



## Clinical trial results:

**A first-in-human, open-label, dose escalation followed by dose expansion phase I/IIa trial to evaluate the safety, preliminary efficacy and pharmacokinetics of intratumoral CyPep-1 monotherapy and in combination with pembrolizumab in patients with advanced solid cancers.**

### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2019-003317-33 |
| Trial protocol           | NL FR ES       |
| Global end of trial date | 05 July 2024   |

### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 02 July 2025 |
| First version publication date | 02 July 2025 |

### Trial information

#### Trial identification

|                       |         |
|-----------------------|---------|
| Sponsor protocol code | CyPep-1 |
|-----------------------|---------|

#### Additional study identifiers

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

Notes:

### Sponsors

|                              |                                                         |
|------------------------------|---------------------------------------------------------|
| Sponsor organisation name    | Cytovation ASA                                          |
| Sponsor organisation address | 5058 Bergen, Bergen, Norway,                            |
| Public contact               | General contact, Cytovation ASA, contact@cytovation.com |
| Scientific contact           | General contact, Cytovation ASA, contact@cytovation.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                       | 05 December 2024 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 05 July 2024     |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 05 July 2024     |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of IT administration of CyPep-1 as monotherapy and in combination with pembrolizumab.

To identify the recommended phase II dose (RP2D) of CyPep-1 as monotherapy and in combination with pembrolizumab.

Protection of trial subjects:

The Dose Escalation Committee (DEC) was comprised of all the Investigators or designees, medical monitor, and representatives of the Sponsor. The decisions on dose escalation and CyPep 1 maximum tolerated dose (MTD)/recommended Phase 2 dose (RP2D) were taken by the DEC after reviewing safety data (including dose-limiting toxicities [DLTs] from all patients who entered Phase I of the study and completed the DLT observation period). The DEC was responsible for the review of all data after all patients in the highest dose cohort completed the DLT observation period and before enrolment of patients in the expansion cohort at RP2D in monotherapy and combination with pembrolizumab cohort was initiated. The decision to de escalate the dose of CyPep-1 based on the observed severity and relatedness of safety events (DLT/treatment limiting toxicity [TLT] criteria for CyPep-1) and to what dose (either dose level of the next lowest dose level from Phase I or 50-70% of current dose level), was also made by the DEC after reviewing available safety data (including TLTs). Based on the review of this data, recommendations were made regarding the further conduct and the scientific and ethical integrity of the study. The final decision to act upon these recommendations was the responsibility of the Sponsor

Background therapy: -

Evidence for comparator: -

|                                                           |               |
|-----------------------------------------------------------|---------------|
| Actual start date of recruitment                          | 30 April 2020 |
| 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 | Netherlands: 42 |
| Country: Number of subjects enrolled | Spain: 4        |
| Country: Number of subjects enrolled | France: 14      |
| Worldwide total number of subjects   | 60              |
| EEA total number of subjects         | 60              |

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)                      | 20 |
| From 65 to 84 years                       | 40 |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

This study was conducted at 7 investigational sites in 3 countries (France, Spain, and The Netherlands). A total of 87 patients were screened for eligibility, with 27 excluded (25 due to screening failures, and 2 not assigned). Of the original 87 patients screened, 60 were eligible and were allocated into corresponding Phase I and II treatment arms

### Pre-assignment

Screening details:

The study consisted of 2 phases and 4 arms. For both phases and all study arms, patients signed the ICF and completed the Screening visit to determine eligibility to participate in the study. Patients stayed in the study until end of study or until confirmed disease progression, unacceptable toxicity, death or discontinuation for any other reason.

### Period 1

|                              |                |
|------------------------------|----------------|
| Period 1 title               | Phase 1        |
| Is this the baseline period? | Yes            |
| Allocation method            | Not applicable |
| Blinding used                | Not blinded    |

Blinding implementation details:

This was an open-label study, blinding not applicable.

### Arms

|                              |          |
|------------------------------|----------|
| Are arms mutually exclusive? | No       |
| <b>Arm title</b>             | Cohort 1 |

Arm description:

Cohort 1: dose escalation at 0.5 mg/mL, n=3

|                                        |                                                                            |
|----------------------------------------|----------------------------------------------------------------------------|
| Arm type                               | Experimental                                                               |
| Investigational medicinal product name | CyPep-1 0.5 mg/mL                                                          |
| Investigational medicinal product code |                                                                            |
| Other name                             |                                                                            |
| Pharmaceutical forms                   | Solution and suspension for suspension for injection in pre-filled syringe |
| Routes of administration               | Intratumoral use                                                           |

Dosage and administration details:

0.5 mL via intratumoral administration

|                  |          |
|------------------|----------|
| <b>Arm title</b> | Cohort 2 |
|------------------|----------|

Arm description:

Cohort 2: 2 mg/mL, n=5

|                                        |                                                                            |
|----------------------------------------|----------------------------------------------------------------------------|
| Arm type                               | Experimental                                                               |
| Investigational medicinal product name | CyPep-1 2.0 mg/mL                                                          |
| Investigational medicinal product code |                                                                            |
| Other name                             |                                                                            |
| Pharmaceutical forms                   | Solution and suspension for suspension for injection in pre-filled syringe |
| Routes of administration               | Intratumoral use                                                           |

Dosage and administration details:

CyPep-1 2.0 mg/mL intratumoral

|                  |          |
|------------------|----------|
| <b>Arm title</b> | Cohort 3 |
|------------------|----------|

Arm description:

Cohort 3: 5 mg/mL, n=6

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

|                                        |                                                |
|----------------------------------------|------------------------------------------------|
| Investigational medicinal product name | CyPep-1 5.0 mg/mL                              |
| Investigational medicinal product code |                                                |
| Other name                             |                                                |
| Pharmaceutical forms                   | Suspension for injection in pre-filled syringe |
| Routes of administration               | Intratumoral use                               |
| Dosage and administration details:     |                                                |
| 5.0 mg/mL via intratumoral             |                                                |

| Number of subjects in period 1 | Cohort 1 | Cohort 2 | Cohort 3 |
|--------------------------------|----------|----------|----------|
| Started                        | 3        | 5        | 6        |
| Completed                      | 0        | 0        | 0        |
| Not completed                  | 3        | 5        | 6        |
| Consent withdrawn by subject   | -        | 1        | -        |
| Death                          | 3        | 4        | 6        |

## Period 2

|                                                        |                |
|--------------------------------------------------------|----------------|
| Period 2 title                                         | Phase 2        |
| Is this the baseline period?                           | No             |
| Allocation method                                      | Not applicable |
| Blinding used                                          | Not blinded    |
| Blinding implementation details:                       |                |
| This was an open-label study, blinding not applicable. |                |

## Arms

|                              |       |
|------------------------------|-------|
| Are arms mutually exclusive? | No    |
| Arm title                    | Arm B |

### Arm description:

The safety and tolerability of CyPep-1 in combination with pembrolizumab was evaluated in a cohort of 15 patients in total, using a staggered approach. Initially, 3 patients received CyPep-1 at RP2D in combination with pembrolizumab once every 6 weeks

|                                        |                                                                            |
|----------------------------------------|----------------------------------------------------------------------------|
| Arm type                               | Experimental                                                               |
| Investigational medicinal product name | CyPep-1 5.0 mg/mL + IV pembrolizumab                                       |
| Investigational medicinal product code |                                                                            |
| Other name                             |                                                                            |
| Pharmaceutical forms                   | Solution and suspension for suspension for injection in pre-filled syringe |
| Routes of administration               | Intratumoral use                                                           |

### Dosage and administration details:

5.0mg/mL via intratumoral administration

|           |                  |
|-----------|------------------|
| Arm title | Arm C (Cohort 4) |
|-----------|------------------|

### Arm description:

the safety and tolerability of at least 2 dose levels of CyPep-1, the RP2D and the dose immediately below that, were evaluated when CyPep-1 was administered IT using ultrasound guidance to one metastatic lesion in the liver (Cohort 4: 2 mg/mL, n=6)

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

|                                                                                                                                                                                                                                                                                        |                                                                            |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------|
| Investigational medicinal product name                                                                                                                                                                                                                                                 | CyPep-1 2.0 mg/mL for liver metastases                                     |
| Investigational medicinal product code                                                                                                                                                                                                                                                 |                                                                            |
| Other name                                                                                                                                                                                                                                                                             |                                                                            |
| Pharmaceutical forms                                                                                                                                                                                                                                                                   | Solution and suspension for suspension for injection in pre-filled syringe |
| Routes of administration                                                                                                                                                                                                                                                               | Intratumoral use                                                           |
| Dosage and administration details:<br>2.0mg/mL via intratumoral administration                                                                                                                                                                                                         |                                                                            |
| <b>Arm title</b>                                                                                                                                                                                                                                                                       | Arm C (Cohort 5)                                                           |
| Arm description:<br>The safety and tolerability of at least 2 dose levels of CyPep-1, the RP2D and the dose immediately below that, were evaluated when CyPep-1 was administered IT using ultrasound guidance to one metastatic lesion in the liver. The RP2D (Cohort 5: 5 mg/mL, n=6) |                                                                            |
| Arm type                                                                                                                                                                                                                                                                               | Experimental                                                               |
| Investigational medicinal product name                                                                                                                                                                                                                                                 | CyPep-1 5.0 mg/mL for liver metastases                                     |
| Investigational medicinal product code                                                                                                                                                                                                                                                 |                                                                            |
| Other name                                                                                                                                                                                                                                                                             |                                                                            |
| Pharmaceutical forms                                                                                                                                                                                                                                                                   | Solution for injection/infusion in pre-filled syringe                      |
| Routes of administration                                                                                                                                                                                                                                                               | Intratumoral use                                                           |
| Dosage and administration details:<br>5.0mg/mL via intratumoral administration                                                                                                                                                                                                         |                                                                            |
| <b>Arm title</b>                                                                                                                                                                                                                                                                       | Arm D                                                                      |
| Arm description:<br>The safety and tolerability of CyPep-1 at RP2D was planned to be further evaluated with focus on assessing efficacy signals of CyPep-1 monotherapy in 30 patients with cutaneous melanoma                                                                          |                                                                            |
| Arm type                                                                                                                                                                                                                                                                               | Experimental                                                               |
| Investigational medicinal product name                                                                                                                                                                                                                                                 | CyPep-1 5.0 mg/mL for melanoma                                             |
| Investigational medicinal product code                                                                                                                                                                                                                                                 |                                                                            |
| Other name                                                                                                                                                                                                                                                                             |                                                                            |
| Pharmaceutical forms                                                                                                                                                                                                                                                                   | Solution and suspension for suspension for injection in pre-filled syringe |
| Routes of administration                                                                                                                                                                                                                                                               | Intratumoral use                                                           |
| Dosage and administration details:<br>5.0mg/mL via intratumoral administration                                                                                                                                                                                                         |                                                                            |
| <b>Arm title</b>                                                                                                                                                                                                                                                                       | Arm A                                                                      |
| Arm description:<br>CyPep-1 5.0mg/mL Monotherapy                                                                                                                                                                                                                                       |                                                                            |
| Arm type                                                                                                                                                                                                                                                                               | Experimental                                                               |
| Investigational medicinal product name                                                                                                                                                                                                                                                 | CyPep-1 5.0 mg/mL Monotherapy                                              |
| Investigational medicinal product code                                                                                                                                                                                                                                                 |                                                                            |
| Other name                                                                                                                                                                                                                                                                             |                                                                            |
| Pharmaceutical forms                                                                                                                                                                                                                                                                   | Solution and suspension for suspension for injection in pre-filled syringe |
| Routes of administration                                                                                                                                                                                                                                                               | Intratumoral use                                                           |
| Dosage and administration details:<br>5.0 mg/mL via intratumoral                                                                                                                                                                                                                       |                                                                            |

| <b>Number of subjects in period 2</b> | Arm B | Arm C (Cohort 4) | Arm C (Cohort 5) |
|---------------------------------------|-------|------------------|------------------|
| Started                               | 15    | 6                | 6                |
| Completed                             | 1     | 1                | 0                |
| Not completed                         | 14    | 5                | 6                |
| Consent withdrawn by subject          | -     | -                | -                |
| Death                                 | 14    | 5                | 5                |
| Termination of the study              | -     | -                | -                |
| Sponsor terminated                    | -     | -                | 1                |

| <b>Number of subjects in period 2</b> | Arm D | Arm A |
|---------------------------------------|-------|-------|
| Started                               | 1     | 18    |
| Completed                             | 0     | 2     |
| Not completed                         | 1     | 16    |
| Consent withdrawn by subject          | 1     | 2     |
| Death                                 | -     | 13    |
| Termination of the study              | -     | 1     |
| Sponsor terminated                    | -     | -     |

## Baseline characteristics

### Reporting groups<sup>[1]</sup>

|                                             |          |
|---------------------------------------------|----------|
| Reporting group title                       | Cohort 1 |
| Reporting group description:                |          |
| Cohort 1: dose escalation at 0.5 mg/mL, n=3 |          |
| Reporting group title                       | Cohort 2 |
| Reporting group description:                |          |
| Cohort 2: 2 mg/mL, n=5                      |          |
| Reporting group title                       | Cohort 3 |
| Reporting group description:                |          |
| Cohort 3: 5 mg/mL, n=6                      |          |

Notes:

[1] - The number of subjects reported to be in the baseline period is not equal to the worldwide number of subjects enrolled in the trial. It is expected that these numbers will be the same.

