Seizure                                         |                |                |                |

|                                                 |                 |                 |                |
|-------------------------------------------------|-----------------|-----------------|----------------|
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 20 (0.00%)  | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0          |
| Syncope                                         |                 |                 |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 20 (0.00%)  | 0 / 15 (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 / 10 (0.00%)  | 0 / 20 (0.00%)  | 0 / 15 (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          |
| Ear and labyrinth disorders                     |                 |                 |                |
| Vertigo                                         |                 |                 |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 20 (0.00%)  | 0 / 15 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0          |
| Gastrointestinal disorders                      |                 |                 |                |
| Abdominal pain                                  |                 |                 |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 1 / 20 (5.00%)  | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0          |
| Diarrhoea                                       |                 |                 |                |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 2 / 20 (10.00%) | 0 / 15 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 1 / 2           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0          |
| Nausea                                          |                 |                 |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 20 (0.00%)  | 0 / 15 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0          |
| Vomiting                                        |                 |                 |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 1 / 20 (5.00%)  | 0 / 15 (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          |

|                                                 |                 |                |                |
|-------------------------------------------------|-----------------|----------------|----------------|
| Enteritis                                       |                 |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 1 / 20 (5.00%) | 0 / 15 (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          |
| Gastrointestinal haemorrhage                    |                 |                |                |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 20 (0.00%) | 0 / 15 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Intestinal obstruction                          |                 |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Intestinal perforation                          |                 |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 1 / 1          |
| Large intestinal obstruction                    |                 |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (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          |
| Obstruction gastric                             |                 |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (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          |
| Pancreatic fistula                              |                 |                |                |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 20 (0.00%) | 0 / 15 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Small intestinal obstruction                    |                 |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (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                         |                 |                |                |

|                                                 |                 |                |                |
|-------------------------------------------------|-----------------|----------------|----------------|
| Biliary dyskinesia                              |                 |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (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          |
| Biliary obstruction                             |                 |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (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          |
| Cholecystitis acute                             |                 |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (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          |
| Hepatic failure                                 |                 |                |                |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 20 (0.00%) | 0 / 15 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 1 / 1           | 0 / 0          | 0 / 0          |
| Skin and subcutaneous tissue disorders          |                 |                |                |
| Angioedema                                      |                 |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Hyperhidrosis                                   |                 |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (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                     | 1 / 10 (10.00%) | 1 / 20 (5.00%) | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0          | 0 / 0          |
| Musculoskeletal and connective tissue disorders |                 |                |                |
| Back pain                                       |                 |                |                |

|                                                 |                 |                |                |
|-------------------------------------------------|-----------------|----------------|----------------|
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 20 (0.00%) | 0 / 15 (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          |
| Fistula                                         |                 |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Pain in extremity                               |                 |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (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          |
| Rhabdomyolysis                                  |                 |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 1 / 20 (5.00%) | 0 / 15 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Infections and infestations                     |                 |                |                |
| Sepsis                                          |                 |                |                |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 1 / 20 (5.00%) | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 1          | 0 / 2          |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0          | 0 / 1          |
| Abdominal infection                             |                 |                |                |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 20 (0.00%) | 0 / 15 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Cellulitis                                      |                 |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (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          |
| Clostridium difficile infection                 |                 |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (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          |
| Sinusitis                                       |                 |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 20 (0.00%) | 0 / 15 (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 / 10 (0.00%) | 1 / 20 (5.00%) | 0 / 15 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Metabolism and nutrition disorders              |                |                |                |
| Dehydration                                     |                |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 20 (0.00%) | 0 / 15 (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          |
| Hyponatraemia                                   |                |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 1 / 20 (5.00%) | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Decreased appetite                              |                |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 20 (0.00%) | 0 / 15 (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          |
| Hyperglycaemia                                  |                |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 1 / 20 (5.00%) | 0 / 15 (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          |
| Hyperkalaemia                                   |                |                |                |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 1 / 20 (5.00%) | 0 / 15 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

| Serious adverse events                            | Dose Expansion Phase: Cohort D: GC | Dose Expansion Phase: Cohort E2: UPS | Dose Expansion Phase: Cohort F: ATC |
|---------------------------------------------------|------------------------------------|--------------------------------------|-------------------------------------|
| Total subjects affected by serious adverse events |                                    |                                      |                                     |
| subjects affected / exposed                       | 0 / 3 (0.00%)                      | 4 / 9 (44.44%)                       | 1 / 3 (33.33%)                      |
| number of deaths (all causes)                     | 0                                  | 1                                    | 3                                   |
| number of deaths resulting from                   | 0                                  | 0                                    | 0                                   |

|                                                                     |               |                |                |
|---------------------------------------------------------------------|---------------|----------------|----------------|
| adverse events                                                      |               |                |                |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |               |                |                |
| Malignant neoplasm progression                                      |               |                |                |
| subjects affected / exposed                                         | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (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          |
| Basal cell carcinoma                                                |               |                |                |
| subjects affected / exposed                                         | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences causally related to treatment / all                     | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0         | 0 / 0          | 0 / 0          |
| Vascular disorders                                                  |               |                |                |
| Deep vein thrombosis                                                |               |                |                |
| subjects affected / exposed                                         | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 3 (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          |
| Haematoma                                                           |               |                |                |
| subjects affected / exposed                                         | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 3 (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          |
| Hypertension                                                        |               |                |                |
| subjects affected / exposed                                         | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (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                |               |                |                |
| Disease progression                                                 |               |                |                |
| subjects affected / exposed                                         | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences causally related to treatment / all                     | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0         | 0 / 0          | 0 / 0          |
| Pyrexia                                                             |               |                |                |
| subjects affected / exposed                                         | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 1 / 3 (33.33%) |
| occurrences causally related to treatment / all                     | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all                          | 0 / 0         | 0 / 0          | 0 / 0          |
| Asthenia                                                            |               |                |                |

|                                                 |               |                |                |
|-------------------------------------------------|---------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (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          |
| Chills                                          |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 1 / 3 (33.33%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Fatigue                                         |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (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          |
| Gait disturbance                                |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 1 / 3 (33.33%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Respiratory, thoracic and mediastinal disorders |               |                |                |
| Hypoxia                                         |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 1 / 3 (33.33%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Acute respiratory failure                       |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (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 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (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          |
| Psychiatric disorders                           |               |                |                |
| Delirium                                        |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 1 / 3 (33.33%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |

|                                                 |               |               |                |
|-------------------------------------------------|---------------|---------------|----------------|
| Investigations                                  |               |               |                |
| Liver function test increased                   |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 3 (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 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 3 (33.33%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Hand fracture                                   |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 3 (33.33%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Splenic rupture                                 |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 3 (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          |
| Subdural haematoma                              |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 3 (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 flutter                                  |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 3 (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 arrest                                  |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 3 (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          |
| Myocarditis                                     |               |               |                |

|                                                 |               |                |               |
|-------------------------------------------------|---------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (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 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 3 (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         |
| Ventricular fibrillation                        |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (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                        |               |                |               |
| Cerebrovascular accident                        |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (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         |
| Dysarthria                                      |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (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         |
| Hypertensive encephalopathy                     |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (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         |
| Neuropathy peripheral                           |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (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 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (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         |
| Syncope                                         |               |                |               |

|                                                 |               |                |               |
|-------------------------------------------------|---------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (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>Blood and lymphatic system disorders</b>     |               |                |               |
| Anaemia                                         |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 3 (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         |
| <b>Ear and labyrinth disorders</b>              |               |                |               |
| Vertigo                                         |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (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>Gastrointestinal disorders</b>               |               |                |               |
| Abdominal pain                                  |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Diarrhoea                                       |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Nausea                                          |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Vomiting                                        |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (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         |
| Enteritis                                       |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (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 haemorrhage                    |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Intestinal obstruction                          |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Intestinal perforation                          |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (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         |
| Large intestinal obstruction                    |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (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         |
| Obstruction gastric                             |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (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         |
| Pancreatic fistula                              |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (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 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (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                         |               |                |               |
| Biliary dyskinesia                              |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 3 (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         |
| Biliary obstruction                             |               |                |               |

|                                                 |               |                |               |
|-------------------------------------------------|---------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (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         |
| Cholecystitis acute                             |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 3 (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         |
| Hepatic failure                                 |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (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 and subcutaneous tissue disorders          |               |                |               |
| Angioedema                                      |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (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         |
| Hyperhidrosis                                   |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (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 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Musculoskeletal and connective tissue disorders |               |                |               |
| Back pain                                       |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (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         |
| Fistula                                         |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |

|                                                 |               |                |               |
|-------------------------------------------------|---------------|----------------|---------------|
| Pain in extremity                               |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 3 (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         |
| Rhabdomyolysis                                  |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (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                     |               |                |               |
| Sepsis                                          |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 3 (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 infection                             |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (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         |
| Cellulitis                                      |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 3 (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         |
| Clostridium difficile infection                 |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (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         |
| Sinusitis                                       |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (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 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Metabolism and nutrition disorders              |               |                |               |

|                                                 |               |               |               |
|-------------------------------------------------|---------------|---------------|---------------|
| Dehydration                                     |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 3 (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         |
| Hyponatraemia                                   |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 3 (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         |
| Decreased appetite                              |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 3 (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         |
| Hyperglycaemia                                  |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 3 (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         |
| Hyperkalaemia                                   |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 3 (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         |

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

| <b>Non-serious adverse events</b>                                   | Dose Escalation<br>Phase: Surufatinib<br>250 mg +<br>Tislelizumab | Dose Escalation<br>Phase: Surufatinib<br>300 mg +<br>Tislelizumab | Dose Expansion<br>Phase: Cohort A:<br>CRC |
|---------------------------------------------------------------------|-------------------------------------------------------------------|-------------------------------------------------------------------|-------------------------------------------|
| Total subjects affected by non-serious adverse events               |                                                                   |                                                                   |                                           |
| subjects affected / exposed                                         | 5 / 6 (83.33%)                                                    | 6 / 6 (100.00%)                                                   | 14 / 15 (93.33%)                          |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                                                   |                                                                   |                                           |
| Neoplasm skin                                                       |                                                                   |                                                                   |                                           |
| subjects affected / exposed                                         | 0 / 6 (0.00%)                                                     | 0 / 6 (0.00%)                                                     | 0 / 15 (0.00%)                            |
| occurrences (all)                                                   | 0                                                                 | 0                                                                 | 0                                         |
| Vascular disorders                                                  |                                                                   |                                                                   |                                           |
| Hypertension                                                        |                                                                   |                                                                   |                                           |

|                                                      |                |                |                  |
|------------------------------------------------------|----------------|----------------|------------------|
| subjects affected / exposed                          | 0 / 6 (0.00%)  | 2 / 6 (33.33%) | 10 / 15 (66.67%) |
| occurrences (all)                                    | 0              | 3              | 23               |
| Flushing                                             |                |                |                  |
| subjects affected / exposed                          | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)   |
| occurrences (all)                                    | 0              | 0              | 0                |
| Hypotension                                          |                |                |                  |
| subjects affected / exposed                          | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 2 / 15 (13.33%)  |
| occurrences (all)                                    | 0              | 0              | 3                |
| Orthostatic hypotension                              |                |                |                  |
| subjects affected / exposed                          | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)   |
| occurrences (all)                                    | 0              | 0              | 0                |
| Vasculitis                                           |                |                |                  |
| subjects affected / exposed                          | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)   |
| occurrences (all)                                    | 0              | 0              | 0                |
| General disorders and administration site conditions |                |                |                  |
| Fatigue                                              |                |                |                  |
| subjects affected / exposed                          | 3 / 6 (50.00%) | 3 / 6 (50.00%) | 6 / 15 (40.00%)  |
| occurrences (all)                                    | 3              | 5              | 9                |
| Oedema peripheral                                    |                |                |                  |
| subjects affected / exposed                          | 1 / 6 (16.67%) | 1 / 6 (16.67%) | 2 / 15 (13.33%)  |
| occurrences (all)                                    | 2              | 1              | 2                |
| Asthenia                                             |                |                |                  |
| subjects affected / exposed                          | 0 / 6 (0.00%)  | 1 / 6 (16.67%) | 3 / 15 (20.00%)  |
| occurrences (all)                                    | 0              | 1              | 3                |
| Pyrexia                                              |                |                |                  |
| subjects affected / exposed                          | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 1 / 15 (6.67%)   |
| occurrences (all)                                    | 0              | 0              | 1                |
| Non-cardiac chest pain                               |                |                |                  |
| subjects affected / exposed                          | 0 / 6 (0.00%)  | 1 / 6 (16.67%) | 1 / 15 (6.67%)   |
| occurrences (all)                                    | 0              | 1              | 1                |
| Chills                                               |                |                |                  |
| subjects affected / exposed                          | 1 / 6 (16.67%) | 1 / 6 (16.67%) | 0 / 15 (0.00%)   |
| occurrences (all)                                    | 1              | 1              | 0                |
| Localised oedema                                     |                |                |                  |

|                             |                |               |                |
|-----------------------------|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 0             | 0              |
| Malaise                     |                |               |                |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 6 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 1              | 0             | 0              |
| Gait disturbance            |                |               |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 0             | 0              |
| Pain                        |                |               |                |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 6 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 1              | 0             | 0              |
| Catheter site haematoma     |                |               |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all)           | 0              | 0             | 1              |
| Catheter site haemorrhage   |                |               |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all)           | 0              | 0             | 1              |
| Facial pain                 |                |               |                |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 6 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 1              | 0             | 0              |
| Influenza like illness      |                |               |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 0             | 0              |
| Injection site pain         |                |               |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 0             | 0              |
| Medical device site pain    |                |               |                |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 6 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 1              | 0             | 0              |
| Mucosal inflammation        |                |               |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 0             | 0              |
| Oedema                      |                |               |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all)           | 0              | 0             | 1              |
| Peripheral swelling         |                |               |                |