Justification: The number of subjects in both the phases are different because the arms are not mutually exclusive. The subjects in Phase 1 (dose escalation) did not roll over into Phase 2 (dose expansion).

| Reporting group values                             | Cohort 1 | Cohort 2 | Cohort 3 |
|----------------------------------------------------|----------|----------|----------|
| Number of subjects                                 | 3        | 5        | 6        |
| Age categorical                                    |          |          |          |
| Units: Subjects                                    |          |          |          |
| In utero                                           | 0        | 0        | 0        |
| Preterm newborn infants (gestational age < 37 wks) | 0        | 0        | 0        |
| Newborns (0-27 days)                               | 0        | 0        | 0        |
| Infants and toddlers (28 days-23 months)           | 0        | 0        | 0        |
| Children (2-11 years)                              | 0        | 0        | 0        |
| Adolescents (12-17 years)                          | 0        | 0        | 0        |
| Adults (18-64 years)                               | 0        | 2        | 2        |
| From 65-84 years                                   | 3        | 3        | 4        |
| 85 years and over                                  | 0        | 0        | 0        |
| Age continuous                                     |          |          |          |
| Units: years                                       |          |          |          |
| median                                             | 53       | 64       | 57.0     |
| standard deviation                                 | ± 11.2   | ± 10.8   | ± 5.9    |
| Gender categorical                                 |          |          |          |
| Units: Subjects                                    |          |          |          |
| Female                                             | 1        | 2        | 2        |
| Male                                               | 2        | 3        | 4        |

| Reporting group values                             | Total |  |  |
|----------------------------------------------------|-------|--|--|
| Number of subjects                                 | 14    |  |  |
| Age categorical                                    |       |  |  |
| Units: Subjects                                    |       |  |  |
| In utero                                           | 0     |  |  |
| Preterm newborn infants (gestational age < 37 wks) | 0     |  |  |
| Newborns (0-27 days)                               | 0     |  |  |
| Infants and toddlers (28 days-23 months)           | 0     |  |  |
| Children (2-11 years)                              | 0     |  |  |

|                           |    |  |  |
|---------------------------|----|--|--|
| Adolescents (12-17 years) | 0  |  |  |
| Adults (18-64 years)      | 4  |  |  |
| From 65-84 years          | 10 |  |  |
| 85 years and over         | 0  |  |  |
| Age continuous            |    |  |  |
| Units: years              |    |  |  |
| median                    |    |  |  |
| standard deviation        | -  |  |  |
| Gender categorical        |    |  |  |
| Units: Subjects           |    |  |  |
| Female                    | 5  |  |  |
| Male                      | 9  |  |  |

## End points

### End points reporting groups

|                                                                                                                                                                                                                                                                                                    |                  |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------|
| Reporting group title                                                                                                                                                                                                                                                                              | Cohort 1         |
| Reporting group description:<br>Cohort 1: dose escalation at 0.5 mg/mL, n=3                                                                                                                                                                                                                        |                  |
| Reporting group title                                                                                                                                                                                                                                                                              | Cohort 2         |
| Reporting group description:<br>Cohort 2: 2 mg/mL, n=5                                                                                                                                                                                                                                             |                  |
| Reporting group title                                                                                                                                                                                                                                                                              | Cohort 3         |
| Reporting group description:<br>Cohort 3: 5 mg/mL, n=6                                                                                                                                                                                                                                             |                  |
| Reporting group title                                                                                                                                                                                                                                                                              | Arm B            |
| Reporting group description:<br>The safety and tolerability of CyPep-1 in combination with pembrolizumab was evaluated in a cohort of 15 patients in total, using a staggered approach. Initially, 3 patients received CyPep-1 at RP2D in combination with pembrolizumab once every 6 weeks        |                  |
| Reporting group title                                                                                                                                                                                                                                                                              | Arm C (Cohort 4) |
| Reporting group description:<br>the safety and tolerability of at least 2 dose levels of CyPep-1, the RP2D and the dose immediately below that, were evaluated when CyPep-1 was administered IT using ultrasound guidance to one metastatic lesion in the liver (Cohort 4: 2 mg/mL, n=6)           |                  |
| Reporting group title                                                                                                                                                                                                                                                                              | Arm C (Cohort 5) |
| Reporting group description:<br>The safety and tolerability of at least 2 dose levels of CyPep-1, the RP2D and the dose immediately below that, were evaluated when CyPep-1 was administered IT using ultrasound guidance to one metastatic lesion in the liver. The RP2D (Cohort 5: 5 mg/mL, n=6) |                  |
| Reporting group title                                                                                                                                                                                                                                                                              | Arm D            |
| Reporting group description:<br>The safety and tolerability of CyPep-1 at RP2D was planned to be further evaluated with focus on assessing efficacy signals of CyPep-1 monotherapy in 30 patients with cutaneous melanoma                                                                          |                  |
| Reporting group title                                                                                                                                                                                                                                                                              | Arm A            |
| Reporting group description:<br>CyPep-1 5.0mg/mL Monotherapy                                                                                                                                                                                                                                       |                  |

### Primary: Type and number of adverse events

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                  |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Type and number of adverse events <sup>[1]</sup> |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                  |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | Primary                                          |
| End point timeframe:<br>From the time of ICF signing until Follow up visit (or until EoT, if it occurred >30 days after the last CyPep-1 administration for Phase I and Arms A, C, and D; for Arm B. After the FU visit, only ongoing AEs or SAEs related to CyPep-1 were collected.                                                                                                                                                                                                                                       |                                                  |
| Notes:<br>[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.<br>Justification: Descriptive statistics was used. The total number/incidence of TEAEs was summarized, including the number of patients with at least one TEAE and the number of TEAEs per cohort and overall. The number of TEAEs per intensity (CTCAE) and relation to study drug was also included and summarized per cohort and overall. |                                                  |

| End point values                                | Cohort 1        | Cohort 2        | Cohort 3        | Arm B           |
|-------------------------------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type                              | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed                     | 3               | 5               | 6               | 15              |
| Units: Number of events                         |                 |                 |                 |                 |
| TEAE                                            | 24              | 37              | 62              | 262             |
| TESAE                                           | 1               | 0               | 0               | 7               |
| CTCAE Grade $\geq 3$                            | 9               | 4               | 5               | 12              |
| TEAE Leading to Study Treatment Discontinuation | 0               | 0               | 1               | 0               |
| Dose-Limiting Toxicity                          | 0               | 0               | 0               | 0               |
| Treatment-Limiting Toxicity                     | 0               | 0               | 0               | 0               |
| Fatal TEAE                                      | 0               | 0               | 0               | 0               |
| TEAE Leading to CyPep-1 Interruption            | 1               | 1               | 1               | 8               |
| TEAE Leading to Pembrolizumab Interruption      | 0               | 0               | 0               | 5               |

| End point values                                | Arm C (Cohort 4) | Arm C (Cohort 5) | Arm D           | Arm A           |
|-------------------------------------------------|------------------|------------------|-----------------|-----------------|
| Subject group type                              | Reporting group  | Reporting group  | Reporting group | Reporting group |
| Number of subjects analysed                     | 6                | 6                | 1               | 18              |
| Units: Number of events                         |                  |                  |                 |                 |
| TEAE                                            | 91               | 91               | 4               | 143             |
| TESAE                                           | 1                | 3                | 0               | 3               |
| CTCAE Grade $\geq 3$                            | 4                | 12               | 0               | 8               |
| TEAE Leading to Study Treatment Discontinuation | 0                | 0                | 0               | 1               |
| Dose-Limiting Toxicity                          | 0                | 2                | 0               | 0               |
| Treatment-Limiting Toxicity                     | 0                | 0                | 0               | 0               |
| Fatal TEAE                                      | 0                | 1                | 0               | 0               |
| TEAE Leading to CyPep-1 Interruption            | 1                | 2                | 0               | 10              |
| TEAE Leading to Pembrolizumab Interruption      | 0                | 0                | 0               | 0               |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Objective response rate (ORR)

|                 |                               |
|-----------------|-------------------------------|
| End point title | Objective response rate (ORR) |
|-----------------|-------------------------------|

End point description:

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

End point timeframe:

28 days after the date of the initial response

| End point values            | Cohort 1        | Cohort 2        | Cohort 3        | Arm B           |
|-----------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type          | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3               | 5               | 6               | 15              |
| Units: percentage           |                 |                 |                 |                 |
| number (not applicable)     |                 |                 |                 |                 |
| Overall Response Rate       | 0               | 0               | 0               | 0               |

| End point values            | Arm C (Cohort 4) | Arm C (Cohort 5) | Arm D           | Arm A           |
|-----------------------------|------------------|------------------|-----------------|-----------------|
| Subject group type          | Reporting group  | Reporting group  | Reporting group | Reporting group |
| Number of subjects analysed | 6                | 6                | 1               | 18              |
| Units: percentage           |                  |                  |                 |                 |
| number (not applicable)     |                  |                  |                 |                 |
| Overall Response Rate       | 16.7             | 0                | 0               | 0               |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Overall Survival

|                                                    |                     |
|----------------------------------------------------|---------------------|
| End point title                                    | Overall Survival    |
| End point description:                             |                     |
| End point type                                     | Other pre-specified |
| End point timeframe:                               |                     |
| from start of study treatment to the date of death |                     |

| End point values              | Cohort 1          | Cohort 2          | Cohort 3           | Arm B             |
|-------------------------------|-------------------|-------------------|--------------------|-------------------|
| Subject group type            | Reporting group   | Reporting group   | Reporting group    | Reporting group   |
| Number of subjects analysed   | 3                 | 5                 | 6                  | 15                |
| Units: Months                 |                   |                   |                    |                   |
| median (full range (min-max)) | 5.2 (2.1 to 21.9) | 5.5 (0.6 to 16.6) | 13.2 (5.3 to 19.8) | 5.8 (1.5 to 26.7) |

| End point values              | Arm C (Cohort 4)  | Arm C (Cohort 5)  | Arm D           | Arm A             |
|-------------------------------|-------------------|-------------------|-----------------|-------------------|
| Subject group type            | Reporting group   | Reporting group   | Reporting group | Reporting group   |
| Number of subjects analysed   | 6                 | 6                 | 1               | 18                |
| Units: Months                 |                   |                   |                 |                   |
| median (full range (min-max)) | 8.3 (3.3 to 26.3) | 4.2 (3.3 to 26.3) | 0 (0 to 0)      | 7.7 (1.0 to 26.2) |

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Progression free survival

|                 |                           |
|-----------------|---------------------------|
| End point title | Progression free survival |
|-----------------|---------------------------|

End point description:

|                |                     |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

time from treatment start until disease relapse or disease progression (based on all lesions, using iRECIST) or death due to any cause, whichever occurred earliest

| End point values              | Cohort 1         | Cohort 2         | Cohort 3          | Arm B            |
|-------------------------------|------------------|------------------|-------------------|------------------|
| Subject group type            | Reporting group  | Reporting group  | Reporting group   | Reporting group  |
| Number of subjects analysed   | 3                | 5                | 6                 | 15               |
| Units: Months                 |                  |                  |                   |                  |
| median (full range (min-max)) | 1.6 (1.2 to 1.9) | 0.9 (0.0 to 9.3) | 2.8 (1.6 to 12.3) | 1.8 (0.0 to 5.4) |

| End point values              | Arm C (Cohort 4) | Arm C (Cohort 5)  | Arm D             | Arm A            |
|-------------------------------|------------------|-------------------|-------------------|------------------|
| Subject group type            | Reporting group  | Reporting group   | Reporting group   | Reporting group  |
| Number of subjects analysed   | 6                | 6                 | 1                 | 18               |
| Units: Months                 |                  |                   |                   |                  |
| median (full range (min-max)) | 2.1 (1.4 to 5.7) | 1.9 (1.8 to 16.6) | 1.9 (1.8 to 16.6) | 1.8 (0.0 to 5.4) |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From the time of ICF signing until Follow up visit (or until EoT, if it occurred >30 days after the last CyPep-1 administration for Phase I and Arms A, C, and D; for Arm B. After the FU visit, only ongoing AEs or SAEs related to CyPep-1 were collected.

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

### Dictionary used

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

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

### Reporting groups

|                       |          |
|-----------------------|----------|
| Reporting group title | Cohort 1 |
|-----------------------|----------|

Reporting group description:

CyPep-1 5.0 mg/mL Monotherapy

|                       |          |
|-----------------------|----------|
| Reporting group title | Cohort 2 |
|-----------------------|----------|

Reporting group description:

CyPep-1 2.0 mg/mL

|                       |          |
|-----------------------|----------|
| Reporting group title | Cohort 3 |
|-----------------------|----------|

Reporting group description:

CyPep-1 5.0 mg/mL

|                       |       |
|-----------------------|-------|
| Reporting group title | Arm A |
|-----------------------|-------|

Reporting group description:

CyPep-1 5.0 mg/mL Monotherapy

|                       |       |
|-----------------------|-------|
| Reporting group title | Arm B |
|-----------------------|-------|

Reporting group description:

CyPep-1 5.0 mg/mL + IV pembrolizumab

|                       |                  |
|-----------------------|------------------|
| Reporting group title | Arm C (Cohort 4) |
|-----------------------|------------------|

Reporting group description:

CyPep-1 2.0 mg/mL for liver metastases

|                       |                  |
|-----------------------|------------------|
| Reporting group title | Arm C (Cohort 5) |
|-----------------------|------------------|

Reporting group description:

CyPep-1 5.0 mg/mL for liver metastases

|                       |       |
|-----------------------|-------|
| Reporting group title | Arm D |
|-----------------------|-------|

Reporting group description:

CyPep-1 5.0 mg/mL for melanoma

| Serious adverse events                            | Cohort 1       | Cohort 2      | Cohort 3      |
|---------------------------------------------------|----------------|---------------|---------------|
| Total subjects affected by serious adverse events |                |               |               |
| subjects affected / exposed                       | 1 / 3 (33.33%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| number of deaths (all causes)                     | 3              | 4             | 6             |
| number of deaths resulting from adverse events    | 0              | 0             | 0             |
| Vascular disorders                                |                |               |               |
| Brachiocephalic vein thrombosis                   |                |               |               |

|                                                      |               |               |               |
|------------------------------------------------------|---------------|---------------|---------------|
| subjects affected / exposed                          | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| 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 |               |               |               |
| Injection site hypersensitivity                      |               |               |               |
| subjects affected / exposed                          | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0         | 0 / 0         | 0 / 0         |
| Injection site ulcer                                 |               |               |               |
| subjects affected / exposed                          | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0         | 0 / 0         | 0 / 0         |
| Face oedema                                          |               |               |               |
| subjects affected / exposed                          | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0         | 0 / 0         | 0 / 0         |
| Injection site inflammation                          |               |               |               |
| subjects affected / exposed                          | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| 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 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| 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                           |               |               |               |
| Rectal haemorrhage                                   |               |               |               |
| subjects affected / exposed                          | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| 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      |               |               |               |
| Dyspnea                                              |               |               |               |

|                                                 |                |               |               |
|-------------------------------------------------|----------------|---------------|---------------|
| subjects affected / exposed                     | 1 / 3 (33.33%) | 0 / 5 (0.00%) | 0 / 6 (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         |
| Endocrine disorders                             |                |               |               |
| Adrenal insufficiency                           |                |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Product issues                                  |                |               |               |
| Device dislocation                              |                |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Infections and infestations                     |                |               |               |
| Pneumonia                                       |                |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| 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              |                |               |               |
| Hypoglycaemia                                   |                |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Malnutrition                                    |                |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Hypercalcemia                                   |                |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| 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>                     | Arm A           | Arm B           | Arm C (Cohort 4) |
| Total subjects affected by serious adverse events |                 |                 |                  |
| subjects affected / exposed                       | 3 / 18 (16.67%) | 2 / 15 (13.33%) | 1 / 6 (16.67%)   |

|                                                      |                |                |               |
|------------------------------------------------------|----------------|----------------|---------------|
| number of deaths (all causes)                        | 13             | 14             | 5             |
| number of deaths resulting from adverse events       | 0              | 0              | 0             |
| Vascular disorders                                   |                |                |               |
| Brachiocephalic vein thrombosis                      |                |                |               |
| subjects affected / exposed                          | 0 / 18 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (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         |
| General disorders and administration site conditions |                |                |               |
| Injection site hypersensitivity                      |                |                |               |
| subjects affected / exposed                          | 1 / 18 (5.56%) | 0 / 15 (0.00%) | 0 / 6 (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         |
| Injection site ulcer                                 |                |                |               |
| subjects affected / exposed                          | 1 / 18 (5.56%) | 0 / 15 (0.00%) | 0 / 6 (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         |
| Face oedema                                          |                |                |               |
| subjects affected / exposed                          | 0 / 18 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (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         |
| Injection site inflammation                          |                |                |               |
| subjects affected / exposed                          | 0 / 18 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (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         |
| Fatigue                                              |                |                |               |
| subjects affected / exposed                          | 0 / 18 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (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                           |                |                |               |
| Rectal haemorrhage                                   |                |                |               |
| subjects affected / exposed                          | 0 / 18 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| 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      |                |                |               |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| Dyspnea                                         |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 7          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Endocrine disorders                             |                |                |                |
| Adrenal insufficiency                           |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 15 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Product issues                                  |                |                |                |
| Device dislocation                              |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (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          |
| Infections and infestations                     |                |                |                |
| Pneumonia                                       |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| 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              |                |                |                |
| Hypoglycaemia                                   |                |                |                |
| subjects affected / exposed                     | 1 / 18 (5.56%) | 0 / 15 (0.00%) | 0 / 6 (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          |
| Malnutrition                                    |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (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          |
| Hypercalcemia                                   |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (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>Serious adverse events</b>                     | Arm C (Cohort 5) | Arm D |  |
| Total subjects affected by serious adverse events |                  |       |  |

|                                                      |                |               |  |
|------------------------------------------------------|----------------|---------------|--|
| subjects affected / exposed                          | 2 / 6 (33.33%) | 0 / 1 (0.00%) |  |
| number of deaths (all causes)                        | 5              | 0             |  |
| number of deaths resulting from adverse events       | 0              | 0             |  |
| Vascular disorders                                   |                |               |  |
| Brachiocephalic vein thrombosis                      |                |               |  |
| subjects affected / exposed                          | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         |  |
| General disorders and administration site conditions |                |               |  |
| Injection site hypersensitivity                      |                |               |  |
| subjects affected / exposed                          | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         |  |
| Injection site ulcer                                 |                |               |  |
| subjects affected / exposed                          | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         |  |
| Face oedema                                          |                |               |  |
| subjects affected / exposed                          | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         |  |
| Injection site inflammation                          |                |               |  |
| subjects affected / exposed                          | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         |  |
| Fatigue                                              |                |               |  |
| subjects affected / exposed                          | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         |  |
| Gastrointestinal disorders                           |                |               |  |
| Rectal haemorrhage                                   |                |               |  |
| subjects affected / exposed                          | 1 / 6 (16.67%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0         |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         |  |
| Respiratory, thoracic and mediastinal                |                |               |  |

|                                                 |                |               |  |
|-------------------------------------------------|----------------|---------------|--|
| disorders                                       |                |               |  |
| Dyspnea                                         |                |               |  |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Endocrine disorders                             |                |               |  |
| Adrenal insufficiency                           |                |               |  |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Product issues                                  |                |               |  |
| Device dislocation                              |                |               |  |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Infections and infestations                     |                |               |  |
| Pneumonia                                       |                |               |  |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Metabolism and nutrition disorders              |                |               |  |
| Hypoglycaemia                                   |                |               |  |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Malnutrition                                    |                |               |  |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Hypercalcemia                                   |                |               |  |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |

| <b>Non-serious adverse events</b>                                   | Cohort 1        | Cohort 2        | Cohort 3        |
|---------------------------------------------------------------------|-----------------|-----------------|-----------------|
| Total subjects affected by non-serious adverse events               |                 |                 |                 |
| subjects affected / exposed                                         | 3 / 3 (100.00%) | 5 / 5 (100.00%) | 6 / 6 (100.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                 |                 |                 |
| Cancer pain                                                         |                 |                 |                 |
| subjects affected / exposed                                         | 0 / 3 (0.00%)   | 2 / 5 (40.00%)  | 2 / 6 (33.33%)  |
| occurrences (all)                                                   | 0               | 4               | 14              |
| Metastases to bone                                                  |                 |                 |                 |
| subjects affected / exposed                                         | 0 / 3 (0.00%)   | 0 / 5 (0.00%)   | 0 / 6 (0.00%)   |
| occurrences (all)                                                   | 0               | 0               | 0               |
| Tumour thrombosis                                                   |                 |                 |                 |
| subjects affected / exposed                                         | 0 / 3 (0.00%)   | 0 / 5 (0.00%)   | 0 / 6 (0.00%)   |
| occurrences (all)                                                   | 0               | 0               | 0               |
| Vascular disorders                                                  |                 |                 |                 |
| Hypotension                                                         |                 |                 |                 |
| subjects affected / exposed                                         | 0 / 3 (0.00%)   | 0 / 5 (0.00%)   | 0 / 6 (0.00%)   |
| occurrences (all)                                                   | 0               | 0               | 0               |
| Brachiocephalic vein thrombosis                                     |                 |                 |                 |
| subjects affected / exposed                                         | 0 / 3 (0.00%)   | 0 / 5 (0.00%)   | 0 / 6 (0.00%)   |
| occurrences (all)                                                   | 0               | 0               | 0               |
| Haematoma                                                           |                 |                 |                 |
| subjects affected / exposed                                         | 0 / 3 (0.00%)   | 0 / 5 (0.00%)   | 0 / 6 (0.00%)   |
| occurrences (all)                                                   | 0               | 0               | 0               |
| Hypertension                                                        |                 |                 |                 |
| subjects affected / exposed                                         | 0 / 3 (0.00%)   | 0 / 5 (0.00%)   | 0 / 6 (0.00%)   |
| occurrences (all)                                                   | 0               | 0               | 0               |
| Peripheral coldness                                                 |                 |                 |                 |
| subjects affected / exposed                                         | 0 / 3 (0.00%)   | 0 / 5 (0.00%)   | 0 / 6 (0.00%)   |
| occurrences (all)                                                   | 0               | 0               | 0               |
| General disorders and administration site conditions                |                 |                 |                 |
| Fatigue                                                             |                 |                 |                 |
| subjects affected / exposed                                         | 0 / 3 (0.00%)   | 3 / 5 (60.00%)  | 3 / 6 (50.00%)  |
| occurrences (all)                                                   | 0               | 3               | 5               |
| Pyrexia                                                             |                 |                 |                 |

|                             |                |                |                 |
|-----------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 5 (0.00%)  | 0 / 6 (0.00%)   |
| occurrences (all)           | 1              | 0              | 0               |
| Oedema peripheral           |                |                |                 |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 5 (0.00%)  | 0 / 6 (0.00%)   |
| occurrences (all)           | 1              | 0              | 0               |
| Influenza like illness      |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 1 / 6 (16.67%)  |
| occurrences (all)           | 0              | 0              | 1               |
| Pain                        |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 5 (20.00%) | 0 / 6 (0.00%)   |
| occurrences (all)           | 0              | 1              | 0               |
| Catheter site haemorrhage   |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 5 (20.00%) | 0 / 6 (0.00%)   |
| occurrences (all)           | 0              | 1              | 0               |
| Injection site reaction     |                |                |                 |
| subjects affected / exposed | 1 / 3 (33.33%) | 4 / 5 (80.00%) | 6 / 6 (100.00%) |
| occurrences (all)           | 2              | 6              | 23              |
| Malaise                     |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 6 (0.00%)   |
| occurrences (all)           | 0              | 0              | 0               |
| Chills                      |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 6 (0.00%)   |
| occurrences (all)           | 0              | 0              | 0               |
| Injection site haematoma    |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 6 (0.00%)   |
| occurrences (all)           | 0              | 0              | 0               |
| Face oedema                 |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 6 (0.00%)   |
| occurrences (all)           | 0              | 0              | 0               |
| Non-cardiac chest pain      |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 6 (0.00%)   |
| occurrences (all)           | 0              | 0              | 0               |
| Asthenia                    |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 6 (0.00%)   |
| occurrences (all)           | 0              | 0              | 0               |
| Inflammation                |                |                |                 |

|                                                                                                                   |                     |                     |                     |
|-------------------------------------------------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)                                                                  | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Injection site injury<br>subjects affected / exposed<br>occurrences (all)                                         | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Immune system disorders<br>Hypersensitivity<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Reproductive system and breast disorders<br>Breast tenderness<br>subjects affected / exposed<br>occurrences (all) | 1 / 3 (33.33%)<br>1 | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Postmenopausal haemorrhage<br>subjects affected / exposed<br>occurrences (all)                                    | 1 / 3 (33.33%)<br>1 | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Respiratory, thoracic and mediastinal disorders<br>Dyspnoea<br>subjects affected / exposed<br>occurrences (all)   | 1 / 3 (33.33%)<br>2 | 1 / 5 (20.00%)<br>1 | 1 / 6 (16.67%)<br>1 |
| Hypoxia<br>subjects affected / exposed<br>occurrences (all)                                                       | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 1 / 6 (16.67%)<br>1 |
| Cough<br>subjects affected / exposed<br>occurrences (all)                                                         | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Pleural effusion<br>subjects affected / exposed<br>occurrences (all)                                              | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Dyspnoea at rest<br>subjects affected / exposed<br>occurrences (all)                                              | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Dyspnoea exertional<br>subjects affected / exposed<br>occurrences (all)                                           | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Laryngeal oedema                                                                                                  |                     |                     |                     |