|                                                                                                              |                     |                     |                     |
|--------------------------------------------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)                                                             | 0 / 6 (0.00%)<br>0  | 1 / 6 (16.67%)<br>1 | 0 / 15 (0.00%)<br>0 |
| Xerosis<br>subjects affected / exposed<br>occurrences (all)                                                  | 0 / 6 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 |
| Immune system disorders<br>Seasonal allergy<br>subjects affected / exposed<br>occurrences (all)              | 0 / 6 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 |
| Hypersensitivity<br>subjects affected / exposed<br>occurrences (all)                                         | 0 / 6 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 |
| Reproductive system and breast disorders<br>Pelvic pain<br>subjects affected / exposed<br>occurrences (all)  | 0 / 6 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 |
| Gynaecomastia<br>subjects affected / exposed<br>occurrences (all)                                            | 0 / 6 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1 |
| Vaginal haemorrhage<br>subjects affected / exposed<br>occurrences (all)                                      | 0 / 6 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 |
| Respiratory, thoracic and mediastinal disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0  | 2 / 6 (33.33%)<br>2 | 0 / 15 (0.00%)<br>0 |
| Dyspnoea<br>subjects affected / exposed<br>occurrences (all)                                                 | 0 / 6 (0.00%)<br>0  | 3 / 6 (50.00%)<br>3 | 1 / 15 (6.67%)<br>1 |
| Epistaxis<br>subjects affected / exposed<br>occurrences (all)                                                | 1 / 6 (16.67%)<br>1 | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 |
| Dysphonia<br>subjects affected / exposed<br>occurrences (all)                                                | 1 / 6 (16.67%)<br>1 | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 |
| Nasal congestion                                                                                             |                     |                     |                     |

|                             |               |                |                |
|-----------------------------|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Pleural effusion            |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%)  | 1 / 15 (6.67%) |
| occurrences (all)           | 0             | 0              | 1              |
| Productive cough            |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Sinus congestion            |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 6 (16.67%) | 1 / 15 (6.67%) |
| occurrences (all)           | 0             | 1              | 1              |
| Atelectasis                 |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Hiccups                     |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Oropharyngeal pain          |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Pneumonitis                 |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Pulmonary haemorrhage       |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Rhinorrhoea                 |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Sneezing                    |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Sputum discoloured          |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Psychiatric disorders       |               |                |                |

|                                      |                |                |                 |
|--------------------------------------|----------------|----------------|-----------------|
| Confusional state                    |                |                |                 |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 1 / 6 (16.67%) | 0 / 15 (0.00%)  |
| occurrences (all)                    | 0              | 1              | 0               |
| Insomnia                             |                |                |                 |
| subjects affected / exposed          | 1 / 6 (16.67%) | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                    | 1              | 0              | 0               |
| Anxiety                              |                |                |                 |
| subjects affected / exposed          | 1 / 6 (16.67%) | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                    | 1              | 0              | 0               |
| Depression                           |                |                |                 |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                    | 0              | 0              | 1               |
| Depressed mood                       |                |                |                 |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0               |
| Irritability                         |                |                |                 |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0               |
| Panic attack                         |                |                |                 |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 1 / 6 (16.67%) | 0 / 15 (0.00%)  |
| occurrences (all)                    | 0              | 1              | 0               |
| Restlessness                         |                |                |                 |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0               |
| Product issues                       |                |                |                 |
| Device occlusion                     |                |                |                 |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                    | 0              | 0              | 1               |
| Investigations                       |                |                |                 |
| Aspartate aminotransferase increased |                |                |                 |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 1 / 6 (16.67%) | 4 / 15 (26.67%) |
| occurrences (all)                    | 0              | 1              | 7               |
| Alanine aminotransferase increased   |                |                |                 |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 1 / 6 (16.67%) | 3 / 15 (20.00%) |
| occurrences (all)                    | 0              | 1              | 3               |
| Blood creatinine increased           |                |                |                 |

|                                        |                |                |                 |
|----------------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed            | 0 / 6 (0.00%)  | 2 / 6 (33.33%) | 5 / 15 (33.33%) |
| occurrences (all)                      | 0              | 3              | 7               |
| Weight decreased                       |                |                |                 |
| subjects affected / exposed            | 1 / 6 (16.67%) | 4 / 6 (66.67%) | 4 / 15 (26.67%) |
| occurrences (all)                      | 1              | 4              | 5               |
| Blood bilirubin increased              |                |                |                 |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 1 / 6 (16.67%) | 3 / 15 (20.00%) |
| occurrences (all)                      | 0              | 1              | 5               |
| Lipase increased                       |                |                |                 |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 2 / 15 (13.33%) |
| occurrences (all)                      | 0              | 0              | 2               |
| Platelet count decreased               |                |                |                 |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 4 / 15 (26.67%) |
| occurrences (all)                      | 0              | 0              | 5               |
| Blood alkaline phosphatase increased   |                |                |                 |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 2 / 15 (13.33%) |
| occurrences (all)                      | 0              | 0              | 2               |
| Blood lactate dehydrogenase increased  |                |                |                 |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                      | 0              | 0              | 1               |
| Amylase increased                      |                |                |                 |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0               |
| Blood creatine phosphokinase increased |                |                |                 |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                      | 0              | 0              | 1               |
| Lymphocyte count decreased             |                |                |                 |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                      | 0              | 0              | 2               |
| Electrocardiogram QT prolonged         |                |                |                 |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0               |
| Neutrophil count decreased             |                |                |                 |

|                                                 |                |               |                |
|-------------------------------------------------|----------------|---------------|----------------|
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all)                               | 0              | 0             | 1              |
| Activated partial thromboplastin time prolonged |                |               |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                               | 0              | 0             | 0              |
| White blood cell count decreased                |                |               |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all)                               | 0              | 0             | 2              |
| Blood creatine increased                        |                |               |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                               | 0              | 0             | 0              |
| Ejection fraction decreased                     |                |               |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                               | 0              | 0             | 0              |
| Troponin T increased                            |                |               |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                               | 0              | 0             | 0              |
| Breath sounds abnormal                          |                |               |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                               | 0              | 0             | 0              |
| Haemoglobin decreased                           |                |               |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                               | 0              | 0             | 0              |
| Neutrophil count increased                      |                |               |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all)                               | 0              | 0             | 1              |
| White blood cell count increased                |                |               |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all)                               | 0              | 0             | 1              |
| Injury, poisoning and procedural complications  |                |               |                |
| Contusion                                       |                |               |                |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 6 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                               | 1              | 0             | 0              |
| Fall                                            |                |               |                |

|                                  |                |                |                 |
|----------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed      | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Infusion related reaction        |                |                |                 |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Incision site discharge          |                |                |                 |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                | 0              | 0              | 1               |
| Postoperative wound complication |                |                |                 |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                | 0              | 0              | 1               |
| Wound dehiscence                 |                |                |                 |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                | 0              | 0              | 2               |
| Cardiac disorders                |                |                |                 |
| Sinus tachycardia                |                |                |                 |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 2 / 6 (33.33%) | 2 / 15 (13.33%) |
| occurrences (all)                | 0              | 2              | 2               |
| Tachycardia                      |                |                |                 |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Aortic valve disease             |                |                |                 |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Atrial fibrillation              |                |                |                 |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Nervous system disorders         |                |                |                 |
| Headache                         |                |                |                 |
| subjects affected / exposed      | 2 / 6 (33.33%) | 0 / 6 (0.00%)  | 2 / 15 (13.33%) |
| occurrences (all)                | 2              | 0              | 2               |
| Dizziness                        |                |                |                 |
| subjects affected / exposed      | 1 / 6 (16.67%) | 1 / 6 (16.67%) | 0 / 15 (0.00%)  |
| occurrences (all)                | 1              | 1              | 0               |
| Dysgeusia                        |                |                |                 |

|                               |                |                |                 |
|-------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed   | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 2 / 15 (13.33%) |
| occurrences (all)             | 0              | 0              | 3               |
| Paraesthesia                  |                |                |                 |
| subjects affected / exposed   | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)             | 0              | 0              | 0               |
| Tremor                        |                |                |                 |
| subjects affected / exposed   | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)             | 0              | 0              | 0               |
| Hypoaesthesia                 |                |                |                 |
| subjects affected / exposed   | 1 / 6 (16.67%) | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)             | 1              | 0              | 0               |
| Lethargy                      |                |                |                 |
| subjects affected / exposed   | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)             | 0              | 0              | 1               |
| Neuropathy peripheral         |                |                |                 |
| subjects affected / exposed   | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)             | 0              | 0              | 0               |
| Peripheral sensory neuropathy |                |                |                 |
| subjects affected / exposed   | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)             | 0              | 0              | 0               |
| Sciatica                      |                |                |                 |
| subjects affected / exposed   | 0 / 6 (0.00%)  | 1 / 6 (16.67%) | 0 / 15 (0.00%)  |
| occurrences (all)             | 0              | 1              | 0               |
| Burning sensation             |                |                |                 |
| subjects affected / exposed   | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)             | 0              | 0              | 0               |
| Dysarthria                    |                |                |                 |
| subjects affected / exposed   | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)             | 0              | 0              | 1               |
| Metabolic encephalopathy      |                |                |                 |
| subjects affected / exposed   | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)             | 0              | 0              | 0               |
| Sinus headache                |                |                |                 |
| subjects affected / exposed   | 0 / 6 (0.00%)  | 1 / 6 (16.67%) | 0 / 15 (0.00%)  |
| occurrences (all)             | 0              | 1              | 0               |
| Somnolence                    |                |                |                 |

|                                                                             |                     |                     |                        |
|-----------------------------------------------------------------------------|---------------------|---------------------|------------------------|
| subjects affected / exposed<br>occurrences (all)                            | 0 / 6 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0    |
| Spinal cord compression<br>subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0    |
| Blood and lymphatic system disorders                                        |                     |                     |                        |
| Anaemia<br>subjects affected / exposed<br>occurrences (all)                 | 1 / 6 (16.67%)<br>2 | 1 / 6 (16.67%)<br>3 | 1 / 15 (6.67%)<br>1    |
| Coagulopathy<br>subjects affected / exposed<br>occurrences (all)            | 0 / 6 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0    |
| Thrombocytosis<br>subjects affected / exposed<br>occurrences (all)          | 0 / 6 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0    |
| Ear and labyrinth disorders                                                 |                     |                     |                        |
| Hypoacusis<br>subjects affected / exposed<br>occurrences (all)              | 0 / 6 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1    |
| Vertigo<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 6 (0.00%)<br>0  | 1 / 6 (16.67%)<br>1 | 0 / 15 (0.00%)<br>0    |
| Ear pruritus<br>subjects affected / exposed<br>occurrences (all)            | 0 / 6 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1    |
| Eye disorders                                                               |                     |                     |                        |
| Vision blurred<br>subjects affected / exposed<br>occurrences (all)          | 0 / 6 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0    |
| Vitreous floaters<br>subjects affected / exposed<br>occurrences (all)       | 0 / 6 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0    |
| Gastrointestinal disorders                                                  |                     |                     |                        |
| Nausea<br>subjects affected / exposed<br>occurrences (all)                  | 3 / 6 (50.00%)<br>3 | 3 / 6 (50.00%)<br>3 | 10 / 15 (66.67%)<br>18 |
| Diarrhoea                                                                   |                     |                     |                        |

|                                  |                |                |                 |
|----------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed      | 1 / 6 (16.67%) | 3 / 6 (50.00%) | 6 / 15 (40.00%) |
| occurrences (all)                | 1              | 4              | 14              |
| Vomiting                         |                |                |                 |
| subjects affected / exposed      | 1 / 6 (16.67%) | 1 / 6 (16.67%) | 7 / 15 (46.67%) |
| occurrences (all)                | 1              | 1              | 13              |
| Abdominal pain                   |                |                |                 |
| subjects affected / exposed      | 2 / 6 (33.33%) | 0 / 6 (0.00%)  | 3 / 15 (20.00%) |
| occurrences (all)                | 3              | 0              | 4               |
| Constipation                     |                |                |                 |
| subjects affected / exposed      | 1 / 6 (16.67%) | 2 / 6 (33.33%) | 2 / 15 (13.33%) |
| occurrences (all)                | 1              | 2              | 4               |
| Flatulence                       |                |                |                 |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 2 / 15 (13.33%) |
| occurrences (all)                | 0              | 0              | 2               |
| Abdominal distension             |                |                |                 |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                | 0              | 0              | 1               |
| Dry mouth                        |                |                |                 |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Stomatitis                       |                |                |                 |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 3 / 15 (20.00%) |
| occurrences (all)                | 0              | 0              | 4               |
| Abdominal pain upper             |                |                |                 |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                | 0              | 0              | 2               |
| Gastrooesophageal reflux disease |                |                |                 |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                | 0              | 0              | 1               |
| Dysphagia                        |                |                |                 |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Haematochezia                    |                |                |                 |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                | 0              | 0              | 1               |
| Ascites                          |                |                |                 |

|                               |               |               |                |
|-------------------------------|---------------|---------------|----------------|
| subjects affected / exposed   | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all)             | 0             | 0             | 1              |
| Dyspepsia                     |               |               |                |
| subjects affected / exposed   | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)             | 0             | 0             | 0              |
| Gastrointestinal disorder     |               |               |                |
| subjects affected / exposed   | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)             | 0             | 0             | 0              |
| Gingival bleeding             |               |               |                |
| subjects affected / exposed   | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)             | 0             | 0             | 0              |
| Ileus                         |               |               |                |
| subjects affected / exposed   | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)             | 0             | 0             | 0              |
| Immune-mediated enterocolitis |               |               |                |
| subjects affected / exposed   | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)             | 0             | 0             | 0              |
| Large intestinal obstruction  |               |               |                |
| subjects affected / exposed   | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all)             | 0             | 0             | 2              |
| Mouth haemorrhage             |               |               |                |
| subjects affected / exposed   | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)             | 0             | 0             | 0              |
| Odynophagia                   |               |               |                |
| subjects affected / exposed   | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)             | 0             | 0             | 0              |
| Oral pain                     |               |               |                |
| subjects affected / exposed   | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all)             | 0             | 0             | 1              |
| Pancreatitis                  |               |               |                |
| subjects affected / exposed   | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)             | 0             | 0             | 0              |
| Proctalgia                    |               |               |                |
| subjects affected / exposed   | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)             | 0             | 0             | 0              |
| Rectal haemorrhage            |               |               |                |