|                                                                                                            |                     |                    |                    |
|------------------------------------------------------------------------------------------------------------|---------------------|--------------------|--------------------|
| subjects affected / exposed<br>occurrences (all)                                                           | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 |
| Pneumonitis<br>subjects affected / exposed<br>occurrences (all)                                            | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 |
| Pneumothorax<br>subjects affected / exposed<br>occurrences (all)                                           | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 |
| Productive cough<br>subjects affected / exposed<br>occurrences (all)                                       | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 |
| Psychiatric disorders<br>Insomnia<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 |
| Depression<br>subjects affected / exposed<br>occurrences (all)                                             | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 |
| Anxiety<br>subjects affected / exposed<br>occurrences (all)                                                | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 |
| Confusional state<br>subjects affected / exposed<br>occurrences (all)                                      | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 |
| Delirium<br>subjects affected / exposed<br>occurrences (all)                                               | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 |
| Product issues<br>Device dislocation<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 |
| Investigations<br>Blood alkaline phosphatase increased<br>subjects affected / exposed<br>occurrences (all) | 1 / 3 (33.33%)<br>1 | 0 / 5 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 |
| Gamma-glutamyltransferase<br>increased                                                                     |                     |                    |                    |

|                                      |                |                |                |
|--------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed          | 1 / 3 (33.33%) | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 2              | 0              | 0              |
| Alanine aminotransferase increased   |                |                |                |
| subjects affected / exposed          | 1 / 3 (33.33%) | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 1              | 0              | 0              |
| Weight decreased                     |                |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 1 / 5 (20.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0              | 1              | 0              |
| Blood bilirubin increased            |                |                |                |
| subjects affected / exposed          | 1 / 3 (33.33%) | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 1              | 0              | 0              |
| Platelet count decreased             |                |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)                    | 0              | 0              | 1              |
| Electrocardiogram QT prolonged       |                |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 1 / 5 (20.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0              | 1              | 0              |
| Lipase increased                     |                |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Blood creatinine increased           |                |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Aspartate aminotransferase increased |                |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Amylase increased                    |                |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Lymphocyte count decreased           |                |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Urine output decreased               |                |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |

|                                                             |               |               |                |
|-------------------------------------------------------------|---------------|---------------|----------------|
| Injury, poisoning and procedural complications              |               |               |                |
| Post procedural complication<br>subjects affected / exposed | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all)                                           | 0             | 0             | 1              |
| Procedural pain<br>subjects affected / exposed              | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                                           | 0             | 0             | 0              |
| Drain site complication<br>subjects affected / exposed      | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                                           | 0             | 0             | 0              |
| Fall<br>subjects affected / exposed                         | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                                           | 0             | 0             | 0              |
| Post procedural erythema<br>subjects affected / exposed     | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                                           | 0             | 0             | 0              |
| Post procedural fever<br>subjects affected / exposed        | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                                           | 0             | 0             | 0              |
| Post procedural haematoma<br>subjects affected / exposed    | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                                           | 0             | 0             | 0              |
| Stoma site erythema<br>subjects affected / exposed          | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                                           | 0             | 0             | 0              |
| Cardiac disorders                                           |               |               |                |
| Myocardial infarction<br>subjects affected / exposed        | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                                           | 0             | 0             | 0              |
| Palpitations<br>subjects affected / exposed                 | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                                           | 0             | 0             | 0              |
| Sinus tachycardia<br>subjects affected / exposed            | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                                           | 0             | 0             | 0              |
| Nervous system disorders                                    |               |               |                |

|                                      |               |                |                |
|--------------------------------------|---------------|----------------|----------------|
| Dizziness                            |               |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%) | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Aphasia                              |               |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%) | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Brachial plexopathy                  |               |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%) | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Depressed level of consciousness     |               |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%) | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Disturbance in attention             |               |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%) | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Headache                             |               |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%) | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Neuropathy peripheral                |               |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%) | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Peripheral sensory neuropathy        |               |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%) | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Presyncope                           |               |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%) | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Somnolence                           |               |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%) | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Blood and lymphatic system disorders |               |                |                |
| Anaemia                              |               |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%) | 2 / 5 (40.00%) | 2 / 6 (33.33%) |
| occurrences (all)                    | 0             | 2              | 3              |
| Ear and labyrinth disorders          |               |                |                |

|                                                                                                |                     |                     |                     |
|------------------------------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| Ear discomfort<br>subjects affected / exposed<br>occurrences (all)                             | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Ear pain<br>subjects affected / exposed<br>occurrences (all)                                   | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Hypoacusis<br>subjects affected / exposed<br>occurrences (all)                                 | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Eye disorders<br>Chalazion<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Gastrointestinal disorders<br>Constipation<br>subjects affected / exposed<br>occurrences (all) | 2 / 3 (66.67%)<br>3 | 1 / 5 (20.00%)<br>1 | 1 / 6 (16.67%)<br>4 |
| Nausea<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 3 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 | 0 / 6 (0.00%)<br>0  |
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)                             | 0 / 3 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 | 0 / 6 (0.00%)<br>0  |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)                                   | 0 / 3 (0.00%)<br>0  | 2 / 5 (40.00%)<br>2 | 0 / 6 (0.00%)<br>0  |
| Rectal haemorrhage<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 3 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 | 0 / 6 (0.00%)<br>0  |
| Dysphagia<br>subjects affected / exposed<br>occurrences (all)                                  | 1 / 3 (33.33%)<br>2 | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Ileus<br>subjects affected / exposed<br>occurrences (all)                                      | 0 / 3 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 | 0 / 6 (0.00%)<br>0  |
| Oesophageal obstruction                                                                        |                     |                     |                     |

|                              |                |               |                |
|------------------------------|----------------|---------------|----------------|
| subjects affected / exposed  | 1 / 3 (33.33%) | 0 / 5 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)            | 1              | 0             | 0              |
| Small intestinal obstruction |                |               |                |
| subjects affected / exposed  | 0 / 3 (0.00%)  | 0 / 5 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all)            | 0              | 0             | 1              |
| Diarrhoea                    |                |               |                |
| subjects affected / exposed  | 0 / 3 (0.00%)  | 0 / 5 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)            | 0              | 0             | 0              |
| Abdominal pain upper         |                |               |                |
| subjects affected / exposed  | 0 / 3 (0.00%)  | 0 / 5 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)            | 0              | 0             | 0              |
| Abdominal distension         |                |               |                |
| subjects affected / exposed  | 0 / 3 (0.00%)  | 0 / 5 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)            | 0              | 0             | 0              |
| Dry mouth                    |                |               |                |
| subjects affected / exposed  | 0 / 3 (0.00%)  | 0 / 5 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)            | 0              | 0             | 0              |
| Abdominal pain lower         |                |               |                |
| subjects affected / exposed  | 0 / 3 (0.00%)  | 0 / 5 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)            | 0              | 0             | 0              |
| Breath odour                 |                |               |                |
| subjects affected / exposed  | 0 / 3 (0.00%)  | 0 / 5 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)            | 0              | 0             | 0              |
| Eructation                   |                |               |                |
| subjects affected / exposed  | 0 / 3 (0.00%)  | 0 / 5 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)            | 0              | 0             | 0              |
| Inguinal hernia              |                |               |                |
| subjects affected / exposed  | 0 / 3 (0.00%)  | 0 / 5 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)            | 0              | 0             | 0              |
| Oedema mouth                 |                |               |                |
| subjects affected / exposed  | 0 / 3 (0.00%)  | 0 / 5 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)            | 0              | 0             | 0              |
| Retching                     |                |               |                |
| subjects affected / exposed  | 0 / 3 (0.00%)  | 0 / 5 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)            | 0              | 0             | 0              |
| Hepatobiliary disorders      |                |               |                |

|                                                                   |                     |                     |                     |
|-------------------------------------------------------------------|---------------------|---------------------|---------------------|
| Hepatic pain<br>subjects affected / exposed<br>occurrences (all)  | 1 / 3 (33.33%)<br>2 | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Skin and subcutaneous tissue disorders                            |                     |                     |                     |
| Alopecia<br>subjects affected / exposed<br>occurrences (all)      | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 1 / 6 (16.67%)<br>1 |
| Eczema<br>subjects affected / exposed<br>occurrences (all)        | 0 / 3 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 | 0 / 6 (0.00%)<br>0  |
| Rash macular<br>subjects affected / exposed<br>occurrences (all)  | 0 / 3 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 | 0 / 6 (0.00%)<br>0  |
| Vitiligo<br>subjects affected / exposed<br>occurrences (all)      | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 1 / 6 (16.67%)<br>1 |
| Erythema<br>subjects affected / exposed<br>occurrences (all)      | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Psoriasis<br>subjects affected / exposed<br>occurrences (all)     | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Rash<br>subjects affected / exposed<br>occurrences (all)          | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Urticaria<br>subjects affected / exposed<br>occurrences (all)     | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Hyperhidrosis<br>subjects affected / exposed<br>occurrences (all) | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Pruritus<br>subjects affected / exposed<br>occurrences (all)      | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Rash pruritic                                                     |                     |                     |                     |

|                                                 |               |                |                |
|-------------------------------------------------|---------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Scar pain                                       |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Skin wound                                      |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Endocrine disorders                             |               |                |                |
| Adrenal insufficiency                           |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Hyperthyroidism                                 |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Musculoskeletal and connective tissue disorders |               |                |                |
| Myalgia                                         |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 5 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)                               | 0             | 0              | 1              |
| Back pain                                       |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 5 (20.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0             | 1              | 0              |
| Flank pain                                      |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 5 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)                               | 0             | 0              | 1              |
| Arthralgia                                      |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Muscle spasms                                   |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Bone pain                                       |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Mobility decreased                              |               |                |                |

|                                   |               |                |                |
|-----------------------------------|---------------|----------------|----------------|
| subjects affected / exposed       | 0 / 3 (0.00%) | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                 | 0             | 0              | 0              |
| Neck pain                         |               |                |                |
| subjects affected / exposed       | 0 / 3 (0.00%) | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                 | 0             | 0              | 0              |
| Pain in extremity                 |               |                |                |
| subjects affected / exposed       | 0 / 3 (0.00%) | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                 | 0             | 0              | 0              |
| Pain in jaw                       |               |                |                |
| subjects affected / exposed       | 0 / 3 (0.00%) | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                 | 0             | 0              | 0              |
| Oedema                            |               |                |                |
| subjects affected / exposed       | 0 / 3 (0.00%) | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                 | 0             | 0              | 0              |
| Infections and infestations       |               |                |                |
| Upper respiratory tract infection |               |                |                |
| subjects affected / exposed       | 0 / 3 (0.00%) | 1 / 5 (20.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                 | 0             | 2              | 0              |
| Pyelonephritis                    |               |                |                |
| subjects affected / exposed       | 0 / 3 (0.00%) | 0 / 5 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)                 | 0             | 0              | 2              |
| COVID-19                          |               |                |                |
| subjects affected / exposed       | 0 / 3 (0.00%) | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                 | 0             | 0              | 0              |
| Nasopharyngitis                   |               |                |                |
| subjects affected / exposed       | 0 / 3 (0.00%) | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                 | 0             | 0              | 0              |
| Pneumonia                         |               |                |                |
| subjects affected / exposed       | 0 / 3 (0.00%) | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                 | 0             | 0              | 0              |
| Paronychia                        |               |                |                |
| subjects affected / exposed       | 0 / 3 (0.00%) | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                 | 0             | 0              | 0              |
| Conjunctivitis                    |               |                |                |
| subjects affected / exposed       | 0 / 3 (0.00%) | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                 | 0             | 0              | 0              |

|                                                                           |                     |                    |                     |
|---------------------------------------------------------------------------|---------------------|--------------------|---------------------|
| Oral fungal infection<br>subjects affected / exposed<br>occurrences (all) | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Sinusitis<br>subjects affected / exposed<br>occurrences (all)             | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Skin infection<br>subjects affected / exposed<br>occurrences (all)        | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Metabolism and nutrition disorders                                        |                     |                    |                     |
| Decreased appetite<br>subjects affected / exposed<br>occurrences (all)    | 1 / 3 (33.33%)<br>1 | 0 / 5 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Hyponatraemia<br>subjects affected / exposed<br>occurrences (all)         | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 1 / 6 (16.67%)<br>1 |
| Hyperglycaemia<br>subjects affected / exposed<br>occurrences (all)        | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Hypokalaemia<br>subjects affected / exposed<br>occurrences (all)          | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Hypercalcaemia<br>subjects affected / exposed<br>occurrences (all)        | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Hypophosphataemia<br>subjects affected / exposed<br>occurrences (all)     | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Hypomagnesaemia<br>subjects affected / exposed<br>occurrences (all)       | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Dehydration<br>subjects affected / exposed<br>occurrences (all)           | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Hyperuricaemia                                                            |                     |                    |                     |

|                             |               |               |               |
|-----------------------------|---------------|---------------|---------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Hypoalbuminaemia            |               |               |               |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Malnutrition                |               |               |               |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Vitamin D deficiency        |               |               |               |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |

| <b>Non-serious adverse events</b>                                   | Arm A             | Arm B             | Arm C (Cohort 4) |
|---------------------------------------------------------------------|-------------------|-------------------|------------------|
| Total subjects affected by non-serious adverse events               |                   |                   |                  |
| subjects affected / exposed                                         | 18 / 18 (100.00%) | 15 / 15 (100.00%) | 6 / 6 (100.00%)  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                   |                   |                  |
| Cancer pain                                                         |                   |                   |                  |
| subjects affected / exposed                                         | 5 / 18 (27.78%)   | 7 / 15 (46.67%)   | 0 / 6 (0.00%)    |
| occurrences (all)                                                   | 8                 | 11                | 0                |
| Metastases to bone                                                  |                   |                   |                  |
| subjects affected / exposed                                         | 0 / 18 (0.00%)    | 0 / 15 (0.00%)    | 0 / 6 (0.00%)    |
| occurrences (all)                                                   | 0                 | 0                 | 0                |
| Tumour thrombosis                                                   |                   |                   |                  |
| subjects affected / exposed                                         | 0 / 18 (0.00%)    | 1 / 15 (6.67%)    | 0 / 6 (0.00%)    |
| occurrences (all)                                                   | 0                 | 1                 | 0                |
| Vascular disorders                                                  |                   |                   |                  |
| Hypotension                                                         |                   |                   |                  |
| subjects affected / exposed                                         | 0 / 18 (0.00%)    | 1 / 15 (6.67%)    | 1 / 6 (16.67%)   |
| occurrences (all)                                                   | 0                 | 1                 | 1                |
| Brachiocephalic vein thrombosis                                     |                   |                   |                  |
| subjects affected / exposed                                         | 0 / 18 (0.00%)    | 1 / 15 (6.67%)    | 0 / 6 (0.00%)    |
| occurrences (all)                                                   | 0                 | 1                 | 0                |
| Haematoma                                                           |                   |                   |                  |
| subjects affected / exposed                                         | 0 / 18 (0.00%)    | 1 / 15 (6.67%)    | 0 / 6 (0.00%)    |
| occurrences (all)                                                   | 0                 | 1                 | 0                |
| Hypertension                                                        |                   |                   |                  |

|                                                      |                  |                  |                |
|------------------------------------------------------|------------------|------------------|----------------|
| subjects affected / exposed                          | 0 / 18 (0.00%)   | 1 / 15 (6.67%)   | 0 / 6 (0.00%)  |
| occurrences (all)                                    | 0                | 1                | 0              |
| Peripheral coldness                                  |                  |                  |                |
| subjects affected / exposed                          | 0 / 18 (0.00%)   | 1 / 15 (6.67%)   | 0 / 6 (0.00%)  |
| occurrences (all)                                    | 0                | 1                | 0              |
| General disorders and administration site conditions |                  |                  |                |
| Fatigue                                              |                  |                  |                |
| subjects affected / exposed                          | 9 / 18 (50.00%)  | 8 / 15 (53.33%)  | 2 / 6 (33.33%) |
| occurrences (all)                                    | 13               | 16               | 5              |
| Pyrexia                                              |                  |                  |                |
| subjects affected / exposed                          | 2 / 18 (11.11%)  | 1 / 15 (6.67%)   | 3 / 6 (50.00%) |
| occurrences (all)                                    | 2                | 1                | 4              |
| Oedema peripheral                                    |                  |                  |                |
| subjects affected / exposed                          | 0 / 18 (0.00%)   | 2 / 15 (13.33%)  | 0 / 6 (0.00%)  |
| occurrences (all)                                    | 0                | 2                | 0              |
| Influenza like illness                               |                  |                  |                |
| subjects affected / exposed                          | 0 / 18 (0.00%)   | 1 / 15 (6.67%)   | 1 / 6 (16.67%) |
| occurrences (all)                                    | 0                | 4                | 1              |
| Pain                                                 |                  |                  |                |
| subjects affected / exposed                          | 0 / 18 (0.00%)   | 1 / 15 (6.67%)   | 0 / 6 (0.00%)  |
| occurrences (all)                                    | 0                | 1                | 0              |
| Catheter site haemorrhage                            |                  |                  |                |
| subjects affected / exposed                          | 0 / 18 (0.00%)   | 0 / 15 (0.00%)   | 0 / 6 (0.00%)  |
| occurrences (all)                                    | 0                | 0                | 0              |
| Injection site reaction                              |                  |                  |                |
| subjects affected / exposed                          | 15 / 18 (83.33%) | 12 / 15 (80.00%) | 5 / 6 (83.33%) |
| occurrences (all)                                    | 60               | 72               | 15             |
| Malaise                                              |                  |                  |                |
| subjects affected / exposed                          | 1 / 18 (5.56%)   | 2 / 15 (13.33%)  | 0 / 6 (0.00%)  |
| occurrences (all)                                    | 1                | 3                | 0              |
| Chills                                               |                  |                  |                |
| subjects affected / exposed                          | 1 / 18 (5.56%)   | 0 / 15 (0.00%)   | 1 / 6 (16.67%) |
| occurrences (all)                                    | 1                | 0                | 1              |
| Injection site haematoma                             |                  |                  |                |

|                                                 |                |                 |                |
|-------------------------------------------------|----------------|-----------------|----------------|
| subjects affected / exposed                     | 1 / 18 (5.56%) | 2 / 15 (13.33%) | 0 / 6 (0.00%)  |
| occurrences (all)                               | 1              | 2               | 0              |
| Face oedema                                     |                |                 |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 2 / 15 (13.33%) | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0              | 2               | 0              |
| Non-cardiac chest pain                          |                |                 |                |
| subjects affected / exposed                     | 1 / 18 (5.56%) | 0 / 15 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)                               | 1              | 0               | 1              |
| Asthenia                                        |                |                 |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 15 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)                               | 0              | 0               | 1              |
| Inflammation                                    |                |                 |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 1 / 15 (6.67%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0              | 1               | 0              |
| Injection site injury                           |                |                 |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 1 / 15 (6.67%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0              | 1               | 0              |
| Immune system disorders                         |                |                 |                |
| Hypersensitivity                                |                |                 |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0              |
| Reproductive system and breast disorders        |                |                 |                |
| Breast tenderness                               |                |                 |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0              |
| Postmenopausal haemorrhage                      |                |                 |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0              |
| Respiratory, thoracic and mediastinal disorders |                |                 |                |
| Dyspnoea                                        |                |                 |                |
| subjects affected / exposed                     | 1 / 18 (5.56%) | 1 / 15 (6.67%)  | 2 / 6 (33.33%) |
| occurrences (all)                               | 1              | 5               | 2              |
| Hypoxia                                         |                |                 |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0              |
| Cough                                           |                |                 |                |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 15 (6.67%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 1              | 2              | 0              |
| Pleural effusion            |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 4              | 0              |
| Dyspnoea at rest            |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0              |
| Dyspnoea exertional         |                |                |                |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0              |
| Laryngeal oedema            |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0              |
| Pneumonitis                 |                |                |                |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0              |
| Pneumothorax                |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0              |
| Productive cough            |                |                |                |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0              |
| Psychiatric disorders       |                |                |                |
| Insomnia                    |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 15 (6.67%) | 1 / 6 (16.67%) |
| occurrences (all)           | 0              | 2              | 1              |
| Depression                  |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 2              | 0              |
| Anxiety                     |                |                |                |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 15 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all)           | 0              | 0              | 1              |
| Confusional state           |                |                |                |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0              |

|                                                                                                            |                     |                      |                     |
|------------------------------------------------------------------------------------------------------------|---------------------|----------------------|---------------------|
| Delirium<br>subjects affected / exposed<br>occurrences (all)                                               | 1 / 18 (5.56%)<br>1 | 0 / 15 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Product issues<br>Device dislocation<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 18 (0.00%)<br>0 | 1 / 15 (6.67%)<br>1  | 0 / 6 (0.00%)<br>0  |
| Investigations<br>Blood alkaline phosphatase increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 18 (0.00%)<br>0 | 1 / 15 (6.67%)<br>5  | 1 / 6 (16.67%)<br>1 |
| Gamma-glutamyltransferase increased<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 18 (0.00%)<br>0 | 1 / 15 (6.67%)<br>1  | 1 / 6 (16.67%)<br>1 |
| Alanine aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 18 (0.00%)<br>0 | 2 / 15 (13.33%)<br>2 | 0 / 6 (0.00%)<br>0  |
| Weight decreased<br>subjects affected / exposed<br>occurrences (all)                                       | 1 / 18 (5.56%)<br>1 | 1 / 15 (6.67%)<br>1  | 0 / 6 (0.00%)<br>0  |
| Blood bilirubin increased<br>subjects affected / exposed<br>occurrences (all)                              | 1 / 18 (5.56%)<br>1 | 0 / 15 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Platelet count decreased<br>subjects affected / exposed<br>occurrences (all)                               | 1 / 18 (5.56%)<br>1 | 0 / 15 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Electrocardiogram QT prolonged<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 18 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Lipase increased<br>subjects affected / exposed<br>occurrences (all)                                       | 1 / 18 (5.56%)<br>1 | 1 / 15 (6.67%)<br>5  | 0 / 6 (0.00%)<br>0  |
| Blood creatinine increased<br>subjects affected / exposed<br>occurrences (all)                             | 1 / 18 (5.56%)<br>1 | 2 / 15 (13.33%)<br>2 | 0 / 6 (0.00%)<br>0  |
| Aspartate aminotransferase increased                                                                       |                     |                      |                     |

|                                                                                  |                     |                      |                     |
|----------------------------------------------------------------------------------|---------------------|----------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)                                 | 0 / 18 (0.00%)<br>0 | 2 / 15 (13.33%)<br>2 | 0 / 6 (0.00%)<br>0  |
| Amylase increased<br>subjects affected / exposed<br>occurrences (all)            | 0 / 18 (0.00%)<br>0 | 1 / 15 (6.67%)<br>1  | 0 / 6 (0.00%)<br>0  |
| Lymphocyte count decreased<br>subjects affected / exposed<br>occurrences (all)   | 0 / 18 (0.00%)<br>0 | 1 / 15 (6.67%)<br>1  | 0 / 6 (0.00%)<br>0  |
| Urine output decreased<br>subjects affected / exposed<br>occurrences (all)       | 0 / 18 (0.00%)<br>0 | 1 / 15 (6.67%)<br>1  | 0 / 6 (0.00%)<br>0  |
| Injury, poisoning and procedural complications                                   |                     |                      |                     |
| Post procedural complication<br>subjects affected / exposed<br>occurrences (all) | 0 / 18 (0.00%)<br>0 | 1 / 15 (6.67%)<br>1  | 0 / 6 (0.00%)<br>0  |
| Procedural pain<br>subjects affected / exposed<br>occurrences (all)              | 0 / 18 (0.00%)<br>0 | 1 / 15 (6.67%)<br>1  | 2 / 6 (33.33%)<br>3 |
| Drain site complication<br>subjects affected / exposed<br>occurrences (all)      | 0 / 18 (0.00%)<br>0 | 1 / 15 (6.67%)<br>1  | 0 / 6 (0.00%)<br>0  |
| Fall<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 18 (0.00%)<br>0 | 1 / 15 (6.67%)<br>1  | 0 / 6 (0.00%)<br>0  |
| Post procedural erythema<br>subjects affected / exposed<br>occurrences (all)     | 0 / 18 (0.00%)<br>0 | 1 / 15 (6.67%)<br>1  | 0 / 6 (0.00%)<br>0  |
| Post procedural fever<br>subjects affected / exposed<br>occurrences (all)        | 0 / 18 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Post procedural haematoma<br>subjects affected / exposed<br>occurrences (all)    | 0 / 18 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0  | 1 / 6 (16.67%)<br>1 |
| Stoma site erythema                                                              |                     |                      |                     |