|                                                                                                                   |                    |                     |                      |
|-------------------------------------------------------------------------------------------------------------------|--------------------|---------------------|----------------------|
| subjects affected / exposed<br>occurrences (all)                                                                  | 0 / 6 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Small intestinal obstruction<br>subjects affected / exposed<br>occurrences (all)                                  | 0 / 6 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  |
| Hepatobiliary disorders<br>Immune-mediated hepatitis<br>subjects affected / exposed<br>occurrences (all)          | 0 / 6 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  |
| Biliary obstruction<br>subjects affected / exposed<br>occurrences (all)                                           | 0 / 6 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  |
| Hepatic artery thrombosis<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 6 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Hepatic cirrhosis<br>subjects affected / exposed<br>occurrences (all)                                             | 0 / 6 (0.00%)<br>0 | 1 / 6 (16.67%)<br>1 | 0 / 15 (0.00%)<br>0  |
| Skin and subcutaneous tissue disorders<br>Rash maculo-papular<br>subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  |
| Pruritus<br>subjects affected / exposed<br>occurrences (all)                                                      | 0 / 6 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  | 1 / 15 (6.67%)<br>2  |
| Rash<br>subjects affected / exposed<br>occurrences (all)                                                          | 0 / 6 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  | 2 / 15 (13.33%)<br>2 |
| Alopecia<br>subjects affected / exposed<br>occurrences (all)                                                      | 0 / 6 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  |
| Dry skin<br>subjects affected / exposed<br>occurrences (all)                                                      | 0 / 6 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Decubitus ulcer                                                                                                   |                    |                     |                      |

|                                             |                |                |                 |
|---------------------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed                 | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 2 / 15 (13.33%) |
| occurrences (all)                           | 0              | 0              | 2               |
| Palmar-plantar erythrodysaesthesia syndrome |                |                |                 |
| subjects affected / exposed                 | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                           | 0              | 0              | 0               |
| Cold sweat                                  |                |                |                 |
| subjects affected / exposed                 | 1 / 6 (16.67%) | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                           | 1              | 0              | 0               |
| Dermatitis acneiform                        |                |                |                 |
| subjects affected / exposed                 | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                           | 0              | 0              | 1               |
| Hyperhidrosis                               |                |                |                 |
| subjects affected / exposed                 | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                           | 0              | 0              | 0               |
| Immune-mediated dermatitis                  |                |                |                 |
| subjects affected / exposed                 | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                           | 0              | 0              | 0               |
| Night sweats                                |                |                |                 |
| subjects affected / exposed                 | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                           | 0              | 0              | 0               |
| Psoriasis                                   |                |                |                 |
| subjects affected / exposed                 | 0 / 6 (0.00%)  | 1 / 6 (16.67%) | 0 / 15 (0.00%)  |
| occurrences (all)                           | 0              | 1              | 0               |
| Skin lesion                                 |                |                |                 |
| subjects affected / exposed                 | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                           | 0              | 0              | 0               |
| Renal and urinary disorders                 |                |                |                 |
| Proteinuria                                 |                |                |                 |
| subjects affected / exposed                 | 0 / 6 (0.00%)  | 2 / 6 (33.33%) | 5 / 15 (33.33%) |
| occurrences (all)                           | 0              | 6              | 13              |
| Haematuria                                  |                |                |                 |
| subjects affected / exposed                 | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                           | 0              | 0              | 1               |
| Urinary retention                           |                |                |                 |

|                             |               |                |                |
|-----------------------------|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Acute kidney injury         |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 6 (16.67%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0             | 1              | 0              |
| Chronic kidney disease      |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%)  | 1 / 15 (6.67%) |
| occurrences (all)           | 0             | 0              | 2              |
| Dysuria                     |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Hydronephrosis              |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%)  | 1 / 15 (6.67%) |
| occurrences (all)           | 0             | 0              | 1              |
| Leukocyturia                |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Micturition disorder        |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Nephrolithiasis             |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Pollakiuria                 |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%)  | 1 / 15 (6.67%) |
| occurrences (all)           | 0             | 0              | 1              |
| Renal pain                  |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Urinary tract pain          |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Urine flow decreased        |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Endocrine disorders         |               |                |                |

|                                                 |                |                |                 |
|-------------------------------------------------|----------------|----------------|-----------------|
| Hypothyroidism                                  |                |                |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 6 (16.67%) | 2 / 15 (13.33%) |
| occurrences (all)                               | 0              | 1              | 2               |
| Inappropriate antidiuretic hormone secretion    |                |                |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0               |
| Musculoskeletal and connective tissue disorders |                |                |                 |
| Arthralgia                                      |                |                |                 |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 1 / 6 (16.67%) | 1 / 15 (6.67%)  |
| occurrences (all)                               | 1              | 1              | 1               |
| Back pain                                       |                |                |                 |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 1 / 6 (16.67%) | 4 / 15 (26.67%) |
| occurrences (all)                               | 1              | 1              | 4               |
| Pain in extremity                               |                |                |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0               |
| Myalgia                                         |                |                |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 6 (16.67%) | 0 / 15 (0.00%)  |
| occurrences (all)                               | 0              | 1              | 0               |
| Muscular weakness                               |                |                |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0               |
| Flank pain                                      |                |                |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0               |
| Neck pain                                       |                |                |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 6 (16.67%) | 0 / 15 (0.00%)  |
| occurrences (all)                               | 0              | 1              | 0               |
| Muscle spasms                                   |                |                |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0               |
| Musculoskeletal chest pain                      |                |                |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 6 (16.67%) | 0 / 15 (0.00%)  |
| occurrences (all)                               | 0              | 1              | 0               |
| Bursitis                                        |                |                |                 |

|                                   |                |                |                 |
|-----------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed       | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                 | 0              | 0              | 0               |
| Muscle atrophy                    |                |                |                 |
| subjects affected / exposed       | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                 | 0              | 0              | 1               |
| Rheumatoid arthritis              |                |                |                 |
| subjects affected / exposed       | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                 | 0              | 0              | 0               |
| Infections and infestations       |                |                |                 |
| COVID-19                          |                |                |                 |
| subjects affected / exposed       | 0 / 6 (0.00%)  | 1 / 6 (16.67%) | 0 / 15 (0.00%)  |
| occurrences (all)                 | 0              | 1              | 0               |
| Urinary tract infection           |                |                |                 |
| subjects affected / exposed       | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 4 / 15 (26.67%) |
| occurrences (all)                 | 0              | 0              | 6               |
| Pneumonia                         |                |                |                 |
| subjects affected / exposed       | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                 | 0              | 0              | 0               |
| Upper respiratory tract infection |                |                |                 |
| subjects affected / exposed       | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                 | 0              | 0              | 0               |
| Clostridium difficile infection   |                |                |                 |
| subjects affected / exposed       | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 2 / 15 (13.33%) |
| occurrences (all)                 | 0              | 0              | 2               |
| Sinusitis                         |                |                |                 |
| subjects affected / exposed       | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                 | 0              | 0              | 0               |
| Eye infection                     |                |                |                 |
| subjects affected / exposed       | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                 | 0              | 0              | 0               |
| Abscess                           |                |                |                 |
| subjects affected / exposed       | 1 / 6 (16.67%) | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                 | 1              | 0              | 0               |
| Bacteriuria                       |                |                |                 |
| subjects affected / exposed       | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                 | 0              | 0              | 0               |

|                                  |               |               |                |
|----------------------------------|---------------|---------------|----------------|
| Bronchitis                       |               |               |                |
| subjects affected / exposed      | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                | 0             | 0             | 0              |
| Cellulitis                       |               |               |                |
| subjects affected / exposed      | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                | 0             | 0             | 0              |
| Conjunctivitis                   |               |               |                |
| subjects affected / exposed      | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                | 0             | 0             | 0              |
| Cystitis                         |               |               |                |
| subjects affected / exposed      | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                | 0             | 0             | 0              |
| Folliculitis                     |               |               |                |
| subjects affected / exposed      | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                | 0             | 0             | 0              |
| Gastrointestinal viral infection |               |               |                |
| subjects affected / exposed      | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                | 0             | 0             | 0              |
| Herpes simplex                   |               |               |                |
| subjects affected / exposed      | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                | 0             | 0             | 0              |
| Kidney infection                 |               |               |                |
| subjects affected / exposed      | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                | 0             | 0             | 0              |
| Nasopharyngitis                  |               |               |                |
| subjects affected / exposed      | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                | 0             | 0             | 0              |
| Pneumonia aspiration             |               |               |                |
| subjects affected / exposed      | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                | 0             | 0             | 0              |
| Rash pustular                    |               |               |                |
| subjects affected / exposed      | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                | 0             | 0             | 0              |
| Respiratory tract infection      |               |               |                |
| subjects affected / exposed      | 0 / 6 (0.00%) | 0 / 6 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                | 0             | 0             | 0              |

|                                    |                |                |                 |
|------------------------------------|----------------|----------------|-----------------|
| Sepsis                             |                |                |                 |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                  | 0              | 0              | 0               |
| Skin infection                     |                |                |                 |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                  | 0              | 0              | 0               |
| Metabolism and nutrition disorders |                |                |                 |
| Decreased appetite                 |                |                |                 |
| subjects affected / exposed        | 1 / 6 (16.67%) | 3 / 6 (50.00%) | 9 / 15 (60.00%) |
| occurrences (all)                  | 1              | 3              | 9               |
| Hypokalaemia                       |                |                |                 |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 5 / 15 (33.33%) |
| occurrences (all)                  | 0              | 0              | 8               |
| Hyponatraemia                      |                |                |                 |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                  | 0              | 0              | 1               |
| Hyperuricaemia                     |                |                |                 |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 1 / 6 (16.67%) | 4 / 15 (26.67%) |
| occurrences (all)                  | 0              | 1              | 4               |
| Hypomagnesaemia                    |                |                |                 |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 4 / 15 (26.67%) |
| occurrences (all)                  | 0              | 0              | 4               |
| Dehydration                        |                |                |                 |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 1 / 6 (16.67%) | 2 / 15 (13.33%) |
| occurrences (all)                  | 0              | 1              | 4               |
| Hyperglycaemia                     |                |                |                 |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 3 / 15 (20.00%) |
| occurrences (all)                  | 0              | 0              | 3               |
| Hypoalbuminaemia                   |                |                |                 |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 6 (0.00%)  | 2 / 15 (13.33%) |
| occurrences (all)                  | 0              | 0              | 2               |
| Hyperkalaemia                      |                |                |                 |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 1 / 6 (16.67%) | 1 / 15 (6.67%)  |
| occurrences (all)                  | 0              | 1              | 1               |
| Hyperphosphataemia                 |                |                |                 |

|                             |               |                |                 |
|-----------------------------|---------------|----------------|-----------------|
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 6 (16.67%) | 0 / 15 (0.00%)  |
| occurrences (all)           | 0             | 1              | 0               |
| Hypoglycaemia               |               |                |                 |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0               |
| Hypophosphataemia           |               |                |                 |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0               |
| Hypercalcaemia              |               |                |                 |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)           | 0             | 0              | 1               |
| Hypocalcaemia               |               |                |                 |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%)  | 2 / 15 (13.33%) |
| occurrences (all)           | 0             | 0              | 2               |
| Food intolerance            |               |                |                 |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0               |
| Hypertriglyceridaemia       |               |                |                 |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0               |

| <b>Non-serious adverse events</b>                                   | Dose Expansion<br>Phase: Cohort B1:<br>Thoracic NETs | Dose Expansion<br>Phase: Cohort B2:<br>GEP NETs | Dose Expansion<br>Phase: Cohort C:<br>SCLC |
|---------------------------------------------------------------------|------------------------------------------------------|-------------------------------------------------|--------------------------------------------|
| Total subjects affected by non-serious adverse events               |                                                      |                                                 |                                            |
| subjects affected / exposed                                         | 10 / 10 (100.00%)                                    | 20 / 20 (100.00%)                               | 15 / 15 (100.00%)                          |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                                      |                                                 |                                            |
| Neoplasm skin                                                       |                                                      |                                                 |                                            |
| subjects affected / exposed                                         | 0 / 10 (0.00%)                                       | 0 / 20 (0.00%)                                  | 0 / 15 (0.00%)                             |
| occurrences (all)                                                   | 0                                                    | 0                                               | 0                                          |
| Vascular disorders                                                  |                                                      |                                                 |                                            |
| Hypertension                                                        |                                                      |                                                 |                                            |
| subjects affected / exposed                                         | 3 / 10 (30.00%)                                      | 9 / 20 (45.00%)                                 | 1 / 15 (6.67%)                             |
| occurrences (all)                                                   | 7                                                    | 37                                              | 1                                          |
| Flushing                                                            |                                                      |                                                 |                                            |
| subjects affected / exposed                                         | 2 / 10 (20.00%)                                      | 2 / 20 (10.00%)                                 | 0 / 15 (0.00%)                             |
| occurrences (all)                                                   | 2                                                    | 3                                               | 0                                          |
| Hypotension                                                         |                                                      |                                                 |                                            |

|                                                      |                 |                  |                 |
|------------------------------------------------------|-----------------|------------------|-----------------|
| subjects affected / exposed                          | 0 / 10 (0.00%)  | 3 / 20 (15.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                                    | 0               | 3                | 0               |
| Orthostatic hypotension                              |                 |                  |                 |
| subjects affected / exposed                          | 0 / 10 (0.00%)  | 0 / 20 (0.00%)   | 1 / 15 (6.67%)  |
| occurrences (all)                                    | 0               | 0                | 1               |
| Vasculitis                                           |                 |                  |                 |
| subjects affected / exposed                          | 1 / 10 (10.00%) | 0 / 20 (0.00%)   | 0 / 15 (0.00%)  |
| occurrences (all)                                    | 1               | 0                | 0               |
| General disorders and administration site conditions |                 |                  |                 |
| Fatigue                                              |                 |                  |                 |
| subjects affected / exposed                          | 5 / 10 (50.00%) | 11 / 20 (55.00%) | 7 / 15 (46.67%) |
| occurrences (all)                                    | 11              | 14               | 8               |
| Oedema peripheral                                    |                 |                  |                 |
| subjects affected / exposed                          | 1 / 10 (10.00%) | 7 / 20 (35.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                                    | 2               | 12               | 0               |
| Asthenia                                             |                 |                  |                 |
| subjects affected / exposed                          | 0 / 10 (0.00%)  | 1 / 20 (5.00%)   | 2 / 15 (13.33%) |
| occurrences (all)                                    | 0               | 1                | 2               |
| Pyrexia                                              |                 |                  |                 |
| subjects affected / exposed                          | 2 / 10 (20.00%) | 3 / 20 (15.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                                    | 2               | 3                | 0               |
| Non-cardiac chest pain                               |                 |                  |                 |
| subjects affected / exposed                          | 1 / 10 (10.00%) | 1 / 20 (5.00%)   | 2 / 15 (13.33%) |
| occurrences (all)                                    | 1               | 2                | 2               |
| Chills                                               |                 |                  |                 |
| subjects affected / exposed                          | 1 / 10 (10.00%) | 3 / 20 (15.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                                    | 1               | 3                | 0               |
| Localised oedema                                     |                 |                  |                 |
| subjects affected / exposed                          | 1 / 10 (10.00%) | 0 / 20 (0.00%)   | 0 / 15 (0.00%)  |
| occurrences (all)                                    | 1               | 0                | 0               |
| Malaise                                              |                 |                  |                 |
| subjects affected / exposed                          | 1 / 10 (10.00%) | 1 / 20 (5.00%)   | 0 / 15 (0.00%)  |
| occurrences (all)                                    | 1               | 1                | 0               |
| Gait disturbance                                     |                 |                  |                 |