|                                                  |                     |                     |                    |
|--------------------------------------------------|---------------------|---------------------|--------------------|
| subjects affected / exposed<br>occurrences (all) | 1 / 18 (5.56%)<br>1 | 0 / 15 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 |
| Cardiac disorders                                |                     |                     |                    |
| Myocardial infarction                            |                     |                     |                    |
| subjects affected / exposed                      | 0 / 18 (0.00%)      | 0 / 15 (0.00%)      | 0 / 6 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                  |
| Palpitations                                     |                     |                     |                    |
| subjects affected / exposed                      | 0 / 18 (0.00%)      | 1 / 15 (6.67%)      | 0 / 6 (0.00%)      |
| occurrences (all)                                | 0                   | 1                   | 0                  |
| Sinus tachycardia                                |                     |                     |                    |
| subjects affected / exposed                      | 0 / 18 (0.00%)      | 0 / 15 (0.00%)      | 0 / 6 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                  |
| Nervous system disorders                         |                     |                     |                    |
| Dizziness                                        |                     |                     |                    |
| subjects affected / exposed                      | 1 / 18 (5.56%)      | 2 / 15 (13.33%)     | 1 / 6 (16.67%)     |
| occurrences (all)                                | 1                   | 2                   | 1                  |
| Aphasia                                          |                     |                     |                    |
| subjects affected / exposed                      | 1 / 18 (5.56%)      | 0 / 15 (0.00%)      | 0 / 6 (0.00%)      |
| occurrences (all)                                | 1                   | 0                   | 0                  |
| Brachial plexopathy                              |                     |                     |                    |
| subjects affected / exposed                      | 0 / 18 (0.00%)      | 1 / 15 (6.67%)      | 0 / 6 (0.00%)      |
| occurrences (all)                                | 0                   | 1                   | 0                  |
| Depressed level of consciousness                 |                     |                     |                    |
| subjects affected / exposed                      | 1 / 18 (5.56%)      | 0 / 15 (0.00%)      | 0 / 6 (0.00%)      |
| occurrences (all)                                | 1                   | 0                   | 0                  |
| Disturbance in attention                         |                     |                     |                    |
| subjects affected / exposed                      | 0 / 18 (0.00%)      | 1 / 15 (6.67%)      | 0 / 6 (0.00%)      |
| occurrences (all)                                | 0                   | 1                   | 0                  |
| Headache                                         |                     |                     |                    |
| subjects affected / exposed                      | 0 / 18 (0.00%)      | 1 / 15 (6.67%)      | 0 / 6 (0.00%)      |
| occurrences (all)                                | 0                   | 1                   | 0                  |
| Neuropathy peripheral                            |                     |                     |                    |
| subjects affected / exposed                      | 0 / 18 (0.00%)      | 1 / 15 (6.67%)      | 0 / 6 (0.00%)      |
| occurrences (all)                                | 0                   | 1                   | 0                  |
| Peripheral sensory neuropathy                    |                     |                     |                    |

|                                                                                                     |                      |                      |                     |
|-----------------------------------------------------------------------------------------------------|----------------------|----------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)                                                    | 0 / 18 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  | 0 / 6 (0.00%)<br>0  |
| Presyncope<br>subjects affected / exposed<br>occurrences (all)                                      | 0 / 18 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  | 1 / 6 (16.67%)<br>1 |
| Somnolence<br>subjects affected / exposed<br>occurrences (all)                                      | 0 / 18 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  | 0 / 6 (0.00%)<br>0  |
| Blood and lymphatic system disorders<br>Anaemia<br>subjects affected / exposed<br>occurrences (all) | 5 / 18 (27.78%)<br>5 | 5 / 15 (33.33%)<br>6 | 2 / 6 (33.33%)<br>2 |
| Ear and labyrinth disorders<br>Ear discomfort<br>subjects affected / exposed<br>occurrences (all)   | 0 / 18 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  | 1 / 6 (16.67%)<br>1 |
| Ear pain<br>subjects affected / exposed<br>occurrences (all)                                        | 0 / 18 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  | 0 / 6 (0.00%)<br>0  |
| Hypoacusis<br>subjects affected / exposed<br>occurrences (all)                                      | 0 / 18 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  | 0 / 6 (0.00%)<br>0  |
| Eye disorders<br>Chalazion<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 18 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  | 0 / 6 (0.00%)<br>0  |
| Gastrointestinal disorders<br>Constipation<br>subjects affected / exposed<br>occurrences (all)      | 1 / 18 (5.56%)<br>1  | 5 / 15 (33.33%)<br>7 | 3 / 6 (50.00%)<br>6 |
| Nausea<br>subjects affected / exposed<br>occurrences (all)                                          | 2 / 18 (11.11%)<br>2 | 5 / 15 (33.33%)<br>9 | 3 / 6 (50.00%)<br>8 |
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)                                  | 1 / 18 (5.56%)<br>3  | 1 / 15 (6.67%)<br>1  | 1 / 6 (16.67%)<br>1 |
| Vomiting                                                                                            |                      |                      |                     |

|                              |                 |                 |                |
|------------------------------|-----------------|-----------------|----------------|
| subjects affected / exposed  | 1 / 18 (5.56%)  | 4 / 15 (26.67%) | 3 / 6 (50.00%) |
| occurrences (all)            | 1               | 5               | 8              |
| Rectal haemorrhage           |                 |                 |                |
| subjects affected / exposed  | 0 / 18 (0.00%)  | 1 / 15 (6.67%)  | 0 / 6 (0.00%)  |
| occurrences (all)            | 0               | 1               | 0              |
| Dysphagia                    |                 |                 |                |
| subjects affected / exposed  | 0 / 18 (0.00%)  | 0 / 15 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)            | 0               | 0               | 1              |
| Ileus                        |                 |                 |                |
| subjects affected / exposed  | 0 / 18 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)            | 0               | 0               | 0              |
| Oesophageal obstruction      |                 |                 |                |
| subjects affected / exposed  | 0 / 18 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)            | 0               | 0               | 0              |
| Small intestinal obstruction |                 |                 |                |
| subjects affected / exposed  | 0 / 18 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)            | 0               | 0               | 0              |
| Diarrhoea                    |                 |                 |                |
| subjects affected / exposed  | 2 / 18 (11.11%) | 2 / 15 (13.33%) | 1 / 6 (16.67%) |
| occurrences (all)            | 3               | 4               | 1              |
| Abdominal pain upper         |                 |                 |                |
| subjects affected / exposed  | 1 / 18 (5.56%)  | 1 / 15 (6.67%)  | 0 / 6 (0.00%)  |
| occurrences (all)            | 1               | 2               | 0              |
| Abdominal distension         |                 |                 |                |
| subjects affected / exposed  | 0 / 18 (0.00%)  | 0 / 15 (0.00%)  | 2 / 6 (33.33%) |
| occurrences (all)            | 0               | 0               | 2              |
| Dry mouth                    |                 |                 |                |
| subjects affected / exposed  | 0 / 18 (0.00%)  | 0 / 15 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)            | 0               | 0               | 1              |
| Abdominal pain lower         |                 |                 |                |
| subjects affected / exposed  | 0 / 18 (0.00%)  | 0 / 15 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)            | 0               | 0               | 1              |
| Breath odour                 |                 |                 |                |
| subjects affected / exposed  | 0 / 18 (0.00%)  | 0 / 15 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)            | 0               | 0               | 1              |
| Eructation                   |                 |                 |                |

|                                        |                |                |                |
|----------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed            | 0 / 18 (0.00%) | 0 / 15 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all)                      | 0              | 0              | 1              |
| Inguinal hernia                        |                |                |                |
| subjects affected / exposed            | 1 / 18 (5.56%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                      | 1              | 0              | 0              |
| Oedema mouth                           |                |                |                |
| subjects affected / exposed            | 0 / 18 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0              | 1              | 0              |
| Retching                               |                |                |                |
| subjects affected / exposed            | 0 / 18 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0              | 1              | 0              |
| Hepatobiliary disorders                |                |                |                |
| Hepatic pain                           |                |                |                |
| subjects affected / exposed            | 0 / 18 (0.00%) | 0 / 15 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all)                      | 0              | 0              | 1              |
| Skin and subcutaneous tissue disorders |                |                |                |
| Alopecia                               |                |                |                |
| subjects affected / exposed            | 0 / 18 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Eczema                                 |                |                |                |
| subjects affected / exposed            | 0 / 18 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Rash macular                           |                |                |                |
| subjects affected / exposed            | 0 / 18 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Vitiligo                               |                |                |                |
| subjects affected / exposed            | 0 / 18 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Erythema                               |                |                |                |
| subjects affected / exposed            | 0 / 18 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0              | 1              | 0              |
| Psoriasis                              |                |                |                |
| subjects affected / exposed            | 0 / 18 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0              | 2              | 0              |
| Rash                                   |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 18 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0              | 2              | 0              |
| Urticaria                                       |                |                |                |
| subjects affected / exposed                     | 1 / 18 (5.56%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                               | 2              | 0              | 0              |
| Hyperhidrosis                                   |                |                |                |
| subjects affected / exposed                     | 1 / 18 (5.56%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                               | 2              | 0              | 0              |
| Pruritus                                        |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0              | 1              | 0              |
| Rash pruritic                                   |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0              | 1              | 0              |
| Scar pain                                       |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 15 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Skin wound                                      |                |                |                |
| subjects affected / exposed                     | 1 / 18 (5.56%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                               | 1              | 0              | 0              |
| Endocrine disorders                             |                |                |                |
| Adrenal insufficiency                           |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 1 / 15 (6.67%) | 1 / 6 (16.67%) |
| occurrences (all)                               | 0              | 1              | 1              |
| Hyperthyroidism                                 |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 0 / 15 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Musculoskeletal and connective tissue disorders |                |                |                |
| Myalgia                                         |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0              | 1              | 0              |
| Back pain                                       |                |                |                |
| subjects affected / exposed                     | 0 / 18 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0              | 1              | 0              |
| Flank pain                                      |                |                |                |

|                                   |                 |                 |                |
|-----------------------------------|-----------------|-----------------|----------------|
| subjects affected / exposed       | 0 / 18 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                 | 0               | 0               | 0              |
| Arthralgia                        |                 |                 |                |
| subjects affected / exposed       | 0 / 18 (0.00%)  | 6 / 15 (40.00%) | 1 / 6 (16.67%) |
| occurrences (all)                 | 0               | 6               | 1              |
| Muscle spasms                     |                 |                 |                |
| subjects affected / exposed       | 1 / 18 (5.56%)  | 1 / 15 (6.67%)  | 1 / 6 (16.67%) |
| occurrences (all)                 | 1               | 1               | 1              |
| Bone pain                         |                 |                 |                |
| subjects affected / exposed       | 0 / 18 (0.00%)  | 0 / 15 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)                 | 0               | 0               | 1              |
| Mobility decreased                |                 |                 |                |
| subjects affected / exposed       | 0 / 18 (0.00%)  | 1 / 15 (6.67%)  | 0 / 6 (0.00%)  |
| occurrences (all)                 | 0               | 1               | 0              |
| Neck pain                         |                 |                 |                |
| subjects affected / exposed       | 0 / 18 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                 | 0               | 0               | 0              |
| Pain in extremity                 |                 |                 |                |
| subjects affected / exposed       | 0 / 18 (0.00%)  | 0 / 15 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)                 | 0               | 0               | 1              |
| Pain in jaw                       |                 |                 |                |
| subjects affected / exposed       | 0 / 18 (0.00%)  | 1 / 15 (6.67%)  | 0 / 6 (0.00%)  |
| occurrences (all)                 | 0               | 1               | 0              |
| Oedema                            |                 |                 |                |
| subjects affected / exposed       | 0 / 18 (0.00%)  | 1 / 15 (6.67%)  | 0 / 6 (0.00%)  |
| occurrences (all)                 | 0               | 1               | 0              |
| Infections and infestations       |                 |                 |                |
| Upper respiratory tract infection |                 |                 |                |
| subjects affected / exposed       | 1 / 18 (5.56%)  | 1 / 15 (6.67%)  | 0 / 6 (0.00%)  |
| occurrences (all)                 | 1               | 1               | 0              |
| Pyelonephritis                    |                 |                 |                |
| subjects affected / exposed       | 0 / 18 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                 | 0               | 0               | 0              |
| COVID-19                          |                 |                 |                |
| subjects affected / exposed       | 3 / 18 (16.67%) | 2 / 15 (13.33%) | 1 / 6 (16.67%) |
| occurrences (all)                 | 3               | 2               | 1              |