|                             |                 |                |                |
|-----------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 10 (0.00%)  | 1 / 20 (5.00%) | 1 / 15 (6.67%) |
| occurrences (all)           | 0               | 1              | 1              |
| Pain                        |                 |                |                |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all)           | 0               | 0              | 1              |
| Catheter site haematoma     |                 |                |                |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0               | 0              | 0              |
| Catheter site haemorrhage   |                 |                |                |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0               | 0              | 0              |
| Facial pain                 |                 |                |                |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0               | 0              | 0              |
| Influenza like illness      |                 |                |                |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 20 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 1               | 0              | 0              |
| Injection site pain         |                 |                |                |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0               | 0              | 0              |
| Medical device site pain    |                 |                |                |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0               | 0              | 0              |
| Mucosal inflammation        |                 |                |                |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0               | 0              | 0              |
| Oedema                      |                 |                |                |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0               | 0              | 0              |
| Peripheral swelling         |                 |                |                |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0               | 0              | 0              |
| Xerosis                     |                 |                |                |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0               | 0              | 0              |
| Immune system disorders     |                 |                |                |

|                                                                         |                      |                      |                      |
|-------------------------------------------------------------------------|----------------------|----------------------|----------------------|
| Seasonal allergy<br>subjects affected / exposed<br>occurrences (all)    | 0 / 10 (0.00%)<br>0  | 2 / 20 (10.00%)<br>2 | 0 / 15 (0.00%)<br>0  |
| Hypersensitivity<br>subjects affected / exposed<br>occurrences (all)    | 1 / 10 (10.00%)<br>1 | 0 / 20 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Reproductive system and breast disorders                                |                      |                      |                      |
| Pelvic pain<br>subjects affected / exposed<br>occurrences (all)         | 1 / 10 (10.00%)<br>1 | 1 / 20 (5.00%)<br>1  | 0 / 15 (0.00%)<br>0  |
| Gynaecomastia<br>subjects affected / exposed<br>occurrences (all)       | 0 / 10 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Vaginal haemorrhage<br>subjects affected / exposed<br>occurrences (all) | 1 / 10 (10.00%)<br>2 | 0 / 20 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Respiratory, thoracic and mediastinal disorders                         |                      |                      |                      |
| Cough<br>subjects affected / exposed<br>occurrences (all)               | 3 / 10 (30.00%)<br>3 | 5 / 20 (25.00%)<br>7 | 3 / 15 (20.00%)<br>3 |
| Dyspnoea<br>subjects affected / exposed<br>occurrences (all)            | 3 / 10 (30.00%)<br>4 | 3 / 20 (15.00%)<br>3 | 2 / 15 (13.33%)<br>2 |
| Epistaxis<br>subjects affected / exposed<br>occurrences (all)           | 1 / 10 (10.00%)<br>1 | 2 / 20 (10.00%)<br>3 | 0 / 15 (0.00%)<br>0  |
| Dysphonia<br>subjects affected / exposed<br>occurrences (all)           | 1 / 10 (10.00%)<br>1 | 2 / 20 (10.00%)<br>2 | 0 / 15 (0.00%)<br>0  |
| Nasal congestion<br>subjects affected / exposed<br>occurrences (all)    | 2 / 10 (20.00%)<br>2 | 1 / 20 (5.00%)<br>1  | 0 / 15 (0.00%)<br>0  |
| Pleural effusion<br>subjects affected / exposed<br>occurrences (all)    | 0 / 10 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Productive cough                                                        |                      |                      |                      |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 10 (10.00%) | 1 / 20 (5.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)           | 2               | 2               | 0               |
| Sinus congestion            |                 |                 |                 |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 20 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Atelectasis                 |                 |                 |                 |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 20 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)           | 1               | 0               | 0               |
| Hiccups                     |                 |                 |                 |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 20 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Oropharyngeal pain          |                 |                 |                 |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 20 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)           | 1               | 0               | 0               |
| Pneumonitis                 |                 |                 |                 |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 20 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Pulmonary haemorrhage       |                 |                 |                 |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 20 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)           | 0               | 0               | 1               |
| Rhinorrhoea                 |                 |                 |                 |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 20 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)           | 1               | 0               | 0               |
| Sneezing                    |                 |                 |                 |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 20 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)           | 0               | 0               | 1               |
| Sputum discoloured          |                 |                 |                 |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 20 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Psychiatric disorders       |                 |                 |                 |
| Confusional state           |                 |                 |                 |
| subjects affected / exposed | 2 / 10 (20.00%) | 2 / 20 (10.00%) | 3 / 15 (20.00%) |
| occurrences (all)           | 2               | 2               | 5               |
| Insomnia                    |                 |                 |                 |
| subjects affected / exposed | 1 / 10 (10.00%) | 1 / 20 (5.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)           | 2               | 1               | 0               |

|                                      |                 |                  |                |
|--------------------------------------|-----------------|------------------|----------------|
| Anxiety                              |                 |                  |                |
| subjects affected / exposed          | 0 / 10 (0.00%)  | 0 / 20 (0.00%)   | 0 / 15 (0.00%) |
| occurrences (all)                    | 0               | 0                | 0              |
| Depression                           |                 |                  |                |
| subjects affected / exposed          | 0 / 10 (0.00%)  | 0 / 20 (0.00%)   | 1 / 15 (6.67%) |
| occurrences (all)                    | 0               | 0                | 1              |
| Depressed mood                       |                 |                  |                |
| subjects affected / exposed          | 0 / 10 (0.00%)  | 0 / 20 (0.00%)   | 0 / 15 (0.00%) |
| occurrences (all)                    | 0               | 0                | 0              |
| Irritability                         |                 |                  |                |
| subjects affected / exposed          | 1 / 10 (10.00%) | 0 / 20 (0.00%)   | 0 / 15 (0.00%) |
| occurrences (all)                    | 1               | 0                | 0              |
| Panic attack                         |                 |                  |                |
| subjects affected / exposed          | 0 / 10 (0.00%)  | 0 / 20 (0.00%)   | 0 / 15 (0.00%) |
| occurrences (all)                    | 0               | 0                | 0              |
| Restlessness                         |                 |                  |                |
| subjects affected / exposed          | 0 / 10 (0.00%)  | 0 / 20 (0.00%)   | 0 / 15 (0.00%) |
| occurrences (all)                    | 0               | 0                | 0              |
| Product issues                       |                 |                  |                |
| Device occlusion                     |                 |                  |                |
| subjects affected / exposed          | 0 / 10 (0.00%)  | 0 / 20 (0.00%)   | 0 / 15 (0.00%) |
| occurrences (all)                    | 0               | 0                | 0              |
| Investigations                       |                 |                  |                |
| Aspartate aminotransferase increased |                 |                  |                |
| subjects affected / exposed          | 3 / 10 (30.00%) | 13 / 20 (65.00%) | 1 / 15 (6.67%) |
| occurrences (all)                    | 11              | 37               | 3              |
| Alanine aminotransferase increased   |                 |                  |                |
| subjects affected / exposed          | 2 / 10 (20.00%) | 11 / 20 (55.00%) | 1 / 15 (6.67%) |
| occurrences (all)                    | 9               | 26               | 2              |
| Blood creatinine increased           |                 |                  |                |
| subjects affected / exposed          | 2 / 10 (20.00%) | 7 / 20 (35.00%)  | 1 / 15 (6.67%) |
| occurrences (all)                    | 2               | 24               | 1              |
| Weight decreased                     |                 |                  |                |
| subjects affected / exposed          | 2 / 10 (20.00%) | 3 / 20 (15.00%)  | 1 / 15 (6.67%) |
| occurrences (all)                    | 7               | 3                | 1              |
| Blood bilirubin increased            |                 |                  |                |

|                                                 |                 |                 |                |
|-------------------------------------------------|-----------------|-----------------|----------------|
| subjects affected / exposed                     | 2 / 10 (20.00%) | 6 / 20 (30.00%) | 1 / 15 (6.67%) |
| occurrences (all)                               | 5               | 12              | 3              |
| Lipase increased                                |                 |                 |                |
| subjects affected / exposed                     | 2 / 10 (20.00%) | 5 / 20 (25.00%) | 1 / 15 (6.67%) |
| occurrences (all)                               | 6               | 16              | 2              |
| Platelet count decreased                        |                 |                 |                |
| subjects affected / exposed                     | 4 / 10 (40.00%) | 4 / 20 (20.00%) | 1 / 15 (6.67%) |
| occurrences (all)                               | 4               | 9               | 1              |
| Blood alkaline phosphatase increased            |                 |                 |                |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 5 / 20 (25.00%) | 0 / 15 (0.00%) |
| occurrences (all)                               | 1               | 9               | 0              |
| Blood lactate dehydrogenase increased           |                 |                 |                |
| subjects affected / exposed                     | 3 / 10 (30.00%) | 4 / 20 (20.00%) | 0 / 15 (0.00%) |
| occurrences (all)                               | 7               | 6               | 0              |
| Amylase increased                               |                 |                 |                |
| subjects affected / exposed                     | 2 / 10 (20.00%) | 3 / 20 (15.00%) | 1 / 15 (6.67%) |
| occurrences (all)                               | 14              | 4               | 1              |
| Blood creatine phosphokinase increased          |                 |                 |                |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 5 / 20 (25.00%) | 0 / 15 (0.00%) |
| occurrences (all)                               | 1               | 7               | 0              |
| Lymphocyte count decreased                      |                 |                 |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 4 / 20 (20.00%) | 0 / 15 (0.00%) |
| occurrences (all)                               | 0               | 10              | 0              |
| Electrocardiogram QT prolonged                  |                 |                 |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 4 / 20 (20.00%) | 0 / 15 (0.00%) |
| occurrences (all)                               | 0               | 6               | 0              |
| Neutrophil count decreased                      |                 |                 |                |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 2 / 20 (10.00%) | 0 / 15 (0.00%) |
| occurrences (all)                               | 1               | 6               | 0              |
| Activated partial thromboplastin time prolonged |                 |                 |                |
| subjects affected / exposed                     | 2 / 10 (20.00%) | 1 / 20 (5.00%)  | 0 / 15 (0.00%) |
| occurrences (all)                               | 3               | 8               | 0              |
| White blood cell count decreased                |                 |                 |                |

|                                                |                |                 |                |
|------------------------------------------------|----------------|-----------------|----------------|
| subjects affected / exposed                    | 0 / 10 (0.00%) | 2 / 20 (10.00%) | 0 / 15 (0.00%) |
| occurrences (all)                              | 0              | 9               | 0              |
| Blood creatine increased                       |                |                 |                |
| subjects affected / exposed                    | 0 / 10 (0.00%) | 2 / 20 (10.00%) | 0 / 15 (0.00%) |
| occurrences (all)                              | 0              | 3               | 0              |
| Ejection fraction decreased                    |                |                 |                |
| subjects affected / exposed                    | 0 / 10 (0.00%) | 0 / 20 (0.00%)  | 1 / 15 (6.67%) |
| occurrences (all)                              | 0              | 0               | 1              |
| Troponin T increased                           |                |                 |                |
| subjects affected / exposed                    | 0 / 10 (0.00%) | 2 / 20 (10.00%) | 0 / 15 (0.00%) |
| occurrences (all)                              | 0              | 2               | 0              |
| Breath sounds abnormal                         |                |                 |                |
| subjects affected / exposed                    | 0 / 10 (0.00%) | 0 / 20 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)                              | 0              | 0               | 0              |
| Haemoglobin decreased                          |                |                 |                |
| subjects affected / exposed                    | 0 / 10 (0.00%) | 0 / 20 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)                              | 0              | 0               | 0              |
| Neutrophil count increased                     |                |                 |                |
| subjects affected / exposed                    | 0 / 10 (0.00%) | 0 / 20 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)                              | 0              | 0               | 0              |
| White blood cell count increased               |                |                 |                |
| subjects affected / exposed                    | 0 / 10 (0.00%) | 0 / 20 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)                              | 0              | 0               | 0              |
| Injury, poisoning and procedural complications |                |                 |                |
| Contusion                                      |                |                 |                |
| subjects affected / exposed                    | 0 / 10 (0.00%) | 1 / 20 (5.00%)  | 1 / 15 (6.67%) |
| occurrences (all)                              | 0              | 1               | 1              |
| Fall                                           |                |                 |                |
| subjects affected / exposed                    | 0 / 10 (0.00%) | 2 / 20 (10.00%) | 0 / 15 (0.00%) |
| occurrences (all)                              | 0              | 3               | 0              |
| Infusion related reaction                      |                |                 |                |
| subjects affected / exposed                    | 0 / 10 (0.00%) | 1 / 20 (5.00%)  | 0 / 15 (0.00%) |
| occurrences (all)                              | 0              | 1               | 0              |
| Incision site discharge                        |                |                 |                |

|                                  |                 |                 |                 |
|----------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed      | 0 / 10 (0.00%)  | 0 / 20 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                | 0               | 0               | 0               |
| Postoperative wound complication |                 |                 |                 |
| subjects affected / exposed      | 0 / 10 (0.00%)  | 0 / 20 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                | 0               | 0               | 0               |
| Wound dehiscence                 |                 |                 |                 |
| subjects affected / exposed      | 0 / 10 (0.00%)  | 0 / 20 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                | 0               | 0               | 0               |
| Cardiac disorders                |                 |                 |                 |
| Sinus tachycardia                |                 |                 |                 |
| subjects affected / exposed      | 0 / 10 (0.00%)  | 0 / 20 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                | 0               | 0               | 0               |
| Tachycardia                      |                 |                 |                 |
| subjects affected / exposed      | 0 / 10 (0.00%)  | 2 / 20 (10.00%) | 0 / 15 (0.00%)  |
| occurrences (all)                | 0               | 3               | 0               |
| Aortic valve disease             |                 |                 |                 |
| subjects affected / exposed      | 0 / 10 (0.00%)  | 0 / 20 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                | 0               | 0               | 0               |
| Atrial fibrillation              |                 |                 |                 |
| subjects affected / exposed      | 1 / 10 (10.00%) | 0 / 20 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                | 1               | 0               | 0               |
| Nervous system disorders         |                 |                 |                 |
| Headache                         |                 |                 |                 |
| subjects affected / exposed      | 2 / 10 (20.00%) | 6 / 20 (30.00%) | 4 / 15 (26.67%) |
| occurrences (all)                | 2               | 7               | 4               |
| Dizziness                        |                 |                 |                 |
| subjects affected / exposed      | 0 / 10 (0.00%)  | 6 / 20 (30.00%) | 2 / 15 (13.33%) |
| occurrences (all)                | 0               | 8               | 2               |
| Dysgeusia                        |                 |                 |                 |
| subjects affected / exposed      | 0 / 10 (0.00%)  | 0 / 20 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                | 0               | 0               | 1               |
| Paraesthesia                     |                 |                 |                 |
| subjects affected / exposed      | 0 / 10 (0.00%)  | 1 / 20 (5.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                | 0               | 1               | 1               |
| Tremor                           |                 |                 |                 |

|                                      |                 |                |                 |
|--------------------------------------|-----------------|----------------|-----------------|
| subjects affected / exposed          | 1 / 10 (10.00%) | 0 / 20 (0.00%) | 1 / 15 (6.67%)  |
| occurrences (all)                    | 1               | 0              | 1               |
| Hypoaesthesia                        |                 |                |                 |
| subjects affected / exposed          | 0 / 10 (0.00%)  | 1 / 20 (5.00%) | 0 / 15 (0.00%)  |
| occurrences (all)                    | 0               | 1              | 0               |
| Lethargy                             |                 |                |                 |
| subjects affected / exposed          | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (0.00%)  |
| occurrences (all)                    | 0               | 0              | 0               |
| Neuropathy peripheral                |                 |                |                 |
| subjects affected / exposed          | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 1 / 15 (6.67%)  |
| occurrences (all)                    | 0               | 0              | 2               |
| Peripheral sensory neuropathy        |                 |                |                 |
| subjects affected / exposed          | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 2 / 15 (13.33%) |
| occurrences (all)                    | 0               | 0              | 2               |
| Sciatica                             |                 |                |                 |
| subjects affected / exposed          | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 1 / 15 (6.67%)  |
| occurrences (all)                    | 0               | 0              | 1               |
| Burning sensation                    |                 |                |                 |
| subjects affected / exposed          | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 1 / 15 (6.67%)  |
| occurrences (all)                    | 0               | 0              | 1               |
| Dysarthria                           |                 |                |                 |
| subjects affected / exposed          | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (0.00%)  |
| occurrences (all)                    | 0               | 0              | 0               |
| Metabolic encephalopathy             |                 |                |                 |
| subjects affected / exposed          | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (0.00%)  |
| occurrences (all)                    | 0               | 0              | 0               |
| Sinus headache                       |                 |                |                 |
| subjects affected / exposed          | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (0.00%)  |
| occurrences (all)                    | 0               | 0              | 0               |
| Somnolence                           |                 |                |                 |
| subjects affected / exposed          | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (0.00%)  |
| occurrences (all)                    | 0               | 0              | 0               |
| Spinal cord compression              |                 |                |                 |
| subjects affected / exposed          | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 1 / 15 (6.67%)  |
| occurrences (all)                    | 0               | 0              | 1               |
| Blood and lymphatic system disorders |                 |                |                 |

|                             |                 |                  |                 |
|-----------------------------|-----------------|------------------|-----------------|
| Anaemia                     |                 |                  |                 |
| subjects affected / exposed | 3 / 10 (30.00%) | 4 / 20 (20.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)           | 3               | 11               | 1               |
| Coagulopathy                |                 |                  |                 |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 20 (0.00%)   | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 0                | 0               |
| Thrombocytosis              |                 |                  |                 |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 20 (0.00%)   | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 0                | 0               |
| Ear and labyrinth disorders |                 |                  |                 |
| Hypacusis                   |                 |                  |                 |
| subjects affected / exposed | 0 / 10 (0.00%)  | 1 / 20 (5.00%)   | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 2                | 0               |
| Vertigo                     |                 |                  |                 |
| subjects affected / exposed | 0 / 10 (0.00%)  | 1 / 20 (5.00%)   | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 1                | 0               |
| Ear pruritus                |                 |                  |                 |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 20 (0.00%)   | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 0                | 0               |
| Eye disorders               |                 |                  |                 |
| Vision blurred              |                 |                  |                 |
| subjects affected / exposed | 1 / 10 (10.00%) | 2 / 20 (10.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)           | 1               | 2                | 1               |
| Vitreous floaters           |                 |                  |                 |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 20 (0.00%)   | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 0                | 0               |
| Gastrointestinal disorders  |                 |                  |                 |
| Nausea                      |                 |                  |                 |
| subjects affected / exposed | 5 / 10 (50.00%) | 12 / 20 (60.00%) | 6 / 15 (40.00%) |
| occurrences (all)           | 10              | 17               | 12              |
| Diarrhoea                   |                 |                  |                 |
| subjects affected / exposed | 3 / 10 (30.00%) | 11 / 20 (55.00%) | 6 / 15 (40.00%) |
| occurrences (all)           | 15              | 19               | 8               |
| Vomiting                    |                 |                  |                 |
| subjects affected / exposed | 3 / 10 (30.00%) | 6 / 20 (30.00%)  | 4 / 15 (26.67%) |
| occurrences (all)           | 4               | 10               | 6               |
| Abdominal pain              |                 |                  |                 |

|                                  |                 |                 |                 |
|----------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed      | 4 / 10 (40.00%) | 4 / 20 (20.00%) | 5 / 15 (33.33%) |
| occurrences (all)                | 8               | 6               | 5               |
| Constipation                     |                 |                 |                 |
| subjects affected / exposed      | 2 / 10 (20.00%) | 2 / 20 (10.00%) | 3 / 15 (20.00%) |
| occurrences (all)                | 2               | 2               | 3               |
| Flatulence                       |                 |                 |                 |
| subjects affected / exposed      | 1 / 10 (10.00%) | 2 / 20 (10.00%) | 1 / 15 (6.67%)  |
| occurrences (all)                | 1               | 2               | 1               |
| Abdominal distension             |                 |                 |                 |
| subjects affected / exposed      | 0 / 10 (0.00%)  | 3 / 20 (15.00%) | 1 / 15 (6.67%)  |
| occurrences (all)                | 0               | 4               | 1               |
| Dry mouth                        |                 |                 |                 |
| subjects affected / exposed      | 2 / 10 (20.00%) | 1 / 20 (5.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                | 2               | 1               | 0               |
| Stomatitis                       |                 |                 |                 |
| subjects affected / exposed      | 0 / 10 (0.00%)  | 2 / 20 (10.00%) | 0 / 15 (0.00%)  |
| occurrences (all)                | 0               | 3               | 0               |
| Abdominal pain upper             |                 |                 |                 |
| subjects affected / exposed      | 1 / 10 (10.00%) | 0 / 20 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                | 1               | 0               | 0               |
| Gastrooesophageal reflux disease |                 |                 |                 |
| subjects affected / exposed      | 0 / 10 (0.00%)  | 2 / 20 (10.00%) | 0 / 15 (0.00%)  |
| occurrences (all)                | 0               | 3               | 0               |
| Dysphagia                        |                 |                 |                 |
| subjects affected / exposed      | 1 / 10 (10.00%) | 0 / 20 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                | 1               | 0               | 1               |
| Haematochezia                    |                 |                 |                 |
| subjects affected / exposed      | 0 / 10 (0.00%)  | 0 / 20 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                | 0               | 0               | 0               |
| Ascites                          |                 |                 |                 |
| subjects affected / exposed      | 0 / 10 (0.00%)  | 0 / 20 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                | 0               | 0               | 0               |
| Dyspepsia                        |                 |                 |                 |
| subjects affected / exposed      | 0 / 10 (0.00%)  | 0 / 20 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                | 0               | 0               | 0               |
| Gastrointestinal disorder        |                 |                 |                 |

|                               |                 |                |                |
|-------------------------------|-----------------|----------------|----------------|
| subjects affected / exposed   | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)             | 0               | 0              | 0              |
| Gingival bleeding             |                 |                |                |
| subjects affected / exposed   | 1 / 10 (10.00%) | 0 / 20 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)             | 1               | 0              | 0              |
| Ileus                         |                 |                |                |
| subjects affected / exposed   | 1 / 10 (10.00%) | 0 / 20 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)             | 1               | 0              | 0              |
| Immune-mediated enterocolitis |                 |                |                |
| subjects affected / exposed   | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)             | 0               | 0              | 0              |
| Large intestinal obstruction  |                 |                |                |
| subjects affected / exposed   | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)             | 0               | 0              | 0              |
| Mouth haemorrhage             |                 |                |                |
| subjects affected / exposed   | 1 / 10 (10.00%) | 0 / 20 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)             | 1               | 0              | 0              |
| Odynophagia                   |                 |                |                |
| subjects affected / exposed   | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)             | 0               | 0              | 0              |
| Oral pain                     |                 |                |                |
| subjects affected / exposed   | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)             | 0               | 0              | 0              |
| Pancreatitis                  |                 |                |                |
| subjects affected / exposed   | 1 / 10 (10.00%) | 0 / 20 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)             | 1               | 0              | 0              |
| Proctalgia                    |                 |                |                |
| subjects affected / exposed   | 1 / 10 (10.00%) | 0 / 20 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)             | 1               | 0              | 0              |
| Rectal haemorrhage            |                 |                |                |
| subjects affected / exposed   | 1 / 10 (10.00%) | 0 / 20 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)             | 1               | 0              | 0              |
| Small intestinal obstruction  |                 |                |                |
| subjects affected / exposed   | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)             | 0               | 0              | 0              |
| Hepatobiliary disorders       |                 |                |                |

|                                                                                                    |                      |                      |                      |
|----------------------------------------------------------------------------------------------------|----------------------|----------------------|----------------------|
| Immune-mediated hepatitis<br>subjects affected / exposed<br>occurrences (all)                      | 2 / 10 (20.00%)<br>3 | 2 / 20 (10.00%)<br>3 | 0 / 15 (0.00%)<br>0  |
| Biliary obstruction<br>subjects affected / exposed<br>occurrences (all)                            | 0 / 10 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Hepatic artery thrombosis<br>subjects affected / exposed<br>occurrences (all)                      | 1 / 10 (10.00%)<br>1 | 0 / 20 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Hepatic cirrhosis<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 10 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Skin and subcutaneous tissue disorders                                                             |                      |                      |                      |
| Rash maculo-papular<br>subjects affected / exposed<br>occurrences (all)                            | 1 / 10 (10.00%)<br>2 | 3 / 20 (15.00%)<br>3 | 0 / 15 (0.00%)<br>0  |
| Pruritus<br>subjects affected / exposed<br>occurrences (all)                                       | 1 / 10 (10.00%)<br>1 | 0 / 20 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  |
| Rash<br>subjects affected / exposed<br>occurrences (all)                                           | 0 / 10 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0  | 2 / 15 (13.33%)<br>2 |
| Alopecia<br>subjects affected / exposed<br>occurrences (all)                                       | 0 / 10 (0.00%)<br>0  | 2 / 20 (10.00%)<br>2 | 0 / 15 (0.00%)<br>0  |
| Dry skin<br>subjects affected / exposed<br>occurrences (all)                                       | 2 / 10 (20.00%)<br>2 | 0 / 20 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  |
| Decubitus ulcer<br>subjects affected / exposed<br>occurrences (all)                                | 0 / 10 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Palmar-plantar erythrodysaesthesia<br>syndrome<br>subjects affected / exposed<br>occurrences (all) | 0 / 10 (0.00%)<br>0  | 2 / 20 (10.00%)<br>2 | 0 / 15 (0.00%)<br>0  |
| Cold sweat                                                                                         |                      |                      |                      |

|                             |                 |                 |                |
|-----------------------------|-----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 20 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0               | 0               | 0              |
| Dermatitis acneiform        |                 |                 |                |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 20 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0               | 0               | 0              |
| Hyperhidrosis               |                 |                 |                |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 20 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 1               | 0               | 0              |
| Immune-mediated dermatitis  |                 |                 |                |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 20 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0               | 0               | 0              |
| Night sweats                |                 |                 |                |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 20 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0               | 0               | 0              |
| Psoriasis                   |                 |                 |                |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 20 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0               | 0               | 0              |
| Skin lesion                 |                 |                 |                |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 20 (0.00%)  | 1 / 15 (6.67%) |
| occurrences (all)           | 0               | 0               | 1              |
| Renal and urinary disorders |                 |                 |                |
| Proteinuria                 |                 |                 |                |
| subjects affected / exposed | 4 / 10 (40.00%) | 9 / 20 (45.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 5               | 47              | 0              |
| Haematuria                  |                 |                 |                |
| subjects affected / exposed | 0 / 10 (0.00%)  | 5 / 20 (25.00%) | 1 / 15 (6.67%) |
| occurrences (all)           | 0               | 5               | 1              |
| Urinary retention           |                 |                 |                |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 20 (0.00%)  | 1 / 15 (6.67%) |
| occurrences (all)           | 0               | 0               | 1              |
| Acute kidney injury         |                 |                 |                |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 20 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0               | 0               | 0              |
| Chronic kidney disease      |                 |                 |                |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 20 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0               | 0               | 0              |