|                                    |                 |                 |                |
|------------------------------------|-----------------|-----------------|----------------|
| Nasopharyngitis                    |                 |                 |                |
| subjects affected / exposed        | 0 / 18 (0.00%)  | 3 / 15 (20.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                  | 0               | 3               | 0              |
| Pneumonia                          |                 |                 |                |
| subjects affected / exposed        | 0 / 18 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 0               | 0               | 0              |
| Paronychia                         |                 |                 |                |
| subjects affected / exposed        | 0 / 18 (0.00%)  | 1 / 15 (6.67%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 0               | 2               | 0              |
| Conjunctivitis                     |                 |                 |                |
| subjects affected / exposed        | 1 / 18 (5.56%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 1               | 0               | 0              |
| Oral fungal infection              |                 |                 |                |
| subjects affected / exposed        | 0 / 18 (0.00%)  | 1 / 15 (6.67%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 0               | 1               | 0              |
| Sinusitis                          |                 |                 |                |
| subjects affected / exposed        | 0 / 18 (0.00%)  | 1 / 15 (6.67%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 0               | 1               | 0              |
| Skin infection                     |                 |                 |                |
| subjects affected / exposed        | 1 / 18 (5.56%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 1               | 0               | 0              |
| Metabolism and nutrition disorders |                 |                 |                |
| Decreased appetite                 |                 |                 |                |
| subjects affected / exposed        | 4 / 18 (22.22%) | 4 / 15 (26.67%) | 2 / 6 (33.33%) |
| occurrences (all)                  | 5               | 7               | 4              |
| Hyponatraemia                      |                 |                 |                |
| subjects affected / exposed        | 0 / 18 (0.00%)  | 1 / 15 (6.67%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 0               | 1               | 0              |
| Hyperglycaemia                     |                 |                 |                |
| subjects affected / exposed        | 1 / 18 (5.56%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 1               | 0               | 0              |
| Hypokalaemia                       |                 |                 |                |
| subjects affected / exposed        | 0 / 18 (0.00%)  | 1 / 15 (6.67%)  | 2 / 6 (33.33%) |
| occurrences (all)                  | 0               | 1               | 3              |
| Hypercalcaemia                     |                 |                 |                |

|                             |                |                 |               |
|-----------------------------|----------------|-----------------|---------------|
| subjects affected / exposed | 1 / 18 (5.56%) | 2 / 15 (13.33%) | 0 / 6 (0.00%) |
| occurrences (all)           | 3              | 3               | 0             |
| Hypophosphataemia           |                |                 |               |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 15 (6.67%)  | 0 / 6 (0.00%) |
| occurrences (all)           | 0              | 1               | 0             |
| Hypomagnesaemia             |                |                 |               |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 15 (6.67%)  | 0 / 6 (0.00%) |
| occurrences (all)           | 0              | 1               | 0             |
| Dehydration                 |                |                 |               |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 15 (6.67%)  | 0 / 6 (0.00%) |
| occurrences (all)           | 0              | 1               | 0             |
| Hyperuricaemia              |                |                 |               |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 15 (0.00%)  | 0 / 6 (0.00%) |
| occurrences (all)           | 1              | 0               | 0             |
| Hypoalbuminaemia            |                |                 |               |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 15 (0.00%)  | 0 / 6 (0.00%) |
| occurrences (all)           | 1              | 0               | 0             |
| Malnutrition                |                |                 |               |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 15 (6.67%)  | 0 / 6 (0.00%) |
| occurrences (all)           | 0              | 1               | 0             |
| Vitamin D deficiency        |                |                 |               |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 15 (0.00%)  | 0 / 6 (0.00%) |
| occurrences (all)           | 1              | 0               | 0             |

| <b>Non-serious adverse events</b>                                   | Arm C (Cohort 5) | Arm D           |  |
|---------------------------------------------------------------------|------------------|-----------------|--|
| Total subjects affected by non-serious adverse events               |                  |                 |  |
| subjects affected / exposed                                         | 6 / 6 (100.00%)  | 1 / 1 (100.00%) |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                  |                 |  |
| Cancer pain                                                         |                  |                 |  |
| subjects affected / exposed                                         | 0 / 6 (0.00%)    | 0 / 1 (0.00%)   |  |
| occurrences (all)                                                   | 0                | 0               |  |
| Metastases to bone                                                  |                  |                 |  |
| subjects affected / exposed                                         | 1 / 6 (16.67%)   | 0 / 1 (0.00%)   |  |
| occurrences (all)                                                   | 3                | 0               |  |
| Tumour thrombosis                                                   |                  |                 |  |

|                                                         |                    |                    |  |
|---------------------------------------------------------|--------------------|--------------------|--|
| subjects affected / exposed<br>occurrences (all)        | 0 / 6 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |  |
| Vascular disorders                                      |                    |                    |  |
| Hypotension                                             |                    |                    |  |
| subjects affected / exposed                             | 1 / 6 (16.67%)     | 0 / 1 (0.00%)      |  |
| occurrences (all)                                       | 1                  | 0                  |  |
| Brachiocephalic vein thrombosis                         |                    |                    |  |
| subjects affected / exposed                             | 0 / 6 (0.00%)      | 0 / 1 (0.00%)      |  |
| occurrences (all)                                       | 0                  | 0                  |  |
| Haematoma                                               |                    |                    |  |
| subjects affected / exposed                             | 0 / 6 (0.00%)      | 0 / 1 (0.00%)      |  |
| occurrences (all)                                       | 0                  | 0                  |  |
| Hypertension                                            |                    |                    |  |
| subjects affected / exposed                             | 0 / 6 (0.00%)      | 0 / 1 (0.00%)      |  |
| occurrences (all)                                       | 0                  | 0                  |  |
| Peripheral coldness                                     |                    |                    |  |
| subjects affected / exposed                             | 0 / 6 (0.00%)      | 0 / 1 (0.00%)      |  |
| occurrences (all)                                       | 0                  | 0                  |  |
| General disorders and administration<br>site conditions |                    |                    |  |
| Fatigue                                                 |                    |                    |  |
| subjects affected / exposed                             | 5 / 6 (83.33%)     | 1 / 1 (100.00%)    |  |
| occurrences (all)                                       | 6                  | 2                  |  |
| Pyrexia                                                 |                    |                    |  |
| subjects affected / exposed                             | 3 / 6 (50.00%)     | 0 / 1 (0.00%)      |  |
| occurrences (all)                                       | 4                  | 0                  |  |
| Oedema peripheral                                       |                    |                    |  |
| subjects affected / exposed                             | 1 / 6 (16.67%)     | 0 / 1 (0.00%)      |  |
| occurrences (all)                                       | 2                  | 0                  |  |
| Influenza like illness                                  |                    |                    |  |
| subjects affected / exposed                             | 1 / 6 (16.67%)     | 0 / 1 (0.00%)      |  |
| occurrences (all)                                       | 1                  | 0                  |  |
| Pain                                                    |                    |                    |  |
| subjects affected / exposed                             | 1 / 6 (16.67%)     | 0 / 1 (0.00%)      |  |
| occurrences (all)                                       | 1                  | 0                  |  |
| Catheter site haemorrhage                               |                    |                    |  |

|                                          |                |                 |  |
|------------------------------------------|----------------|-----------------|--|
| subjects affected / exposed              | 0 / 6 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                        | 0              | 0               |  |
| Injection site reaction                  |                |                 |  |
| subjects affected / exposed              | 5 / 6 (83.33%) | 1 / 1 (100.00%) |  |
| occurrences (all)                        | 26             | 2               |  |
| Malaise                                  |                |                 |  |
| subjects affected / exposed              | 0 / 6 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                        | 0              | 0               |  |
| Chills                                   |                |                 |  |
| subjects affected / exposed              | 1 / 6 (16.67%) | 0 / 1 (0.00%)   |  |
| occurrences (all)                        | 1              | 0               |  |
| Injection site haematoma                 |                |                 |  |
| subjects affected / exposed              | 0 / 6 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                        | 0              | 0               |  |
| Face oedema                              |                |                 |  |
| subjects affected / exposed              | 0 / 6 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                        | 0              | 0               |  |
| Non-cardiac chest pain                   |                |                 |  |
| subjects affected / exposed              | 0 / 6 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                        | 0              | 0               |  |
| Asthenia                                 |                |                 |  |
| subjects affected / exposed              | 0 / 6 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                        | 0              | 0               |  |
| Inflammation                             |                |                 |  |
| subjects affected / exposed              | 0 / 6 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                        | 0              | 0               |  |
| Injection site injury                    |                |                 |  |
| subjects affected / exposed              | 0 / 6 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                        | 0              | 0               |  |
| Immune system disorders                  |                |                 |  |
| Hypersensitivity                         |                |                 |  |
| subjects affected / exposed              | 1 / 6 (16.67%) | 0 / 1 (0.00%)   |  |
| occurrences (all)                        | 2              | 0               |  |
| Reproductive system and breast disorders |                |                 |  |

|                                                                                |                     |                    |  |
|--------------------------------------------------------------------------------|---------------------|--------------------|--|
| Breast tenderness<br>subjects affected / exposed<br>occurrences (all)          | 0 / 6 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Postmenopausal haemorrhage<br>subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Respiratory, thoracic and mediastinal disorders                                |                     |                    |  |
| Dyspnoea<br>subjects affected / exposed<br>occurrences (all)                   | 2 / 6 (33.33%)<br>5 | 0 / 1 (0.00%)<br>0 |  |
| Hypoxia<br>subjects affected / exposed<br>occurrences (all)                    | 1 / 6 (16.67%)<br>2 | 0 / 1 (0.00%)<br>0 |  |
| Cough<br>subjects affected / exposed<br>occurrences (all)                      | 1 / 6 (16.67%)<br>4 | 0 / 1 (0.00%)<br>0 |  |
| Pleural effusion<br>subjects affected / exposed<br>occurrences (all)           | 0 / 6 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Dyspnoea at rest<br>subjects affected / exposed<br>occurrences (all)           | 0 / 6 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Dyspnoea exertional<br>subjects affected / exposed<br>occurrences (all)        | 0 / 6 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Laryngeal oedema<br>subjects affected / exposed<br>occurrences (all)           | 0 / 6 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Pneumonitis<br>subjects affected / exposed<br>occurrences (all)                | 0 / 6 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Pneumothorax<br>subjects affected / exposed<br>occurrences (all)               | 0 / 6 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Productive cough                                                               |                     |                    |  |

|                                                  |                    |                    |  |
|--------------------------------------------------|--------------------|--------------------|--|
| subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |  |
| Psychiatric disorders                            |                    |                    |  |
| Insomnia                                         |                    |                    |  |
| subjects affected / exposed                      | 0 / 6 (0.00%)      | 0 / 1 (0.00%)      |  |
| occurrences (all)                                | 0                  | 0                  |  |
| Depression                                       |                    |                    |  |
| subjects affected / exposed                      | 0 / 6 (0.00%)      | 0 / 1 (0.00%)      |  |
| occurrences (all)                                | 0                  | 0                  |  |
| Anxiety                                          |                    |                    |  |
| subjects affected / exposed                      | 0 / 6 (0.00%)      | 0 / 1 (0.00%)      |  |
| occurrences (all)                                | 0                  | 0                  |  |
| Confusional state                                |                    |                    |  |
| subjects affected / exposed                      | 0 / 6 (0.00%)      | 0 / 1 (0.00%)      |  |
| occurrences (all)                                | 0                  | 0                  |  |
| Delirium                                         |                    |                    |  |
| subjects affected / exposed                      | 0 / 6 (0.00%)      | 0 / 1 (0.00%)      |  |
| occurrences (all)                                | 0                  | 0                  |  |
| Product issues                                   |                    |                    |  |
| Device dislocation                               |                    |                    |  |
| subjects affected / exposed                      | 0 / 6 (0.00%)      | 0 / 1 (0.00%)      |  |
| occurrences (all)                                | 0                  | 0                  |  |
| Investigations                                   |                    |                    |  |
| Blood alkaline phosphatase increased             |                    |                    |  |
| subjects affected / exposed                      | 0 / 6 (0.00%)      | 0 / 1 (0.00%)      |  |
| occurrences (all)                                | 0                  | 0                  |  |
| Gamma-glutamyltransferase increased              |                    |                    |  |
| subjects affected / exposed                      | 0 / 6 (0.00%)      | 0 / 1 (0.00%)      |  |
| occurrences (all)                                | 0                  | 0                  |  |
| Alanine aminotransferase increased               |                    |                    |  |
| subjects affected / exposed                      | 0 / 6 (0.00%)      | 0 / 1 (0.00%)      |  |
| occurrences (all)                                | 0                  | 0                  |  |
| Weight decreased                                 |                    |                    |  |
| subjects affected / exposed                      | 0 / 6 (0.00%)      | 0 / 1 (0.00%)      |  |
| occurrences (all)                                | 0                  | 0                  |  |
| Blood bilirubin increased                        |                    |                    |  |

|                                                |                |               |  |
|------------------------------------------------|----------------|---------------|--|
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                              | 0              | 0             |  |
| Platelet count decreased                       |                |               |  |
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                              | 0              | 0             |  |
| Electrocardiogram QT prolonged                 |                |               |  |
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                              | 0              | 0             |  |
| Lipase increased                               |                |               |  |
| subjects affected / exposed                    | 1 / 6 (16.67%) | 0 / 1 (0.00%) |  |
| occurrences (all)                              | 1              | 0             |  |
| Blood creatinine increased                     |                |               |  |
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                              | 0              | 0             |  |
| Aspartate aminotransferase increased           |                |               |  |
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                              | 0              | 0             |  |
| Amylase increased                              |                |               |  |
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                              | 0              | 0             |  |
| Lymphocyte count decreased                     |                |               |  |
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                              | 0              | 0             |  |
| Urine output decreased                         |                |               |  |
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                              | 0              | 0             |  |
| Injury, poisoning and procedural complications |                |               |  |
| Post procedural complication                   |                |               |  |
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                              | 0              | 0             |  |
| Procedural pain                                |                |               |  |
| subjects affected / exposed                    | 1 / 6 (16.67%) | 0 / 1 (0.00%) |  |
| occurrences (all)                              | 1              | 0             |  |
| Drain site complication                        |                |               |  |