|                                                 |                 |                 |                |
|-------------------------------------------------|-----------------|-----------------|----------------|
| Dysuria                                         |                 |                 |                |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 20 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)                               | 1               | 0               | 0              |
| Hydronephrosis                                  |                 |                 |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 20 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)                               | 0               | 0               | 0              |
| Leukocyturia                                    |                 |                 |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 20 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)                               | 0               | 0               | 0              |
| Micturition disorder                            |                 |                 |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 20 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)                               | 0               | 0               | 0              |
| Nephrolithiasis                                 |                 |                 |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 20 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)                               | 0               | 0               | 0              |
| Pollakiuria                                     |                 |                 |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 20 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)                               | 0               | 0               | 0              |
| Renal pain                                      |                 |                 |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 20 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)                               | 0               | 0               | 0              |
| Urinary tract pain                              |                 |                 |                |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 20 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)                               | 1               | 0               | 0              |
| Urine flow decreased                            |                 |                 |                |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 20 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)                               | 1               | 0               | 0              |
| Endocrine disorders                             |                 |                 |                |
| Hypothyroidism                                  |                 |                 |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 2 / 20 (10.00%) | 0 / 15 (0.00%) |
| occurrences (all)                               | 0               | 2               | 0              |
| Inappropriate antidiuretic hormone secretion    |                 |                 |                |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 20 (0.00%)  | 1 / 15 (6.67%) |
| occurrences (all)                               | 0               | 0               | 1              |
| Musculoskeletal and connective tissue disorders |                 |                 |                |

|                             |                 |                 |                |
|-----------------------------|-----------------|-----------------|----------------|
| Arthralgia                  |                 |                 |                |
| subjects affected / exposed | 3 / 10 (30.00%) | 8 / 20 (40.00%) | 1 / 15 (6.67%) |
| occurrences (all)           | 4               | 24              | 1              |
| Back pain                   |                 |                 |                |
| subjects affected / exposed | 1 / 10 (10.00%) | 4 / 20 (20.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 1               | 7               | 0              |
| Pain in extremity           |                 |                 |                |
| subjects affected / exposed | 2 / 10 (20.00%) | 4 / 20 (20.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 2               | 8               | 0              |
| Myalgia                     |                 |                 |                |
| subjects affected / exposed | 1 / 10 (10.00%) | 3 / 20 (15.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 2               | 4               | 0              |
| Muscular weakness           |                 |                 |                |
| subjects affected / exposed | 1 / 10 (10.00%) | 3 / 20 (15.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 1               | 4               | 0              |
| Flank pain                  |                 |                 |                |
| subjects affected / exposed | 2 / 10 (20.00%) | 1 / 20 (5.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 2               | 1               | 0              |
| Neck pain                   |                 |                 |                |
| subjects affected / exposed | 0 / 10 (0.00%)  | 2 / 20 (10.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0               | 2               | 0              |
| Muscle spasms               |                 |                 |                |
| subjects affected / exposed | 0 / 10 (0.00%)  | 2 / 20 (10.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0               | 2               | 0              |
| Musculoskeletal chest pain  |                 |                 |                |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 20 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0               | 0               | 0              |
| Bursitis                    |                 |                 |                |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 20 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 1               | 0               | 0              |
| Muscle atrophy              |                 |                 |                |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 20 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0               | 0               | 0              |
| Rheumatoid arthritis        |                 |                 |                |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 20 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0               | 0               | 0              |

|                                                                                             |                      |                      |                     |
|---------------------------------------------------------------------------------------------|----------------------|----------------------|---------------------|
| Infections and infestations<br>COVID-19<br>subjects affected / exposed<br>occurrences (all) | 2 / 10 (20.00%)<br>2 | 3 / 20 (15.00%)<br>3 | 1 / 15 (6.67%)<br>1 |
| Urinary tract infection<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 10 (0.00%)<br>0  | 1 / 20 (5.00%)<br>1  | 1 / 15 (6.67%)<br>1 |
| Pneumonia<br>subjects affected / exposed<br>occurrences (all)                               | 1 / 10 (10.00%)<br>1 | 1 / 20 (5.00%)<br>2  | 0 / 15 (0.00%)<br>0 |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)       | 1 / 10 (10.00%)<br>1 | 2 / 20 (10.00%)<br>3 | 0 / 15 (0.00%)<br>0 |
| Clostridium difficile infection<br>subjects affected / exposed<br>occurrences (all)         | 0 / 10 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 |
| Sinusitis<br>subjects affected / exposed<br>occurrences (all)                               | 1 / 10 (10.00%)<br>1 | 2 / 20 (10.00%)<br>3 | 0 / 15 (0.00%)<br>0 |
| Eye infection<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 10 (0.00%)<br>0  | 1 / 20 (5.00%)<br>1  | 1 / 15 (6.67%)<br>1 |
| Abscess<br>subjects affected / exposed<br>occurrences (all)                                 | 0 / 10 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 |
| Bacteriuria<br>subjects affected / exposed<br>occurrences (all)                             | 0 / 10 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 |
| Bronchitis<br>subjects affected / exposed<br>occurrences (all)                              | 1 / 10 (10.00%)<br>1 | 0 / 20 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 |
| Cellulitis<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 10 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 |
| Conjunctivitis                                                                              |                      |                      |                     |

|                                    |                 |                |                |
|------------------------------------|-----------------|----------------|----------------|
| subjects affected / exposed        | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all)                  | 0               | 0              | 1              |
| Cystitis                           |                 |                |                |
| subjects affected / exposed        | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                  | 0               | 0              | 0              |
| Folliculitis                       |                 |                |                |
| subjects affected / exposed        | 1 / 10 (10.00%) | 0 / 20 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                  | 1               | 0              | 0              |
| Gastrointestinal viral infection   |                 |                |                |
| subjects affected / exposed        | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all)                  | 0               | 0              | 1              |
| Herpes simplex                     |                 |                |                |
| subjects affected / exposed        | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                  | 0               | 0              | 0              |
| Kidney infection                   |                 |                |                |
| subjects affected / exposed        | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all)                  | 0               | 0              | 1              |
| Nasopharyngitis                    |                 |                |                |
| subjects affected / exposed        | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                  | 0               | 0              | 0              |
| Pneumonia aspiration               |                 |                |                |
| subjects affected / exposed        | 1 / 10 (10.00%) | 0 / 20 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                  | 1               | 0              | 0              |
| Rash pustular                      |                 |                |                |
| subjects affected / exposed        | 1 / 10 (10.00%) | 0 / 20 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                  | 1               | 0              | 0              |
| Respiratory tract infection        |                 |                |                |
| subjects affected / exposed        | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                  | 0               | 0              | 0              |
| Sepsis                             |                 |                |                |
| subjects affected / exposed        | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                  | 0               | 0              | 0              |
| Skin infection                     |                 |                |                |
| subjects affected / exposed        | 0 / 10 (0.00%)  | 0 / 20 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                  | 0               | 0              | 0              |
| Metabolism and nutrition disorders |                 |                |                |

|                                                                        |                       |                        |                      |
|------------------------------------------------------------------------|-----------------------|------------------------|----------------------|
| Decreased appetite<br>subjects affected / exposed<br>occurrences (all) | 4 / 10 (40.00%)<br>10 | 11 / 20 (55.00%)<br>13 | 3 / 15 (20.00%)<br>3 |
| Hypokalaemia<br>subjects affected / exposed<br>occurrences (all)       | 2 / 10 (20.00%)<br>2  | 5 / 20 (25.00%)<br>8   | 2 / 15 (13.33%)<br>2 |
| Hyponatraemia<br>subjects affected / exposed<br>occurrences (all)      | 2 / 10 (20.00%)<br>2  | 7 / 20 (35.00%)<br>36  | 3 / 15 (20.00%)<br>7 |
| Hyperuricaemia<br>subjects affected / exposed<br>occurrences (all)     | 2 / 10 (20.00%)<br>6  | 3 / 20 (15.00%)<br>7   | 0 / 15 (0.00%)<br>0  |
| Hypomagnesaemia<br>subjects affected / exposed<br>occurrences (all)    | 1 / 10 (10.00%)<br>1  | 4 / 20 (20.00%)<br>6   | 1 / 15 (6.67%)<br>1  |
| Dehydration<br>subjects affected / exposed<br>occurrences (all)        | 1 / 10 (10.00%)<br>2  | 1 / 20 (5.00%)<br>1    | 4 / 15 (26.67%)<br>4 |
| Hyperglycaemia<br>subjects affected / exposed<br>occurrences (all)     | 2 / 10 (20.00%)<br>8  | 5 / 20 (25.00%)<br>17  | 0 / 15 (0.00%)<br>0  |
| Hypoalbuminaemia<br>subjects affected / exposed<br>occurrences (all)   | 1 / 10 (10.00%)<br>1  | 3 / 20 (15.00%)<br>4   | 0 / 15 (0.00%)<br>0  |
| Hyperkalaemia<br>subjects affected / exposed<br>occurrences (all)      | 0 / 10 (0.00%)<br>0   | 3 / 20 (15.00%)<br>3   | 0 / 15 (0.00%)<br>0  |
| Hyperphosphataemia<br>subjects affected / exposed<br>occurrences (all) | 0 / 10 (0.00%)<br>0   | 4 / 20 (20.00%)<br>11  | 0 / 15 (0.00%)<br>0  |
| Hypoglycaemia<br>subjects affected / exposed<br>occurrences (all)      | 0 / 10 (0.00%)<br>0   | 4 / 20 (20.00%)<br>4   | 0 / 15 (0.00%)<br>0  |
| Hypophosphataemia<br>subjects affected / exposed<br>occurrences (all)  | 0 / 10 (0.00%)<br>0   | 4 / 20 (20.00%)<br>6   | 0 / 15 (0.00%)<br>0  |

|                                                                           |                      |                     |                     |
|---------------------------------------------------------------------------|----------------------|---------------------|---------------------|
| Hypercalcaemia<br>subjects affected / exposed<br>occurrences (all)        | 0 / 10 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0 | 1 / 15 (6.67%)<br>1 |
| Hypocalcaemia<br>subjects affected / exposed<br>occurrences (all)         | 0 / 10 (0.00%)<br>0  | 1 / 20 (5.00%)<br>1 | 0 / 15 (0.00%)<br>0 |
| Food intolerance<br>subjects affected / exposed<br>occurrences (all)      | 0 / 10 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0 |
| Hypertriglyceridaemia<br>subjects affected / exposed<br>occurrences (all) | 1 / 10 (10.00%)<br>1 | 0 / 20 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0 |

| <b>Non-serious adverse events</b>                                                                                                           | Dose Expansion<br>Phase: Cohort D: GC | Dose Expansion<br>Phase: Cohort E2:<br>UPS | Dose Expansion<br>Phase: Cohort F:<br>ATC |
|---------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------|--------------------------------------------|-------------------------------------------|
| Total subjects affected by non-serious<br>adverse events<br>subjects affected / exposed                                                     | 3 / 3 (100.00%)                       | 8 / 9 (88.89%)                             | 3 / 3 (100.00%)                           |
| Neoplasms benign, malignant and<br>unspecified (incl cysts and polyps)<br>Neoplasm skin<br>subjects affected / exposed<br>occurrences (all) | 0 / 3 (0.00%)<br>0                    | 0 / 9 (0.00%)<br>0                         | 1 / 3 (33.33%)<br>1                       |
| Vascular disorders<br>Hypertension<br>subjects affected / exposed<br>occurrences (all)                                                      | 1 / 3 (33.33%)<br>4                   | 4 / 9 (44.44%)<br>8                        | 2 / 3 (66.67%)<br>4                       |
| Flushing<br>subjects affected / exposed<br>occurrences (all)                                                                                | 1 / 3 (33.33%)<br>1                   | 0 / 9 (0.00%)<br>0                         | 0 / 3 (0.00%)<br>0                        |
| Hypotension<br>subjects affected / exposed<br>occurrences (all)                                                                             | 0 / 3 (0.00%)<br>0                    | 0 / 9 (0.00%)<br>0                         | 0 / 3 (0.00%)<br>0                        |
| Orthostatic hypotension<br>subjects affected / exposed<br>occurrences (all)                                                                 | 0 / 3 (0.00%)<br>0                    | 0 / 9 (0.00%)<br>0                         | 0 / 3 (0.00%)<br>0                        |
| Vasculitis<br>subjects affected / exposed<br>occurrences (all)                                                                              | 0 / 3 (0.00%)<br>0                    | 0 / 9 (0.00%)<br>0                         | 0 / 3 (0.00%)<br>0                        |

|                                                      |                 |                |                |
|------------------------------------------------------|-----------------|----------------|----------------|
| General disorders and administration site conditions |                 |                |                |
| Fatigue                                              |                 |                |                |
| subjects affected / exposed                          | 3 / 3 (100.00%) | 4 / 9 (44.44%) | 1 / 3 (33.33%) |
| occurrences (all)                                    | 4               | 6              | 2              |
| Oedema peripheral                                    |                 |                |                |
| subjects affected / exposed                          | 1 / 3 (33.33%)  | 3 / 9 (33.33%) | 0 / 3 (0.00%)  |
| occurrences (all)                                    | 1               | 4              | 0              |
| Asthenia                                             |                 |                |                |
| subjects affected / exposed                          | 0 / 3 (0.00%)   | 4 / 9 (44.44%) | 0 / 3 (0.00%)  |
| occurrences (all)                                    | 0               | 4              | 0              |
| Pyrexia                                              |                 |                |                |
| subjects affected / exposed                          | 0 / 3 (0.00%)   | 2 / 9 (22.22%) | 0 / 3 (0.00%)  |
| occurrences (all)                                    | 0               | 3              | 0              |
| Non-cardiac chest pain                               |                 |                |                |
| subjects affected / exposed                          | 1 / 3 (33.33%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                                    | 1               | 0              | 0              |
| Chills                                               |                 |                |                |
| subjects affected / exposed                          | 0 / 3 (0.00%)   | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                                    | 0               | 0              | 0              |
| Localised oedema                                     |                 |                |                |
| subjects affected / exposed                          | 0 / 3 (0.00%)   | 0 / 9 (0.00%)  | 2 / 3 (66.67%) |
| occurrences (all)                                    | 0               | 0              | 2              |
| Malaise                                              |                 |                |                |
| subjects affected / exposed                          | 0 / 3 (0.00%)   | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                                    | 0               | 0              | 0              |
| Gait disturbance                                     |                 |                |                |
| subjects affected / exposed                          | 0 / 3 (0.00%)   | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                                    | 0               | 0              | 0              |
| Pain                                                 |                 |                |                |
| subjects affected / exposed                          | 0 / 3 (0.00%)   | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                                    | 0               | 0              | 0              |
| Catheter site haematoma                              |                 |                |                |
| subjects affected / exposed                          | 0 / 3 (0.00%)   | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                                    | 0               | 0              | 0              |
| Catheter site haemorrhage                            |                 |                |                |

|                                          |               |                |               |
|------------------------------------------|---------------|----------------|---------------|
| subjects affected / exposed              | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                        | 0             | 0              | 0             |
| Facial pain                              |               |                |               |
| subjects affected / exposed              | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                        | 0             | 0              | 0             |
| Influenza like illness                   |               |                |               |
| subjects affected / exposed              | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                        | 0             | 0              | 0             |
| Injection site pain                      |               |                |               |
| subjects affected / exposed              | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 3 (0.00%) |
| occurrences (all)                        | 0             | 1              | 0             |
| Medical device site pain                 |               |                |               |
| subjects affected / exposed              | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                        | 0             | 0              | 0             |
| Mucosal inflammation                     |               |                |               |
| subjects affected / exposed              | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 3 (0.00%) |
| occurrences (all)                        | 0             | 2              | 0             |
| Oedema                                   |               |                |               |
| subjects affected / exposed              | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                        | 0             | 0              | 0             |
| Peripheral swelling                      |               |                |               |
| subjects affected / exposed              | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                        | 0             | 0              | 0             |
| Xerosis                                  |               |                |               |
| subjects affected / exposed              | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 3 (0.00%) |
| occurrences (all)                        | 0             | 1              | 0             |
| Immune system disorders                  |               |                |               |
| Seasonal allergy                         |               |                |               |
| subjects affected / exposed              | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                        | 0             | 0              | 0             |
| Hypersensitivity                         |               |                |               |
| subjects affected / exposed              | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                        | 0             | 0              | 0             |
| Reproductive system and breast disorders |               |                |               |

|                                                 |               |                |               |
|-------------------------------------------------|---------------|----------------|---------------|
| Pelvic pain                                     |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0             |
| Gynaecomastia                                   |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0             |
| Vaginal haemorrhage                             |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0             |
| Respiratory, thoracic and mediastinal disorders |               |                |               |
| Cough                                           |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 2 / 9 (22.22%) | 0 / 3 (0.00%) |
| occurrences (all)                               | 0             | 2              | 0             |
| Dyspnoea                                        |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 3 / 9 (33.33%) | 0 / 3 (0.00%) |
| occurrences (all)                               | 0             | 5              | 0             |
| Epistaxis                                       |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 3 (0.00%) |
| occurrences (all)                               | 0             | 2              | 0             |
| Dysphonia                                       |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0             |
| Nasal congestion                                |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0             |
| Pleural effusion                                |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 2 / 9 (22.22%) | 0 / 3 (0.00%) |
| occurrences (all)                               | 0             | 2              | 0             |
| Productive cough                                |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0             |
| Sinus congestion                                |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0             |
| Atelectasis                                     |               |                |               |

|                             |                |                |               |
|-----------------------------|----------------|----------------|---------------|
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Hiccups                     |                |                |               |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)           | 1              | 0              | 0             |
| Oropharyngeal pain          |                |                |               |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Pneumonitis                 |                |                |               |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 9 (11.11%) | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 1              | 0             |
| Pulmonary haemorrhage       |                |                |               |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Rhinorrhoea                 |                |                |               |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Sneezing                    |                |                |               |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Sputum discoloured          |                |                |               |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 9 (11.11%) | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 1              | 0             |
| Psychiatric disorders       |                |                |               |
| Confusional state           |                |                |               |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 9 (11.11%) | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 1              | 0             |
| Insomnia                    |                |                |               |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)           | 1              | 0              | 0             |
| Anxiety                     |                |                |               |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 9 (11.11%) | 0 / 3 (0.00%) |
| occurrences (all)           | 1              | 1              | 0             |
| Depression                  |                |                |               |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 9 (11.11%) | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 1              | 0             |

|                                                                                                            |                     |                     |                     |
|------------------------------------------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| Depressed mood<br>subjects affected / exposed<br>occurrences (all)                                         | 0 / 3 (0.00%)<br>0  | 1 / 9 (11.11%)<br>1 | 0 / 3 (0.00%)<br>0  |
| Irritability<br>subjects affected / exposed<br>occurrences (all)                                           | 0 / 3 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Panic attack<br>subjects affected / exposed<br>occurrences (all)                                           | 0 / 3 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Restlessness<br>subjects affected / exposed<br>occurrences (all)                                           | 0 / 3 (0.00%)<br>0  | 1 / 9 (11.11%)<br>1 | 0 / 3 (0.00%)<br>0  |
| Product issues<br>Device occlusion<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 3 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Investigations<br>Aspartate aminotransferase increased<br>subjects affected / exposed<br>occurrences (all) | 1 / 3 (33.33%)<br>2 | 0 / 9 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Alanine aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)                     | 1 / 3 (33.33%)<br>1 | 0 / 9 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Blood creatinine increased<br>subjects affected / exposed<br>occurrences (all)                             | 0 / 3 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  | 1 / 3 (33.33%)<br>2 |
| Weight decreased<br>subjects affected / exposed<br>occurrences (all)                                       | 2 / 3 (66.67%)<br>2 | 1 / 9 (11.11%)<br>2 | 0 / 3 (0.00%)<br>0  |
| Blood bilirubin increased<br>subjects affected / exposed<br>occurrences (all)                              | 1 / 3 (33.33%)<br>1 | 0 / 9 (0.00%)<br>0  | 1 / 3 (33.33%)<br>2 |
| Lipase increased<br>subjects affected / exposed<br>occurrences (all)                                       | 0 / 3 (0.00%)<br>0  | 1 / 9 (11.11%)<br>1 | 2 / 3 (66.67%)<br>3 |
| Platelet count decreased                                                                                   |                     |                     |                     |

|                                                 |               |                |                |
|-------------------------------------------------|---------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Blood alkaline phosphatase increased            |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Blood lactate dehydrogenase increased           |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Amylase increased                               |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)                               | 0             | 0              | 3              |
| Blood creatine phosphokinase increased          |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Lymphocyte count decreased                      |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0             | 1              | 0              |
| Electrocardiogram QT prolonged                  |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Neutrophil count decreased                      |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Activated partial thromboplastin time prolonged |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| White blood cell count decreased                |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Blood creatine increased                        |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Ejection fraction decreased                     |               |                |                |

|                                                |                |                |               |
|------------------------------------------------|----------------|----------------|---------------|
| subjects affected / exposed                    | 1 / 3 (33.33%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                              | 1              | 0              | 0             |
| Troponin T increased                           |                |                |               |
| subjects affected / exposed                    | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0             |
| Breath sounds abnormal                         |                |                |               |
| subjects affected / exposed                    | 0 / 3 (0.00%)  | 1 / 9 (11.11%) | 0 / 3 (0.00%) |
| occurrences (all)                              | 0              | 2              | 0             |
| Haemoglobin decreased                          |                |                |               |
| subjects affected / exposed                    | 0 / 3 (0.00%)  | 1 / 9 (11.11%) | 0 / 3 (0.00%) |
| occurrences (all)                              | 0              | 5              | 0             |
| Neutrophil count increased                     |                |                |               |
| subjects affected / exposed                    | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0             |
| White blood cell count increased               |                |                |               |
| subjects affected / exposed                    | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0             |
| Injury, poisoning and procedural complications |                |                |               |
| Contusion                                      |                |                |               |
| subjects affected / exposed                    | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0             |
| Fall                                           |                |                |               |
| subjects affected / exposed                    | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0             |
| Infusion related reaction                      |                |                |               |
| subjects affected / exposed                    | 0 / 3 (0.00%)  | 1 / 9 (11.11%) | 0 / 3 (0.00%) |
| occurrences (all)                              | 0              | 2              | 0             |
| Incision site discharge                        |                |                |               |
| subjects affected / exposed                    | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0             |
| Postoperative wound complication               |                |                |               |
| subjects affected / exposed                    | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0             |
| Wound dehiscence                               |                |                |               |

|                                                  |                    |                    |                    |
|--------------------------------------------------|--------------------|--------------------|--------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 3 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0 |
| Cardiac disorders                                |                    |                    |                    |
| Sinus tachycardia                                |                    |                    |                    |
| subjects affected / exposed                      | 0 / 3 (0.00%)      | 0 / 9 (0.00%)      | 0 / 3 (0.00%)      |
| occurrences (all)                                | 0                  | 0                  | 0                  |
| Tachycardia                                      |                    |                    |                    |
| subjects affected / exposed                      | 0 / 3 (0.00%)      | 0 / 9 (0.00%)      | 0 / 3 (0.00%)      |
| occurrences (all)                                | 0                  | 0                  | 0                  |
| Aortic valve disease                             |                    |                    |                    |
| subjects affected / exposed                      | 1 / 3 (33.33%)     | 0 / 9 (0.00%)      | 0 / 3 (0.00%)      |
| occurrences (all)                                | 1                  | 0                  | 0                  |
| Atrial fibrillation                              |                    |                    |                    |
| subjects affected / exposed                      | 0 / 3 (0.00%)      | 0 / 9 (0.00%)      | 0 / 3 (0.00%)      |
| occurrences (all)                                | 0                  | 0                  | 0                  |
| Nervous system disorders                         |                    |                    |                    |
| Headache                                         |                    |                    |                    |
| subjects affected / exposed                      | 0 / 3 (0.00%)      | 3 / 9 (33.33%)     | 0 / 3 (0.00%)      |
| occurrences (all)                                | 0                  | 4                  | 0                  |
| Dizziness                                        |                    |                    |                    |
| subjects affected / exposed                      | 0 / 3 (0.00%)      | 0 / 9 (0.00%)      | 0 / 3 (0.00%)      |
| occurrences (all)                                | 0                  | 0                  | 0                  |
| Dysgeusia                                        |                    |                    |                    |
| subjects affected / exposed                      | 0 / 3 (0.00%)      | 2 / 9 (22.22%)     | 0 / 3 (0.00%)      |
| occurrences (all)                                | 0                  | 2                  | 0                  |
| Paraesthesia                                     |                    |                    |                    |
| subjects affected / exposed                      | 0 / 3 (0.00%)      | 1 / 9 (11.11%)     | 0 / 3 (0.00%)      |
| occurrences (all)                                | 0                  | 1                  | 0                  |
| Tremor                                           |                    |                    |                    |
| subjects affected / exposed                      | 0 / 3 (0.00%)      | 1 / 9 (11.11%)     | 0 / 3 (0.00%)      |
| occurrences (all)                                | 0                  | 1                  | 0                  |
| Hypoaesthesia                                    |                    |                    |                    |
| subjects affected / exposed                      | 0 / 3 (0.00%)      | 0 / 9 (0.00%)      | 0 / 3 (0.00%)      |
| occurrences (all)                                | 0                  | 0                  | 0                  |
| Lethargy                                         |                    |                    |                    |

|                                      |                |                |                |
|--------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed          | 1 / 3 (33.33%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                    | 1              | 0              | 0              |
| Neuropathy peripheral                |                |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 1 / 9 (11.11%) | 0 / 3 (0.00%)  |
| occurrences (all)                    | 0              | 1              | 0              |
| Peripheral sensory neuropathy        |                |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Sciatica                             |                |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Burning sensation                    |                |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Dysarthria                           |                |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Metabolic encephalopathy             |                |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 1 / 9 (11.11%) | 0 / 3 (0.00%)  |
| occurrences (all)                    | 0              | 1              | 0              |
| Sinus headache                       |                |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Somnolence                           |                |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)                    | 0              | 0              | 2              |
| Spinal cord compression              |                |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Blood and lymphatic system disorders |                |                |                |
| Anaemia                              |                |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 2 / 9 (22.22%) | 1 / 3 (33.33%) |
| occurrences (all)                    | 0              | 2              | 1              |
| Coagulopathy                         |                |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 1 / 9 (11.11%) | 0 / 3 (0.00%)  |
| occurrences (all)                    | 0              | 1              | 0              |

|                                                                       |                      |                      |                     |
|-----------------------------------------------------------------------|----------------------|----------------------|---------------------|
| Thrombocytosis<br>subjects affected / exposed<br>occurrences (all)    | 0 / 3 (0.00%)<br>0   | 1 / 9 (11.11%)<br>1  | 0 / 3 (0.00%)<br>0  |
| Ear and labyrinth disorders                                           |                      |                      |                     |
| Hypoacusis<br>subjects affected / exposed<br>occurrences (all)        | 0 / 3 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0   | 0 / 3 (0.00%)<br>0  |
| Vertigo<br>subjects affected / exposed<br>occurrences (all)           | 0 / 3 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0   | 0 / 3 (0.00%)<br>0  |
| Ear pruritus<br>subjects affected / exposed<br>occurrences (all)      | 0 / 3 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0   | 0 / 3 (0.00%)<br>0  |
| Eye disorders                                                         |                      |                      |                     |
| Vision blurred<br>subjects affected / exposed<br>occurrences (all)    | 0 / 3 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0   | 0 / 3 (0.00%)<br>0  |
| Vitreous floaters<br>subjects affected / exposed<br>occurrences (all) | 0 / 3 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0   | 1 / 3 (33.33%)<br>2 |
| Gastrointestinal disorders                                            |                      |                      |                     |
| Nausea<br>subjects affected / exposed<br>occurrences (all)            | 3 / 3 (100.00%)<br>4 | 4 / 9 (44.44%)<br>7  | 0 / 3 (0.00%)<br>0  |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)         | 3 / 3 (100.00%)<br>7 | 4 / 9 (44.44%)<br>16 | 1 / 3 (33.33%)<br>1 |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)          | 0 / 3 (0.00%)<br>0   | 3 / 9 (33.33%)<br>5  | 0 / 3 (0.00%)<br>0  |
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)    | 2 / 3 (66.67%)<br>3  | 2 / 9 (22.22%)<br>2  | 0 / 3 (0.00%)<br>0  |
| Constipation<br>subjects affected / exposed<br>occurrences (all)      | 1 / 3 (33.33%)<br>1  | 3 / 9 (33.33%)<br>3  | 2 / 3 (66.67%)<br>2 |
| Flatulence                                                            |                      |                      |                     |