|                                                  |                     |                    |  |
|--------------------------------------------------|---------------------|--------------------|--|
| subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Fall                                             |                     |                    |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Post procedural erythema                         |                     |                    |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Post procedural fever                            |                     |                    |  |
| subjects affected / exposed<br>occurrences (all) | 1 / 6 (16.67%)<br>1 | 0 / 1 (0.00%)<br>0 |  |
| Post procedural haematoma                        |                     |                    |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Stoma site erythema                              |                     |                    |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Cardiac disorders                                |                     |                    |  |
| Myocardial infarction                            |                     |                    |  |
| subjects affected / exposed<br>occurrences (all) | 1 / 6 (16.67%)<br>1 | 0 / 1 (0.00%)<br>0 |  |
| Palpitations                                     |                     |                    |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Sinus tachycardia                                |                     |                    |  |
| subjects affected / exposed<br>occurrences (all) | 1 / 6 (16.67%)<br>1 | 0 / 1 (0.00%)<br>0 |  |
| Nervous system disorders                         |                     |                    |  |
| Dizziness                                        |                     |                    |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Aphasia                                          |                     |                    |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Brachial plexopathy                              |                     |                    |  |

|                                      |                |               |  |
|--------------------------------------|----------------|---------------|--|
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                    | 0              | 0             |  |
| Depressed level of consciousness     |                |               |  |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                    | 0              | 0             |  |
| Disturbance in attention             |                |               |  |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                    | 0              | 0             |  |
| Headache                             |                |               |  |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                    | 0              | 0             |  |
| Neuropathy peripheral                |                |               |  |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                    | 0              | 0             |  |
| Peripheral sensory neuropathy        |                |               |  |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                    | 0              | 0             |  |
| Presyncope                           |                |               |  |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                    | 0              | 0             |  |
| Somnolence                           |                |               |  |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                    | 0              | 0             |  |
| Blood and lymphatic system disorders |                |               |  |
| Anaemia                              |                |               |  |
| subjects affected / exposed          | 3 / 6 (50.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)                    | 3              | 0             |  |
| Ear and labyrinth disorders          |                |               |  |
| Ear discomfort                       |                |               |  |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                    | 0              | 0             |  |
| Ear pain                             |                |               |  |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                    | 0              | 0             |  |
| Hypoacusis                           |                |               |  |

|                                                                                                |                     |                    |  |
|------------------------------------------------------------------------------------------------|---------------------|--------------------|--|
| subjects affected / exposed<br>occurrences (all)                                               | 0 / 6 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Eye disorders<br>Chalazion<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 6 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Gastrointestinal disorders<br>Constipation<br>subjects affected / exposed<br>occurrences (all) | 1 / 6 (16.67%)<br>1 | 0 / 1 (0.00%)<br>0 |  |
| Nausea<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 6 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)                             | 0 / 6 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)                                   | 0 / 6 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Rectal haemorrhage<br>subjects affected / exposed<br>occurrences (all)                         | 1 / 6 (16.67%)<br>1 | 0 / 1 (0.00%)<br>0 |  |
| Dysphagia<br>subjects affected / exposed<br>occurrences (all)                                  | 0 / 6 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Ileus<br>subjects affected / exposed<br>occurrences (all)                                      | 0 / 6 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Oesophageal obstruction<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 6 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Small intestinal obstruction<br>subjects affected / exposed<br>occurrences (all)               | 0 / 6 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Diarrhoea                                                                                      |                     |                    |  |

|                                        |                |               |  |
|----------------------------------------|----------------|---------------|--|
| subjects affected / exposed            | 1 / 6 (16.67%) | 0 / 1 (0.00%) |  |
| occurrences (all)                      | 1              | 0             |  |
| Abdominal pain upper                   |                |               |  |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                      | 0              | 0             |  |
| Abdominal distension                   |                |               |  |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                      | 0              | 0             |  |
| Dry mouth                              |                |               |  |
| subjects affected / exposed            | 1 / 6 (16.67%) | 0 / 1 (0.00%) |  |
| occurrences (all)                      | 1              | 0             |  |
| Abdominal pain lower                   |                |               |  |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                      | 0              | 0             |  |
| Breath odour                           |                |               |  |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                      | 0              | 0             |  |
| Eructation                             |                |               |  |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                      | 0              | 0             |  |
| Inguinal hernia                        |                |               |  |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                      | 0              | 0             |  |
| Oedema mouth                           |                |               |  |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                      | 0              | 0             |  |
| Retching                               |                |               |  |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                      | 0              | 0             |  |
| Hepatobiliary disorders                |                |               |  |
| Hepatic pain                           |                |               |  |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                      | 0              | 0             |  |
| Skin and subcutaneous tissue disorders |                |               |  |
| Alopecia                               |                |               |  |

|                             |                |               |  |
|-----------------------------|----------------|---------------|--|
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)           | 0              | 0             |  |
| Eczema                      |                |               |  |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)           | 0              | 0             |  |
| Rash macular                |                |               |  |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)           | 0              | 0             |  |
| Vitiligo                    |                |               |  |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)           | 0              | 0             |  |
| Erythema                    |                |               |  |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 1 (0.00%) |  |
| occurrences (all)           | 1              | 0             |  |
| Psoriasis                   |                |               |  |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)           | 0              | 0             |  |
| Rash                        |                |               |  |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)           | 0              | 0             |  |
| Urticaria                   |                |               |  |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)           | 0              | 0             |  |
| Hyperhidrosis               |                |               |  |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)           | 0              | 0             |  |
| Pruritus                    |                |               |  |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)           | 0              | 0             |  |
| Rash pruritic               |                |               |  |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)           | 0              | 0             |  |
| Scar pain                   |                |               |  |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)           | 0              | 0             |  |
| Skin wound                  |                |               |  |

|                                                  |                    |                    |  |
|--------------------------------------------------|--------------------|--------------------|--|
| subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |  |
| Endocrine disorders                              |                    |                    |  |
| Adrenal insufficiency                            |                    |                    |  |
| subjects affected / exposed                      | 0 / 6 (0.00%)      | 0 / 1 (0.00%)      |  |
| occurrences (all)                                | 0                  | 0                  |  |
| Hyperthyroidism                                  |                    |                    |  |
| subjects affected / exposed                      | 0 / 6 (0.00%)      | 0 / 1 (0.00%)      |  |
| occurrences (all)                                | 0                  | 0                  |  |
| Musculoskeletal and connective tissue disorders  |                    |                    |  |
| Myalgia                                          |                    |                    |  |
| subjects affected / exposed                      | 1 / 6 (16.67%)     | 0 / 1 (0.00%)      |  |
| occurrences (all)                                | 3                  | 0                  |  |
| Back pain                                        |                    |                    |  |
| subjects affected / exposed                      | 0 / 6 (0.00%)      | 0 / 1 (0.00%)      |  |
| occurrences (all)                                | 0                  | 0                  |  |
| Flank pain                                       |                    |                    |  |
| subjects affected / exposed                      | 1 / 6 (16.67%)     | 0 / 1 (0.00%)      |  |
| occurrences (all)                                | 1                  | 0                  |  |
| Arthralgia                                       |                    |                    |  |
| subjects affected / exposed                      | 2 / 6 (33.33%)     | 0 / 1 (0.00%)      |  |
| occurrences (all)                                | 3                  | 0                  |  |
| Muscle spasms                                    |                    |                    |  |
| subjects affected / exposed                      | 0 / 6 (0.00%)      | 0 / 1 (0.00%)      |  |
| occurrences (all)                                | 0                  | 0                  |  |
| Bone pain                                        |                    |                    |  |
| subjects affected / exposed                      | 0 / 6 (0.00%)      | 0 / 1 (0.00%)      |  |
| occurrences (all)                                | 0                  | 0                  |  |
| Mobility decreased                               |                    |                    |  |
| subjects affected / exposed                      | 0 / 6 (0.00%)      | 0 / 1 (0.00%)      |  |
| occurrences (all)                                | 0                  | 0                  |  |
| Neck pain                                        |                    |                    |  |
| subjects affected / exposed                      | 1 / 6 (16.67%)     | 0 / 1 (0.00%)      |  |
| occurrences (all)                                | 1                  | 0                  |  |
| Pain in extremity                                |                    |                    |  |

|                                   |                |               |  |
|-----------------------------------|----------------|---------------|--|
| subjects affected / exposed       | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                 | 0              | 0             |  |
| Pain in jaw                       |                |               |  |
| subjects affected / exposed       | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                 | 0              | 0             |  |
| Oedema                            |                |               |  |
| subjects affected / exposed       | 1 / 6 (16.67%) | 0 / 1 (0.00%) |  |
| occurrences (all)                 | 1              | 0             |  |
| Infections and infestations       |                |               |  |
| Upper respiratory tract infection |                |               |  |
| subjects affected / exposed       | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                 | 0              | 0             |  |
| Pyelonephritis                    |                |               |  |
| subjects affected / exposed       | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                 | 0              | 0             |  |
| COVID-19                          |                |               |  |
| subjects affected / exposed       | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                 | 0              | 0             |  |
| Nasopharyngitis                   |                |               |  |
| subjects affected / exposed       | 1 / 6 (16.67%) | 0 / 1 (0.00%) |  |
| occurrences (all)                 | 1              | 0             |  |
| Pneumonia                         |                |               |  |
| subjects affected / exposed       | 1 / 6 (16.67%) | 0 / 1 (0.00%) |  |
| occurrences (all)                 | 1              | 0             |  |
| Paronychia                        |                |               |  |
| subjects affected / exposed       | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                 | 0              | 0             |  |
| Conjunctivitis                    |                |               |  |
| subjects affected / exposed       | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                 | 0              | 0             |  |
| Oral fungal infection             |                |               |  |
| subjects affected / exposed       | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                 | 0              | 0             |  |
| Sinusitis                         |                |               |  |
| subjects affected / exposed       | 0 / 6 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                 | 0              | 0             |  |

|                                                                        |                     |                    |  |
|------------------------------------------------------------------------|---------------------|--------------------|--|
| Skin infection<br>subjects affected / exposed<br>occurrences (all)     | 0 / 6 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Metabolism and nutrition disorders                                     |                     |                    |  |
| Decreased appetite<br>subjects affected / exposed<br>occurrences (all) | 2 / 6 (33.33%)<br>2 | 0 / 1 (0.00%)<br>0 |  |
| Hyponatraemia<br>subjects affected / exposed<br>occurrences (all)      | 0 / 6 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Hyperglycaemia<br>subjects affected / exposed<br>occurrences (all)     | 0 / 6 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Hypokalaemia<br>subjects affected / exposed<br>occurrences (all)       | 2 / 6 (33.33%)<br>3 | 0 / 1 (0.00%)<br>0 |  |
| Hypercalcaemia<br>subjects affected / exposed<br>occurrences (all)     | 0 / 6 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Hypophosphataemia<br>subjects affected / exposed<br>occurrences (all)  | 1 / 6 (16.67%)<br>1 | 0 / 1 (0.00%)<br>0 |  |
| Hypomagnesaemia<br>subjects affected / exposed<br>occurrences (all)    | 1 / 6 (16.67%)<br>2 | 0 / 1 (0.00%)<br>0 |  |
| Dehydration<br>subjects affected / exposed<br>occurrences (all)        | 0 / 6 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Hyperuricaemia<br>subjects affected / exposed<br>occurrences (all)     | 0 / 6 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Hypoalbuminaemia<br>subjects affected / exposed<br>occurrences (all)   | 0 / 6 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Malnutrition                                                           |                     |                    |  |

|                             |               |               |  |
|-----------------------------|---------------|---------------|--|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)           | 0             | 0             |  |
| Vitamin D deficiency        |               |               |  |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)           | 0             | 0             |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment                                                                                                                                                                                                                                                                                                                                                 |
|------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 18 November 2019 | <ul style="list-style-type: none"><li>• Removal Day 2 from Schedule of Events</li><li>• Clarification prophylactic hydration requirement</li><li>• Update non-clinical data</li><li>• Clarification of risks and benefits</li><li>• Clarification SUSAR definition</li><li>• Clarification safety analysis will be performed for RP2D selection</li></ul> |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date          | Interruption                                                                | Restart date |
|---------------|-----------------------------------------------------------------------------|--------------|
| 01 April 2020 | Temporary halt of recruitment due to the COVID-19 pandemic Apr2020- May2020 | 01 June 2020 |

Notes:

### Limitations and caveats

None reported