|                                  |                |                |                |
|----------------------------------|----------------|----------------|----------------|
| subjects affected / exposed      | 0 / 3 (0.00%)  | 1 / 9 (11.11%) | 0 / 3 (0.00%)  |
| occurrences (all)                | 0              | 1              | 0              |
| Abdominal distension             |                |                |                |
| subjects affected / exposed      | 1 / 3 (33.33%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                | 1              | 0              | 0              |
| Dry mouth                        |                |                |                |
| subjects affected / exposed      | 0 / 3 (0.00%)  | 2 / 9 (22.22%) | 1 / 3 (33.33%) |
| occurrences (all)                | 0              | 3              | 1              |
| Stomatitis                       |                |                |                |
| subjects affected / exposed      | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0              |
| Abdominal pain upper             |                |                |                |
| subjects affected / exposed      | 0 / 3 (0.00%)  | 1 / 9 (11.11%) | 0 / 3 (0.00%)  |
| occurrences (all)                | 0              | 1              | 0              |
| Gastrooesophageal reflux disease |                |                |                |
| subjects affected / exposed      | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0              |
| Dysphagia                        |                |                |                |
| subjects affected / exposed      | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0              |
| Haematochezia                    |                |                |                |
| subjects affected / exposed      | 0 / 3 (0.00%)  | 1 / 9 (11.11%) | 0 / 3 (0.00%)  |
| occurrences (all)                | 0              | 1              | 0              |
| Ascites                          |                |                |                |
| subjects affected / exposed      | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0              |
| Dyspepsia                        |                |                |                |
| subjects affected / exposed      | 0 / 3 (0.00%)  | 1 / 9 (11.11%) | 0 / 3 (0.00%)  |
| occurrences (all)                | 0              | 1              | 0              |
| Gastrointestinal disorder        |                |                |                |
| subjects affected / exposed      | 0 / 3 (0.00%)  | 1 / 9 (11.11%) | 0 / 3 (0.00%)  |
| occurrences (all)                | 0              | 1              | 0              |
| Gingival bleeding                |                |                |                |
| subjects affected / exposed      | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0              |
| Ileus                            |                |                |                |

|                               |               |                |               |
|-------------------------------|---------------|----------------|---------------|
| subjects affected / exposed   | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)             | 0             | 0              | 0             |
| Immune-mediated enterocolitis |               |                |               |
| subjects affected / exposed   | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 3 (0.00%) |
| occurrences (all)             | 0             | 1              | 0             |
| Large intestinal obstruction  |               |                |               |
| subjects affected / exposed   | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)             | 0             | 0              | 0             |
| Mouth haemorrhage             |               |                |               |
| subjects affected / exposed   | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)             | 0             | 0              | 0             |
| Odynophagia                   |               |                |               |
| subjects affected / exposed   | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 3 (0.00%) |
| occurrences (all)             | 0             | 1              | 0             |
| Oral pain                     |               |                |               |
| subjects affected / exposed   | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)             | 0             | 0              | 0             |
| Pancreatitis                  |               |                |               |
| subjects affected / exposed   | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)             | 0             | 0              | 0             |
| Proctalgia                    |               |                |               |
| subjects affected / exposed   | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)             | 0             | 0              | 0             |
| Rectal haemorrhage            |               |                |               |
| subjects affected / exposed   | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)             | 0             | 0              | 0             |
| Small intestinal obstruction  |               |                |               |
| subjects affected / exposed   | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)             | 0             | 0              | 0             |
| Hepatobiliary disorders       |               |                |               |
| Immune-mediated hepatitis     |               |                |               |
| subjects affected / exposed   | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)             | 0             | 0              | 0             |
| Biliary obstruction           |               |                |               |
| subjects affected / exposed   | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)             | 0             | 0              | 0             |

|                                                                                                    |                     |                     |                     |
|----------------------------------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| Hepatic artery thrombosis<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 3 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Hepatic cirrhosis<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 3 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Skin and subcutaneous tissue disorders                                                             |                     |                     |                     |
| Rash maculo-papular<br>subjects affected / exposed<br>occurrences (all)                            | 1 / 3 (33.33%)<br>2 | 1 / 9 (11.11%)<br>2 | 1 / 3 (33.33%)<br>1 |
| Pruritus<br>subjects affected / exposed<br>occurrences (all)                                       | 1 / 3 (33.33%)<br>2 | 2 / 9 (22.22%)<br>2 | 0 / 3 (0.00%)<br>0  |
| Rash<br>subjects affected / exposed<br>occurrences (all)                                           | 0 / 3 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Alopecia<br>subjects affected / exposed<br>occurrences (all)                                       | 0 / 3 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Dry skin<br>subjects affected / exposed<br>occurrences (all)                                       | 0 / 3 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Decubitus ulcer<br>subjects affected / exposed<br>occurrences (all)                                | 0 / 3 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Palmar-plantar erythrodysaesthesia<br>syndrome<br>subjects affected / exposed<br>occurrences (all) | 0 / 3 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Cold sweat<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 3 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Dermatitis acneiform<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 3 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Hyperhidrosis                                                                                      |                     |                     |                     |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Immune-mediated dermatitis  |                |                |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 9 (11.11%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0              |
| Night sweats                |                |                |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)           | 0              | 0              | 1              |
| Psoriasis                   |                |                |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Skin lesion                 |                |                |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Renal and urinary disorders |                |                |                |
| Proteinuria                 |                |                |                |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 9 (11.11%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 1              | 10             | 0              |
| Haematuria                  |                |                |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 9 (11.11%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0              |
| Urinary retention           |                |                |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)           | 0              | 0              | 1              |
| Acute kidney injury         |                |                |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Chronic kidney disease      |                |                |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Dysuria                     |                |                |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Hydronephrosis              |                |                |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |

|                                                 |               |                |                |
|-------------------------------------------------|---------------|----------------|----------------|
| Leukocyturia                                    |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0             | 2              | 0              |
| Micturition disorder                            |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0             | 2              | 0              |
| Nephrolithiasis                                 |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0             | 1              | 0              |
| Pollakiuria                                     |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Renal pain                                      |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0             | 1              | 0              |
| Urinary tract pain                              |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Urine flow decreased                            |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Endocrine disorders                             |               |                |                |
| Hypothyroidism                                  |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 1 / 3 (33.33%) |
| occurrences (all)                               | 0             | 1              | 1              |
| Inappropriate antidiuretic hormone secretion    |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Musculoskeletal and connective tissue disorders |               |                |                |
| Arthralgia                                      |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Back pain                                       |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 2 / 9 (22.22%) | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0             | 2              | 0              |
| Pain in extremity                               |               |                |                |

|                             |                |                |               |
|-----------------------------|----------------|----------------|---------------|
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 9 (11.11%) | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 1              | 0             |
| Myalgia                     |                |                |               |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 9 (11.11%) | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 1              | 0             |
| Muscular weakness           |                |                |               |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)           | 1              | 0              | 0             |
| Flank pain                  |                |                |               |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Neck pain                   |                |                |               |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Muscle spasms               |                |                |               |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Musculoskeletal chest pain  |                |                |               |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 9 (11.11%) | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 1              | 0             |
| Bursitis                    |                |                |               |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Muscle atrophy              |                |                |               |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Rheumatoid arthritis        |                |                |               |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 9 (11.11%) | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 2              | 0             |
| Infections and infestations |                |                |               |
| COVID-19                    |                |                |               |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 9 (11.11%) | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 1              | 0             |
| Urinary tract infection     |                |                |               |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 9 (11.11%) | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 1              | 0             |

|                                   |               |                |                |
|-----------------------------------|---------------|----------------|----------------|
| Pneumonia                         |               |                |                |
| subjects affected / exposed       | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 1 / 3 (33.33%) |
| occurrences (all)                 | 0             | 1              | 1              |
| Upper respiratory tract infection |               |                |                |
| subjects affected / exposed       | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 3 (0.00%)  |
| occurrences (all)                 | 0             | 1              | 0              |
| Clostridium difficile infection   |               |                |                |
| subjects affected / exposed       | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 3 (0.00%)  |
| occurrences (all)                 | 0             | 2              | 0              |
| Sinusitis                         |               |                |                |
| subjects affected / exposed       | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                 | 0             | 0              | 0              |
| Eye infection                     |               |                |                |
| subjects affected / exposed       | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                 | 0             | 0              | 0              |
| Abscess                           |               |                |                |
| subjects affected / exposed       | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                 | 0             | 0              | 0              |
| Bacteriuria                       |               |                |                |
| subjects affected / exposed       | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 3 (0.00%)  |
| occurrences (all)                 | 0             | 1              | 0              |
| Bronchitis                        |               |                |                |
| subjects affected / exposed       | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                 | 0             | 0              | 0              |
| Cellulitis                        |               |                |                |
| subjects affected / exposed       | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)                 | 0             | 0              | 1              |
| Conjunctivitis                    |               |                |                |
| subjects affected / exposed       | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                 | 0             | 0              | 0              |
| Cystitis                          |               |                |                |
| subjects affected / exposed       | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 3 (0.00%)  |
| occurrences (all)                 | 0             | 1              | 0              |
| Folliculitis                      |               |                |                |
| subjects affected / exposed       | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                 | 0             | 0              | 0              |

|                                                                                      |                      |                     |                     |
|--------------------------------------------------------------------------------------|----------------------|---------------------|---------------------|
| Gastrointestinal viral infection<br>subjects affected / exposed<br>occurrences (all) | 0 / 3 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Herpes simplex<br>subjects affected / exposed<br>occurrences (all)                   | 1 / 3 (33.33%)<br>1  | 0 / 9 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Kidney infection<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 3 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 3 (0.00%)<br>0   | 1 / 9 (11.11%)<br>1 | 0 / 3 (0.00%)<br>0  |
| Pneumonia aspiration<br>subjects affected / exposed<br>occurrences (all)             | 0 / 3 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Rash pustular<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 3 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)      | 0 / 3 (0.00%)<br>0   | 1 / 9 (11.11%)<br>1 | 0 / 3 (0.00%)<br>0  |
| Sepsis<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 3 (0.00%)<br>0   | 1 / 9 (11.11%)<br>1 | 0 / 3 (0.00%)<br>0  |
| Skin infection<br>subjects affected / exposed<br>occurrences (all)                   | 1 / 3 (33.33%)<br>1  | 0 / 9 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Metabolism and nutrition disorders                                                   |                      |                     |                     |
| Decreased appetite<br>subjects affected / exposed<br>occurrences (all)               | 3 / 3 (100.00%)<br>3 | 3 / 9 (33.33%)<br>4 | 1 / 3 (33.33%)<br>1 |
| Hypokalaemia<br>subjects affected / exposed<br>occurrences (all)                     | 1 / 3 (33.33%)<br>1  | 1 / 9 (11.11%)<br>1 | 0 / 3 (0.00%)<br>0  |
| Hyponatraemia                                                                        |                      |                     |                     |

|                             |                |                |               |
|-----------------------------|----------------|----------------|---------------|
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 9 (11.11%) | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 2              | 0             |
| Hyperuricaemia              |                |                |               |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 9 (11.11%) | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 1              | 0             |
| Hypomagnesaemia             |                |                |               |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 9 (11.11%) | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 1              | 0             |
| Dehydration                 |                |                |               |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)           | 1              | 0              | 0             |
| Hyperglycaemia              |                |                |               |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Hypoalbuminaemia            |                |                |               |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 9 (11.11%) | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 1              | 0             |
| Hyperkalaemia               |                |                |               |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Hyperphosphataemia          |                |                |               |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Hypoglycaemia               |                |                |               |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)           | 1              | 0              | 0             |
| Hypophosphataemia           |                |                |               |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Hypercalcaemia              |                |                |               |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 9 (11.11%) | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 1              | 0             |
| Hypocalcaemia               |                |                |               |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Food intolerance            |                |                |               |

|                             |               |                |               |
|-----------------------------|---------------|----------------|---------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 3 (0.00%) |
| occurrences (all)           | 0             | 1              | 0             |
| Hypertriglyceridaemia       |               |                |               |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
|------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 19 March 2021    | The purpose of this amendment was to align the protocol across sponsor programs (inclusion/exclusion criteria) and to make administrative corrections to errors identified in the original protocol, v 1.                                                                                                                                                                                                                                                                                                                                                                                                                       |
| 10 October 2021  | The purpose of this amendment was to add a cohort in the dose expansion phase to further evaluate the efficacy and safety of surufatinib, to define the RP2D, to align the protocol across sponsor programs and to make administrative changes.                                                                                                                                                                                                                                                                                                                                                                                 |
| 16 March 2022    | The purpose of this amendment was to update the inclusion criteria, to provide guidance for diagnosis and management of infusion-related and hypersensitivity reactions and immune-related adverse events, to update the company name following a change, and to make administrative changes.                                                                                                                                                                                                                                                                                                                                   |
| 30 November 2022 | The purpose of this amendment was to provide notification that further enrollment to all study cohorts was halted based upon the strategic evaluation of surufatinib in the United States and Europe with HUTCHMED as the study Sponsor. This change was not based on any concern for patient safety or efficacy relative to surufatinib treatment. Currently enrolled patients who were deriving clinical benefit from treatment with surufatinib could continue to participate in the study as per the protocol. There was no planned interruption in the supply of surufatinib to clinical trial sites with active patients. |
| 29 November 2023 | The purpose of this amendment was to provide notification of the termination of this study based on the strategic re-evaluation of the clinical development of surufatinib in the United States and Europe. This change was not based on any concern for patient safety or efficacy relative to surufatinib and/or tislelizumab treatment.                                                                                                                                                                                                                                                                                      |

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.

The study was terminated based on the strategic re-evaluation of the clinical development of surufatinib in the United States and Europe with no safety concerns.

Notes: