



## Clinical trial results:

**A phase II randomized, placebo-controlled, double-blind, dose-escalation study to evaluate safety, pharmacokinetics and pharmacodynamic dose response relationship of IFX-1 in patients undergoing complex cardiac surgery (CARDIAC)**

### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2015-003036-12  |
| Trial protocol           | DE              |
| Global end of trial date | 24 January 2017 |

### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 14 May 2021  |
| First version publication date | 14 May 2021  |

### Trial information

#### Trial identification

|                       |            |
|-----------------------|------------|
| Sponsor protocol code | IFX-1-P2.2 |
|-----------------------|------------|

#### Additional study identifiers

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

Notes:

### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | InflaRx GmbH   |
| Sponsor organisation address | Winzerlaer Str.2, Jena, Germany, 07745                       |
| Public contact               | InflaRx GmbH, InflaRx GmbH, +49 3641508 180, info@inflarx.de |
| Scientific contact           | InflaRx GmbH, InflaRx GmbH, +49 3641508 180, info@inflarx.de |

Notes:

### Paediatric regulatory details

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

Notes:

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**Results analysis stage**

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|  |                 |
|--|-----------------|
| Analysis stage                                       | Final           |
| Date of interim/final analysis                       | 20 October 2017 |
| Is this the analysis of the primary completion data? | Yes             |
| Primary completion date                              | 24 January 2017 |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 24 January 2017 |
| Was the trial ended prematurely?                     | No              |

Notes:

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**General information about the trial**

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Main objective of the trial:

To evaluate the effect of four different doses of IFX-1 on interleukin (IL)-6 peak levels in patients undergoing complex cardiac surgery compared to placebo.

Protection of trial subjects:

The study was conducted in accordance with the ethical principles of the Declaration of Helsinki (Version Fortaleza 2013), as well as all pertinent laws and the International Conference on Harmonization (ICH) guidelines for Good Clinical Practice (GCP) issued in June 1996 and CPMP/ICH/135/95 from September 1997. The study only started after obtaining a positive evaluation by the leading ethics committee and approval from the respective federal authority.

Only subjects that met all inclusion criteria and no exclusion criteria were to enter the study. All patients were free to discontinue their participation in the study at any time.

Background therapy: -

Evidence for comparator: -

|   |              |
|---|--------------|
| Actual start date of recruitment                          | 06 June 2016 |
| Long term follow-up planned                               | No           |
| Independent data monitoring committee (IDMC) involvement? | Yes          |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

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|                                      |              |
|--------------------------------------|--------------|
| Country: Number of subjects enrolled | Germany: 115 |
| Worldwide total number of subjects   | 115          |
| EEA total number of subjects         | 115          |

Notes:

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**Subjects enrolled per age group**

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|   |    |
|---|----|
| 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)                      | 30 |
| From 65 to 84 years                       | 84 |

|                   |   |
|-------------------|---|
| 85 years and over | 1 |
|-------------------|---|

## Subject disposition

### Recruitment

#### Recruitment details:

The study included patients of 18 years or older with a planned cardiac surgical procedure with cardiopulmonary bypass. The study was conducted at 10 sites in Germany, 9 of which enrolled patients between 06 Jun 2016 and 24 Jan 2017. Due to missing age data, not the 120 patients enrolled but only the 115 patients randomized are presented above.

### Pre-assignment

#### Screening details:

All 120 patients were screened for eligibility before participating in the active treatment phase of the study. Subjects were not to be entered to the trial treatment if any of the eligibility criteria were violated. Of the 120 patients, 115 patients were randomized and of these, 104 were treated.

### Period 1

|                              |                                 |
|------------------------------|---------------------------------|
| Period 1 title               | Overall period (overall period) |
| Is this the baseline period? | Yes                             |
| Allocation method            | Randomised - controlled         |
| Blinding used                | Double blind                    |
| Roles blinded                | Subject, Investigator, Carer    |

#### Blinding implementation details:

To ensure adequate blinding after reconstitution, standard measures will be taken for the investigational medicinal product (IMP, e.g., same container/closure system, storage conditions, color, and foaming property). In addition, each reconstituted IMP that is transferred to the operating room is only labeled with blinded information. In general, access to study documents containing information on IFX-1 level and treatment groups will be restricted to unblinded personnel.

### Arms

|                              |         |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes     |
| <b>Arm title</b>             | Placebo |

#### Arm description:

Subjects in this arm were administered a single intravenous administration of placebo with doses corresponding to the IFX-1 dose cohorts. The ratio between IFX-1 and placebo within one dose cohort was 4:1. All four placebo dose cohorts of 1, 2, 4 or 8 mg/kg body weight (bw) are presented combined. Dosing started after completion of anaesthesia and was finished prior to start of surgery.

|  |                 |
|--|-----------------|
| Arm type                               | Placebo         |
| Investigational medicinal product name | Placebo         |
| Investigational medicinal product code |                 |
| Other name                             |                 |
| Pharmaceutical forms                   | Infusion        |
| Routes of administration               | Intravenous use |

#### Dosage and administration details:

Administration of 1, 2, 4 or 8 mg/kg bw placebo as an intravenous infusion via infusomat over 30 minutes (min), and within 30 min after completion of successful anaesthesia. Placebo matching the IFX-1 was supplied in 10 mL glass vials containing the equivalent colourless phosphat buffered saline solution with polysorbate 80 without the active pharmaceutical ingredient. For patients with a body weight between 100 and 130 kg, the dose calculation was based on 100 kg body weight.

|                  |                  |
|------------------|------------------|
| <b>Arm title</b> | 1 mg/kg bw IFX-1 |
|------------------|------------------|

#### Arm description:

Subjects in this arm were administered a single intravenous administration of 1 mg/kg bw IFX-1. Dosing started after completion of anaesthesia and was finished prior to start of surgery.

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

|  |                    |
|--|--------------------|
| Investigational medicinal product name | IFX-1              |
| Investigational medicinal product code |                    |
| Other name                             |                    |
| Pharmaceutical forms                   | Injection          |
| Routes of administration               | Intracavernous use |

**Dosage and administration details:**

Administration of 1 mg/kg bw IFX-1 as an intravenous infusion via infusomat over 30 min, and within 30 min after completion of successful anaesthesia.

IFX-1 was formulated in a phosphate buffered saline and polysorbate 80 and was supplied in 10 mL glass vials in strength of 10 mg/mL.

For patients with a body weight between 100 and 130 kg, the dose calculation was based on 100 kg body weight.

|                  |                  |
|------------------|------------------|
| <b>Arm title</b> | 2 mg/kg bw IFX-1 |
|------------------|------------------|

**Arm description:**

Subjects in this arm were administered a single intravenous administration of 2 mg/kg bw IFX-1. Dosing started after completion of anaesthesia and was finished prior to start of surgery.

|  |                    |
|--|--------------------|
| Arm type                               | Experimental       |
| Investigational medicinal product name | IFX-1              |
| Investigational medicinal product code |                    |
| Other name                             |                    |
| Pharmaceutical forms                   | Injection          |
| Routes of administration               | Intracavernous use |

**Dosage and administration details:**

Administration of 2 mg/kg bw IFX-1 as an intravenous infusion via infusomat over 30 min, and within 30 min after completion of successful anaesthesia.

IFX-1 was formulated in a phosphate buffered saline and polysorbate 80 and was supplied in 10 mL glass vials in strength of 10 mg/mL.

For patients with a body weight between 100 and 130 kg, the dose calculation was based on 100 kg body weight.

|                  |                  |
|------------------|------------------|
| <b>Arm title</b> | 4 mg/kg bw IFX-1 |
|------------------|------------------|

**Arm description:**

Subjects in this arm were administered a single intravenous administration of 4 mg/kg bw IFX-1. Dosing started after completion of anaesthesia and was finished prior to start of surgery.

|  |                    |
|--|--------------------|
| Arm type                               | Experimental       |
| Investigational medicinal product name | IFX-1              |
| Investigational medicinal product code |                    |
| Other name                             |                    |
| Pharmaceutical forms                   | Injection          |
| Routes of administration               | Intracavernous use |

**Dosage and administration details:**

Administration of 4 mg/kg bw IFX-1 as an intravenous infusion via infusomat over 30 min, and within 30 min after completion of successful anaesthesia.

IFX-1 was formulated in a phosphate buffered saline and polysorbate 80 and was supplied in 10 mL glass vials in strength of 10 mg/mL.

For patients with a body weight between 100 and 130 kg, the dose calculation was based on 100 kg body weight.

|                  |                  |
|------------------|------------------|
| <b>Arm title</b> | 8 mg/kg bw IFX-1 |
|------------------|------------------|

**Arm description:**

Subjects in this arm were administered a single intravenous administration of 8 mg/kg bw IFX-1. Dosing started after completion of anaesthesia and was finished prior to start of surgery.

|  |                    |
|--|--------------------|
| Arm type                               | Experimental       |
| Investigational medicinal product name | IFX-1              |
| Investigational medicinal product code |                    |
| Other name                             |                    |
| Pharmaceutical forms                   | Injection          |
| Routes of administration               | Intracavernous use |

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**Dosage and administration details:**

Administration of 8 mg/kg bw IFX-1 as an intravenous infusion via infusomat over 30 min, and within 30 min after completion of successful anaesthesia.

IFX-1 was formulated in a phosphate buffered saline and polysorbate 80 and was supplied in 10 mL glass vials in strength of 10 mg/mL.

For patients with a body weight between 100 and 130 kg, the dose calculation was based on 100 kg body weight.

| <b>Number of subjects in period 1<sup>[1]</sup></b> | Placebo | 1 mg/kg bw IFX-1 | 2 mg/kg bw IFX-1 |
|---|---------|------------------|------------------|
| Started   | 23      | 21               | 19               |
| Completed   | 23      | 19               | 19               |
| Not completed                                       | 0       | 2                | 0                |
| Adverse event, serious fatal                        | -       | 2                | -                |

| <b>Number of subjects in period 1<sup>[1]</sup></b> | 4 mg/kg bw IFX-1 | 8 mg/kg bw IFX-1 |
|---|------------------|------------------|
| Started   | 21               | 20               |
| Completed   | 21               | 20               |
| Not completed                                       | 0                | 0                |
| Adverse event, serious fatal                        | -                | -                |

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**Notes:**

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

Justification: Baseline characteristics are based on patients who were randomized after successfully completing the screening period and received study medication (Safety Population).

## Baseline characteristics

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### Reporting groups

|                       |                |
|-----------------------|----------------|
| Reporting group title | Overall period |
|-----------------------|----------------|

Reporting group description:

Safety population (SAF): all subjects who received study drug, irrespective of whether the infusion was completed. Analyses on the SAF were performed according to the actual dose the subjects received.

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| Reporting group values | Overall period | Total |  |
|------------------------|----------------|-------|--|
| Number of subjects     | 104            | 104   |  |
| Age categorical        |                |       |  |
| Units: Subjects        |                |       |  |
| Adults (18-64 years)   | 29             | 29    |  |
| From 65 to 84 years    | 74             | 74    |  |
| 85 years and over      | 1              | 1     |  |
| Gender categorical     |                |       |  |
| Units: Subjects        |                |       |  |
| Female                 | 28             | 28    |  |
| Male                   | 76             | 76    |  |

## End points

### End points reporting groups

|   |                  |
|---|------------------|
| Reporting group title   | Placebo          |
| Reporting group description:<br>Subjects in this arm were administered a single intravenous administration of placebo with doses corresponding to the IFX-1 dose cohorts. The ratio between IFX-1 and placebo within one dose cohort was 4:1. All four placebo dose cohorts of 1, 2, 4 or 8 mg/kg body weight (bw) are presented combined. Dosing started after completion of anaesthesia and was finished prior to start of surgery. |                  |
| Reporting group title   | 1 mg/kg bw IFX-1 |
| Reporting group description:<br>Subjects in this arm were administered a single intravenous administration of 1 mg/kg bw IFX-1. Dosing started after completion of anaesthesia and was finished prior to start of surgery.  |                  |
| Reporting group title   | 2 mg/kg bw IFX-1 |
| Reporting group description:<br>Subjects in this arm were administered a single intravenous administration of 2 mg/kg bw IFX-1. Dosing started after completion of anaesthesia and was finished prior to start of surgery.  |                  |
| Reporting group title   | 4 mg/kg bw IFX-1 |
| Reporting group description:<br>Subjects in this arm were administered a single intravenous administration of 4 mg/kg bw IFX-1. Dosing started after completion of anaesthesia and was finished prior to start of surgery.  |                  |
| Reporting group title   | 8 mg/kg bw IFX-1 |
| Reporting group description:<br>Subjects in this arm were administered a single intravenous administration of 8 mg/kg bw IFX-1. Dosing started after completion of anaesthesia and was finished prior to start of surgery.  |                  |

### Primary: IL-6 peak level

|  |                 |
|--|-----------------|
| End point title  | IL-6 peak level |
| End point description:<br>IL-6 peak level: For each subject, the highest IL-6 level measured at any time point from prior to study drug administration until 24 hours (h) after start of cardiopulmonary bypass.<br>Values > 1500 pg/mL were set to 1500 pg/mL for the purpose of determining the IL-6 peak.<br>Full Analysis Set (FAS): All randomized and treated subjects who had sufficient IL-6 data. IL-6 data were regarded as sufficient if the available blood samples allowed a statement about the IL-6 peak for the subject. Analyses on the FAS were performed according to the randomized dose group. Subjects who were randomized but not treated were excluded from this analysis set. |                 |
| End point type   | Primary         |
| End point timeframe:<br>From prior to study drug administration until Visit 9, 24 h after start of cardiopulmonary bypass.   |                 |

| End point values                     | Placebo           | 1 mg/kg bw IFX-1  | 2 mg/kg bw IFX-1  | 4 mg/kg bw IFX-1  |
|--------------------------------------|-------------------|-------------------|-------------------|-------------------|
| Subject group type                   | Reporting group   | Reporting group   | Reporting group   | Reporting group   |
| Number of subjects analysed          | 23 <sup>[1]</sup> | 21 <sup>[2]</sup> | 19 <sup>[3]</sup> | 21 <sup>[4]</sup> |
| Units: pg/mL                         |                   |                   |                   |                   |
| arithmetic mean (standard deviation) | 679.21 (± 492.64) | 718.19 (± 465.43) | 664.31 (± 455.88) | 550.09 (± 361.17) |



Notes:

[1] - FAS

[2] - FAS

[3] - FAS

[4] - FAS

|                                      |                   |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| <b>End point values</b>              | 8 mg/kg bw IFX-1  |  |  |  |
| Subject group type                   | Reporting group   |  |  |  |
| Number of subjects analysed          | 20 <sup>[5]</sup> |  |  |  |
| Units: pg/mL                         |                   |  |  |  |
| arithmetic mean (standard deviation) | 673.92 (± 483.01) |  |  |  |

Notes:

[5] - FAS

## Statistical analyses

|                                   |                     |
|-----------------------------------|---------------------|
| <b>Statistical analysis title</b> | Kruskal-Wallis test |
|-----------------------------------|---------------------|

Statistical analysis description:

For continuous data, the standard statistics (sample size, number of missing values, mean, standard deviation [SD], minimum, Q1, median, Q3, and maximum) were presented. Continuous data at each visit / analysis day / time point were compared using the Kruskal-Wallis test, assessing an overall difference between dose groups.

|   |   |
|---|---|
| Comparison groups                       | Placebo v 1 mg/kg bw IFX-1 v 2 mg/kg bw IFX-1 v 4 mg/kg bw IFX-1 v 8 mg/kg bw IFX-1 |
| Number of subjects included in analysis | 104   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | other <sup>[6]</sup>  |
| P-value                                 | = 0.8611  |
| Method                                  | Kruskal-wallis  |

Notes:

[6] - Continuous data at each visit / analysis day / time point were compared using the Kruskal-Wallis test, assessing an overall difference between dose groups.

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from First Patient First Visit until Last Patient Last Visit. All adverse events are reported in this record from first study drug administration on Day 1 until Day 29 (last visit).

Adverse event reporting additional description:

SAF

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

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 19.0   |

### Reporting groups

|                       |                 |
|-----------------------|-----------------|
| Reporting group title | 1mg/kg bw IFX-1 |
|-----------------------|-----------------|

Reporting group description:

Subjects in this arm were administered a single intravenous administration of 1 mg/kg bw IFX-1. Dosing started after completion of anaesthesia and was finished prior to start of surgery.

|                       |                 |
|-----------------------|-----------------|
| Reporting group title | 2mg/kg bw IFX-1 |
|-----------------------|-----------------|

Reporting group description:

Subjects in this arm were administered a single intravenous administration of 2 mg/kg bw IFX-1. Dosing started after completion of anaesthesia and was finished prior to start of surgery.

|                       |                 |
|-----------------------|-----------------|
| Reporting group title | 4mg/kg bw IFX-1 |
|-----------------------|-----------------|

Reporting group description:

Subjects in this arm were administered a single intravenous administration of 4 mg/kg bw IFX-1. Dosing started after completion of anaesthesia and was finished prior to start of surgery.

|                       |                 |
|-----------------------|-----------------|
| Reporting group title | 8mg/kg bw IFX-1 |
|-----------------------|-----------------|

Reporting group description:

Subjects in this arm were administered a single intravenous administration of 8 mg/kg bw IFX-1. Dosing started after completion of anaesthesia and was finished prior to start of surgery.

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

Reporting group description:

Subjects in this arm were administered a single intravenous administration of placebo with doses corresponding to the IFX-1 dose cohorts. The ratio between IFX-1 and placebo within one dose cohort was 4:1. All four placebo dose cohorts of 1, 2, 4 or 8 mg/kg body weight (bw) are presented combined. Dosing started after completion of anaesthesia and was finished prior to start of surgery.

| Serious adverse events                            | 1mg/kg bw IFX-1                   | 2mg/kg bw IFX-1 | 4mg/kg bw IFX-1 |
|---|-----------------------------------|-----------------|-----------------|
| Total subjects affected by serious adverse events |                                   |                 |                 |
| subjects affected / exposed                       | 9 / 23 (39.13%)                   | 7 / 18 (38.89%) | 6 / 21 (28.57%) |
| number of deaths (all causes)                     | 2                                 | 0               | 0               |
| number of deaths resulting from adverse events    | 2                                 | 0               | 0               |
| Vascular disorders                                |                                   |                 |                 |
| Haematoma   | Additional description: Haematoma |                 |                 |
| subjects affected / exposed                       | 1 / 23 (4.35%)                    | 0 / 18 (0.00%)  | 0 / 21 (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           |

|   |   |                |                |
|---|---|----------------|----------------|
| Haemodynamic instability<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                | Additional description: Haemodynamic instability                |                |                |
|   | 1 / 23 (4.35%)  | 0 / 18 (0.00%) | 0 / 21 (0.00%) |
|   | 0 / 1   | 0 / 0          | 0 / 0          |
|   | 0 / 0   | 0 / 0          | 0 / 0          |
| Haemorrhage<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                             | Additional description: Haemorrhage                             |                |                |
|   | 0 / 23 (0.00%)  | 0 / 18 (0.00%) | 1 / 21 (4.76%) |
|   | 0 / 0   | 0 / 0          | 0 / 1          |
|   | 0 / 0   | 0 / 0          | 0 / 0          |
| Peripheral artery thrombosis<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all            | Additional description: Peripheral artery thrombosis            |                |                |
|   | 1 / 23 (4.35%)  | 0 / 18 (0.00%) | 0 / 21 (0.00%) |
|   | 0 / 1   | 0 / 0          | 0 / 0          |
|   | 0 / 0   | 0 / 0          | 0 / 0          |
| General disorders and administration site conditions  |   |                |                |
| General physical health deterioration<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all   | Additional description: General physical health deterioration   |                |                |
|   | 1 / 23 (4.35%)  | 0 / 18 (0.00%) | 0 / 21 (0.00%) |
|   | 0 / 1   | 0 / 0          | 0 / 0          |
|   | 0 / 0   | 0 / 0          | 0 / 0          |
| Impaired healing<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                        | Additional description: Impaired healing                        |                |                |
|   | 2 / 23 (8.70%)  | 0 / 18 (0.00%) | 0 / 21 (0.00%) |
|   | 0 / 2   | 0 / 0          | 0 / 0          |
|   | 0 / 0   | 0 / 0          | 0 / 0          |
| Multiple organ dysfunction syndrome<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all     | Additional description: Multiple organ dysfunction syndrome     |                |                |
|   | 0 / 23 (0.00%)  | 0 / 18 (0.00%) | 0 / 21 (0.00%) |
|   | 0 / 0   | 0 / 0          | 0 / 0          |
|   | 0 / 0   | 0 / 0          | 0 / 0          |
| Pyrexia<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                                 | Additional description: Pyrexia                                 |                |                |
|   | 0 / 23 (0.00%)  | 0 / 18 (0.00%) | 1 / 21 (4.76%) |
|   | 0 / 0   | 0 / 0          | 0 / 1          |
|   | 0 / 0   | 0 / 0          | 0 / 0          |
| Systemic inflammatory response syndrome<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all | Additional description: Systemic inflammatory response syndrome |                |                |
|   | 2 / 23 (8.70%)  | 0 / 18 (0.00%) | 0 / 21 (0.00%) |
|   | 0 / 2   | 0 / 0          | 0 / 0          |
|   | 0 / 1   | 0 / 0          | 0 / 0          |

|   |  |                 |                |
|---|--|-----------------|----------------|
| Respiratory, thoracic and mediastinal disorders |  |                 |                |
| Haemothorax                                     | Additional description: Haemothorax              |                 |                |
| subjects affected / exposed                     | 1 / 23 (4.35%)                                   | 1 / 18 (5.56%)  | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 1           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0           | 0 / 0          |
| Mediastinal haemorrhage                         | Additional description: Mediastinal haemorrhage  |                 |                |
| subjects affected / exposed                     | 0 / 23 (0.00%)                                   | 1 / 18 (5.56%)  | 0 / 21 (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          |
| Pleural effusion                                | Additional description: Pleural effusion         |                 |                |
| subjects affected / exposed                     | 0 / 23 (0.00%)                                   | 2 / 18 (11.11%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 2           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0           | 0 / 0          |
| Pulmonary oedema                                | Additional description: Pulmonary oedema         |                 |                |
| subjects affected / exposed                     | 0 / 23 (0.00%)                                   | 1 / 18 (5.56%)  | 0 / 21 (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          |
| Respiratory failure                             | Additional description: Respiratory failure      |                 |                |
| subjects affected / exposed                     | 1 / 23 (4.35%)                                   | 0 / 18 (0.00%)  | 2 / 21 (9.52%) |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0           | 0 / 2          |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0           | 0 / 0          |
| Psychiatric disorders                           |  |                 |                |
| Delirium  | Additional description: Delirium                 |                 |                |
| subjects affected / exposed                     | 0 / 23 (0.00%)                                   | 1 / 18 (5.56%)  | 1 / 21 (4.76%) |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1           | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0           | 0 / 0          |
| Transient psychosis                             | Additional description: Transient psychosis      |                 |                |
| subjects affected / exposed                     | 0 / 23 (0.00%)                                   | 0 / 18 (0.00%)  | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0           | 0 / 0          |
| Investigations                                  |  |                 |                |
| Blood pressure decreased                        | Additional description: Blood pressure decreased |                 |                |

|   |   |                |                |
|---|---|----------------|----------------|
| subjects affected / exposed                     | 0 / 23 (0.00%)  | 1 / 18 (5.56%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 2          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          | 0 / 0          |
| Injury, poisoning and procedural complications  |   |                |                |
| Post procedural haemorrhage                     | Additional description: Post procedural haemorrhage                   |                |                |
| subjects affected / exposed                     | 1 / 23 (4.35%)  | 0 / 18 (0.00%) | 0 / 21 (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          |
| Postoperative thoracic procedure complication   | Additional description: Postoperative thoracic procedure complication |                |                |
| subjects affected / exposed                     | 0 / 23 (0.00%)  | 0 / 18 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          | 0 / 0          |
| Cardiac disorders                               |   |                |                |
| Arteriospasm coronary                           | Additional description: Arteriospasm coronary                         |                |                |
| subjects affected / exposed                     | 0 / 23 (0.00%)  | 0 / 18 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          | 0 / 0          |
| Atrial fibrillation                             | Additional description: Atrial fibrillation                           |                |                |
| subjects affected / exposed                     | 0 / 23 (0.00%)  | 0 / 18 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          | 0 / 0          |
| Atrioventricular block complete                 | Additional description: Atrioventricular block complete               |                |                |
| subjects affected / exposed                     | 0 / 23 (0.00%)  | 0 / 18 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          | 0 / 0          |
| Cardiac arrest                                  | Additional description: Cardiac arrest                                |                |                |
| subjects affected / exposed                     | 0 / 23 (0.00%)  | 1 / 18 (5.56%) | 1 / 21 (4.76%) |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 4          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          | 0 / 0          |
| Cardiac tamponade                               | Additional description: Cardiac tamponade                             |                |                |
| subjects affected / exposed                     | 3 / 23 (13.04%)   | 1 / 18 (5.56%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3   | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          | 0 / 0          |

|  |   |                |                |
|--|---|----------------|----------------|
| Cardiogenic shock<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                        | Additional description: Cardiogenic shock           |                |                |
|  | 1 / 23 (4.35%)                                      | 0 / 18 (0.00%) | 0 / 21 (0.00%) |
|  | 0 / 1   | 0 / 0          | 0 / 0          |
|  | 0 / 0   | 0 / 0          | 0 / 0          |
| Haemorrhage coronary artery<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all              | Additional description: Haemorrhage coronary artery |                |                |
|  | 0 / 23 (0.00%)                                      | 0 / 18 (0.00%) | 1 / 21 (4.76%) |
|  | 0 / 0   | 0 / 0          | 0 / 1          |
|  | 0 / 0   | 0 / 0          | 0 / 0          |
| Low cardiac output syndrome<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all              | Additional description: Low cardiac output syndrome |                |                |
|  | 1 / 23 (4.35%)                                      | 0 / 18 (0.00%) | 0 / 21 (0.00%) |
|  | 0 / 1   | 0 / 0          | 0 / 0          |
|  | 0 / 0   | 0 / 0          | 0 / 0          |
| Myocardial haemorrhage<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                   | Additional description: Myocardial haemorrhage      |                |                |
|  | 0 / 23 (0.00%)                                      | 1 / 18 (5.56%) | 0 / 21 (0.00%) |
|  | 0 / 0   | 0 / 1          | 0 / 0          |
|  | 0 / 0   | 0 / 0          | 0 / 0          |
| Pericardial effusion<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                     | Additional description: Pericardial effusion        |                |                |
|  | 2 / 23 (8.70%)                                      | 0 / 18 (0.00%) | 1 / 21 (4.76%) |
|  | 0 / 3   | 0 / 0          | 0 / 1          |
|  | 0 / 0   | 0 / 0          | 0 / 0          |
| Right ventricular failure<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                | Additional description: Right ventricular failure   |                |                |
|  | 1 / 23 (4.35%)                                      | 0 / 18 (0.00%) | 0 / 21 (0.00%) |
|  | 0 / 1   | 0 / 0          | 0 / 0          |
|  | 0 / 0   | 0 / 0          | 0 / 0          |
| Ventricular fibrillation<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                 | Additional description: Ventricular fibrillation    |                |                |
|  | 0 / 23 (0.00%)                                      | 0 / 18 (0.00%) | 0 / 21 (0.00%) |
|  | 0 / 0   | 0 / 0          | 0 / 0          |
|  | 0 / 0   | 0 / 0          | 0 / 0          |
| Nervous system disorders<br>Brain injury<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all | Additional description: Brain injury                |                |                |
|  | 0 / 23 (0.00%)                                      | 1 / 18 (5.56%) | 0 / 21 (0.00%) |
|  | 0 / 0   | 0 / 1          | 0 / 0          |
|  | 0 / 0   | 0 / 0          | 0 / 0          |
| Brain stem stroke  | Additional description: Brain stem stroke           |                |                |
|  |   |                |                |

|   |   |                |                |
|---|---|----------------|----------------|
| subjects affected / exposed                     | 0 / 23 (0.00%)  | 0 / 18 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          | 0 / 0          |
| Cerebral infarction                             | Additional description: Cerebral infarction                   |                |                |
| subjects affected / exposed                     | 1 / 23 (4.35%)  | 0 / 18 (0.00%) | 0 / 21 (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          |
| Intensive care unit acquired weakness           | Additional description: Intensive care unit acquired weakness |                |                |
| subjects affected / exposed                     | 0 / 23 (0.00%)  | 0 / 18 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          | 0 / 0          |
| Thrombotic stroke                               | Additional description: Thrombotic stroke                     |                |                |
| subjects affected / exposed                     | 0 / 23 (0.00%)  | 0 / 18 (0.00%) | 1 / 21 (4.76%) |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          | 0 / 0          |
| Blood and lymphatic system disorders            |   |                |                |
| Anaemia   | Additional description: Anaemia                               |                |                |
| subjects affected / exposed                     | 0 / 23 (0.00%)  | 0 / 18 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          | 0 / 0          |
| Coagulopathy                                    | Additional description: Coagulopathy                          |                |                |
| subjects affected / exposed                     | 1 / 23 (4.35%)  | 0 / 18 (0.00%) | 0 / 21 (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          |
| Gastrointestinal disorders                      |   |                |                |
| Duodenal ulcer haemorrhage                      | Additional description: Duodenal ulcer haemorrhage            |                |                |
| subjects affected / exposed                     | 0 / 23 (0.00%)  | 1 / 18 (5.56%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 2          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          | 0 / 0          |
| Intestinal haemorrhage                          | Additional description: Intestinal haemorrhage                |                |                |
| subjects affected / exposed                     | 0 / 23 (0.00%)  | 0 / 18 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          | 0 / 0          |

|  |  |                |                |
|--|--|----------------|----------------|
| Intestinal ischaemia<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                               | Additional description: Intestinal ischaemia               |                |                |
|  | 1 / 23 (4.35%)   | 0 / 18 (0.00%) | 0 / 21 (0.00%) |
|  | 0 / 1  | 0 / 0          | 0 / 0          |
|  | 0 / 1  | 0 / 0          | 0 / 0          |
| Upper gastrointestinal haemorrhage<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                 | Additional description: Upper gastrointestinal haemorrhage |                |                |
|  | 0 / 23 (0.00%)   | 0 / 18 (0.00%) | 0 / 21 (0.00%) |
|  | 0 / 0  | 0 / 0          | 0 / 0          |
|  | 0 / 0  | 0 / 0          | 0 / 0          |
| Hepatobiliary disorders<br>Hepatic failure<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all         | Additional description: Hepatic failure                    |                |                |
|  | 1 / 23 (4.35%)   | 0 / 18 (0.00%) | 0 / 21 (0.00%) |
|  | 0 / 1  | 0 / 0          | 0 / 0          |
|  | 0 / 1  | 0 / 0          | 0 / 0          |
| Renal and urinary disorders<br>Acute kidney injury<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all | Additional description: Acute kidney injury                |                |                |
|  | 1 / 23 (4.35%)   | 0 / 18 (0.00%) | 1 / 21 (4.76%) |
|  | 0 / 1  | 0 / 0          | 0 / 1          |
|  | 0 / 0  | 0 / 0          | 0 / 0          |
| End stage renal disease<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                            | Additional description: End stage renal disease            |                |                |
|  | 0 / 23 (0.00%)   | 0 / 18 (0.00%) | 0 / 21 (0.00%) |
|  | 0 / 0  | 0 / 0          | 0 / 0          |
|  | 0 / 0  | 0 / 0          | 0 / 0          |
| Renal failure<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                                      | Additional description: Renal failure                      |                |                |
|  | 2 / 23 (8.70%)   | 0 / 18 (0.00%) | 0 / 21 (0.00%) |
|  | 0 / 2  | 0 / 0          | 0 / 0          |
|  | 0 / 0  | 0 / 0          | 0 / 0          |
| Urinary bladder varices<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                            | Additional description: Urinary bladder varices            |                |                |
|  | 0 / 23 (0.00%)   | 1 / 18 (5.56%) | 0 / 21 (0.00%) |
|  | 0 / 0  | 0 / 1          | 0 / 0          |
|  | 0 / 0  | 0 / 0          | 0 / 0          |
| Infections and infestations<br>Abdominal abscess   | Additional description: Abdominal abscess                  |                |                |
|  |  |                |                |



|   |   |                |                |
|---|---|----------------|----------------|
| subjects affected / exposed                     | 0 / 23 (0.00%)                                      | 0 / 18 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          | 0 / 0          |
| Endocarditis staphylococcal                     | Additional description: Endocarditis staphylococcal |                |                |
| subjects affected / exposed                     | 0 / 23 (0.00%)                                      | 0 / 18 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          | 0 / 0          |
| Enterococcal sepsis                             | Additional description: Enterococcal sepsis         |                |                |
| subjects affected / exposed                     | 0 / 23 (0.00%)                                      | 0 / 18 (0.00%) | 1 / 21 (4.76%) |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          | 0 / 0          |
| Gastroenteritis norovirus                       | Additional description: Gastroenteritis norovirus   |                |                |
| subjects affected / exposed                     | 0 / 23 (0.00%)                                      | 0 / 18 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          | 0 / 0          |
| Influenza                                       | Additional description: Influenza                   |                |                |
| subjects affected / exposed                     | 0 / 23 (0.00%)                                      | 0 / 18 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          | 0 / 0          |
| Mediastinitis                                   | Additional description: Mediastinitis               |                |                |
| subjects affected / exposed                     | 0 / 23 (0.00%)                                      | 0 / 18 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          | 0 / 0          |
| Nosocomial infection                            | Additional description: Nosocomial infection        |                |                |
| subjects affected / exposed                     | 0 / 23 (0.00%)                                      | 0 / 18 (0.00%) | 1 / 21 (4.76%) |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          | 0 / 0          |
| Pneumonia                                       | Additional description: Pneumonia                   |                |                |
| subjects affected / exposed                     | 0 / 23 (0.00%)                                      | 0 / 18 (0.00%) | 1 / 21 (4.76%) |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          | 0 / 0          |
| Pneumonia haemophilus                           | Additional description: Pneumonia haemophilus       |                |                |

|   |   |                |                |
|---|---|----------------|----------------|
| subjects affected / exposed                     | 1 / 23 (4.35%)  | 0 / 18 (0.00%) | 0 / 21 (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          |
| Sepsis  | Additional description: Sepsis                                  |                |                |
| subjects affected / exposed                     | 0 / 23 (0.00%)  | 0 / 18 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          | 0 / 0          |
| Severe invasive streptococcal infection         | Additional description: Severe invasive streptococcal infection |                |                |
| subjects affected / exposed                     | 0 / 23 (0.00%)  | 1 / 18 (5.56%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          | 0 / 0          |
| Urinary tract infection                         | Additional description: Urinary tract infection                 |                |                |
| subjects affected / exposed                     | 0 / 23 (0.00%)  | 0 / 18 (0.00%) | 1 / 21 (4.76%) |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          | 0 / 0          |
| Wound infection                                 | Additional description: Wound infection                         |                |                |
| subjects affected / exposed                     | 0 / 23 (0.00%)  | 0 / 18 (0.00%) | 0 / 21 (0.00%) |
| 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>                     | 8mg/kg bw IFX-1                                  | Placebo         |  |
|---|--|-----------------|--|
| Total subjects affected by serious adverse events |  |                 |  |
| subjects affected / exposed                       | 10 / 20 (50.00%)                                 | 7 / 22 (31.82%) |  |
| number of deaths (all causes)                     | 0  | 0               |  |
| number of deaths resulting from adverse events    | 0  | 0               |  |
| Vascular disorders                                | Additional description: Haematoma                |                 |  |
| Haematoma   |  |                 |  |
| subjects affected / exposed                       | 0 / 20 (0.00%)                                   | 0 / 22 (0.00%)  |  |
| occurrences causally related to treatment / all   | 0 / 0  | 0 / 0           |  |
| deaths causally related to treatment / all        | 0 / 0  | 0 / 0           |  |
| Haemodynamic instability                          | Additional description: Haemodynamic instability |                 |  |
| subjects affected / exposed                       | 0 / 20 (0.00%)                                   | 0 / 22 (0.00%)  |  |
| occurrences causally related to treatment / all   | 0 / 0  | 0 / 0           |  |
| deaths causally related to treatment / all        | 0 / 0  | 0 / 0           |  |

|   |   |                |  |
|---|---|----------------|--|
| Haemorrhage<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                             | Additional description: Haemorrhage                             |                |  |
|   | 0 / 20 (0.00%)  | 0 / 22 (0.00%) |  |
|   | 0 / 0   | 0 / 0          |  |
|   | 0 / 0   | 0 / 0          |  |
| Peripheral artery thrombosis<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all            | Additional description: Peripheral artery thrombosis            |                |  |
|   | 0 / 20 (0.00%)  | 0 / 22 (0.00%) |  |
|   | 0 / 0   | 0 / 0          |  |
|   | 0 / 0   | 0 / 0          |  |
| General disorders and administration site conditions  |   |                |  |
| General physical health deterioration<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all   | Additional description: General physical health deterioration   |                |  |
|   | 0 / 20 (0.00%)  | 0 / 22 (0.00%) |  |
|   | 0 / 0   | 0 / 0          |  |
|   | 0 / 0   | 0 / 0          |  |
| Impaired healing<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                        | Additional description: Impaired healing                        |                |  |
|   | 0 / 20 (0.00%)  | 0 / 22 (0.00%) |  |
|   | 0 / 0   | 0 / 0          |  |
|   | 0 / 0   | 0 / 0          |  |
| Multiple organ dysfunction syndrome<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all     | Additional description: Multiple organ dysfunction syndrome     |                |  |
|   | 1 / 20 (5.00%)  | 0 / 22 (0.00%) |  |
|   | 0 / 1   | 0 / 0          |  |
|   | 0 / 0   | 0 / 0          |  |
| Pyrexia<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                                 | Additional description: Pyrexia                                 |                |  |
|   | 0 / 20 (0.00%)  | 0 / 22 (0.00%) |  |
|   | 0 / 0   | 0 / 0          |  |
|   | 0 / 0   | 0 / 0          |  |
| Systemic inflammatory response syndrome<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all | Additional description: Systemic inflammatory response syndrome |                |  |
|   | 1 / 20 (5.00%)  | 0 / 22 (0.00%) |  |
|   | 0 / 1   | 0 / 0          |  |
|   | 0 / 0   | 0 / 0          |  |
| Respiratory, thoracic and mediastinal disorders   |   |                |  |
| Haemothorax   | Additional description: Haemothorax                             |                |  |
|   |   |                |  |

|   |  |                |  |
|---|--|----------------|--|
| subjects affected / exposed                     | 0 / 20 (0.00%)                                   | 0 / 22 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0          |  |
| Mediastinal haemorrhage                         | Additional description: Mediastinal haemorrhage  |                |  |
| subjects affected / exposed                     | 0 / 20 (0.00%)                                   | 0 / 22 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0          |  |
| Pleural effusion                                | Additional description: Pleural effusion         |                |  |
| subjects affected / exposed                     | 1 / 20 (5.00%)                                   | 0 / 22 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0          |  |
| Pulmonary oedema                                | Additional description: Pulmonary oedema         |                |  |
| subjects affected / exposed                     | 0 / 20 (0.00%)                                   | 0 / 22 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0          |  |
| Respiratory failure                             | Additional description: Respiratory failure      |                |  |
| subjects affected / exposed                     | 2 / 20 (10.00%)                                  | 1 / 22 (4.55%) |  |
| occurrences causally related to treatment / all | 0 / 3  | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0          |  |
| Psychiatric disorders                           |  |                |  |
| Delirium  | Additional description: Delirium                 |                |  |
| subjects affected / exposed                     | 0 / 20 (0.00%)                                   | 0 / 22 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0          |  |
| Transient psychosis                             | Additional description: Transient psychosis      |                |  |
| subjects affected / exposed                     | 0 / 20 (0.00%)                                   | 1 / 22 (4.55%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0          |  |
| Investigations                                  |  |                |  |
| Blood pressure decreased                        | Additional description: Blood pressure decreased |                |  |
| subjects affected / exposed                     | 0 / 20 (0.00%)                                   | 0 / 22 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0          |  |
| Injury, poisoning and procedural                |  |                |  |

|   |   |                 |                |
|---|---|-----------------|----------------|
| complications                                 | Additional description: Post procedural haemorrhage                   |                 |                |
|   | Post procedural haemorrhage subjects affected / exposed               | 0 / 20 (0.00%)  | 0 / 22 (0.00%) |
|   | occurrences causally related to treatment / all                       | 0 / 0           | 0 / 0          |
|   | deaths causally related to treatment / all                            | 0 / 0           | 0 / 0          |
| Postoperative thoracic procedure complication | Additional description: Postoperative thoracic procedure complication |                 |                |
|   | subjects affected / exposed   | 0 / 20 (0.00%)  | 1 / 22 (4.55%) |
|   | occurrences causally related to treatment / all                       | 0 / 0           | 0 / 1          |
|   | deaths causally related to treatment / all                            | 0 / 0           | 0 / 0          |
| Cardiac disorders                             |   |                 |                |
|   | Additional description: Arteriospasm coronary                         |                 |                |
|   | Arteriospasm coronary subjects affected / exposed                     | 1 / 20 (5.00%)  | 0 / 22 (0.00%) |
|   | occurrences causally related to treatment / all                       | 0 / 1           | 0 / 0          |
| Atrial fibrillation                           | Additional description: Atrial fibrillation                           |                 |                |
|   | subjects affected / exposed   | 2 / 20 (10.00%) | 0 / 22 (0.00%) |
|   | occurrences causally related to treatment / all                       | 0 / 2           | 0 / 0          |
|   | deaths causally related to treatment / all                            | 0 / 0           | 0 / 0          |
| Atrioventricular block complete               | Additional description: Atrioventricular block complete               |                 |                |
|   | subjects affected / exposed   | 1 / 20 (5.00%)  | 1 / 22 (4.55%) |
|   | occurrences causally related to treatment / all                       | 0 / 1           | 0 / 1          |
|   | deaths causally related to treatment / all                            | 0 / 0           | 0 / 0          |
| Cardiac arrest                                | Additional description: Cardiac arrest                                |                 |                |
|   | subjects affected / exposed   | 0 / 20 (0.00%)  | 0 / 22 (0.00%) |
|   | occurrences causally related to treatment / all                       | 0 / 0           | 0 / 0          |
|   | deaths causally related to treatment / all                            | 0 / 0           | 0 / 0          |
| Cardiac tamponade                             | Additional description: Cardiac tamponade                             |                 |                |
|   | subjects affected / exposed   | 1 / 20 (5.00%)  | 0 / 22 (0.00%) |
|   | occurrences causally related to treatment / all                       | 0 / 1           | 0 / 0          |
|   | deaths causally related to treatment / all                            | 0 / 0           | 0 / 0          |
| Cardiogenic shock                             | Additional description: Cardiogenic shock                             |                 |                |
|   | subjects affected / exposed   | 0 / 20 (0.00%)  | 0 / 22 (0.00%) |
|   | occurrences causally related to treatment / all                       | 0 / 0           | 0 / 0          |
|   | deaths causally related to treatment / all                            | 0 / 0           | 0 / 0          |

|  |   |                |  |
|--|---|----------------|--|
| Haemorrhage coronary artery<br>subjects affected / exposed | Additional description: Haemorrhage coronary artery |                |  |
|  | 0 / 20 (0.00%)                                      | 0 / 22 (0.00%) |  |
|  | 0 / 0   | 0 / 0          |  |
|  | 0 / 0   | 0 / 0          |  |
| Low cardiac output syndrome<br>subjects affected / exposed | Additional description: Low cardiac output syndrome |                |  |
|  | 0 / 20 (0.00%)                                      | 0 / 22 (0.00%) |  |
|  | 0 / 0   | 0 / 0          |  |
|  | 0 / 0   | 0 / 0          |  |
| Myocardial haemorrhage<br>subjects affected / exposed      | Additional description: Myocardial haemorrhage      |                |  |
|  | 0 / 20 (0.00%)                                      | 0 / 22 (0.00%) |  |
|  | 0 / 0   | 0 / 0          |  |
|  | 0 / 0   | 0 / 0          |  |
| Pericardial effusion<br>subjects affected / exposed        | Additional description: Pericardial effusion        |                |  |
|  | 0 / 20 (0.00%)                                      | 0 / 22 (0.00%) |  |
|  | 0 / 0   | 0 / 0          |  |
|  | 0 / 0   | 0 / 0          |  |
| Right ventricular failure<br>subjects affected / exposed   | Additional description: Right ventricular failure   |                |  |
|  | 1 / 20 (5.00%)                                      | 0 / 22 (0.00%) |  |
|  | 0 / 1   | 0 / 0          |  |
|  | 0 / 0   | 0 / 0          |  |
| Ventricular fibrillation<br>subjects affected / exposed    | Additional description: Ventricular fibrillation    |                |  |
|  | 1 / 20 (5.00%)                                      | 0 / 22 (0.00%) |  |
|  | 0 / 3   | 0 / 0          |  |
|  | 0 / 0   | 0 / 0          |  |
| Nervous system disorders                                   |   |                |  |
| Brain injury<br>subjects affected / exposed                | Additional description: Brain injury                |                |  |
|  | 0 / 20 (0.00%)                                      | 0 / 22 (0.00%) |  |
|  | 0 / 0   | 0 / 0          |  |
|  | 0 / 0   | 0 / 0          |  |
| Brain stem stroke<br>subjects affected / exposed           | Additional description: Brain stem stroke           |                |  |
|  | 1 / 20 (5.00%)                                      | 0 / 22 (0.00%) |  |
|  | 0 / 1   | 0 / 0          |  |
|  | 0 / 0   | 0 / 0          |  |
| Cerebral infarction  |   |                |  |
| Additional description: Cerebral infarction                |   |                |  |

|   |   |                |  |
|---|---|----------------|--|
| subjects affected / exposed                     | 0 / 20 (0.00%)  | 0 / 22 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          |  |
| Intensive care unit acquired weakness           | Additional description: Intensive care unit acquired weakness |                |  |
| subjects affected / exposed                     | 1 / 20 (5.00%)  | 0 / 22 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          |  |
| Thrombotic stroke                               | Additional description: Thrombotic stroke                     |                |  |
| subjects affected / exposed                     | 0 / 20 (0.00%)  | 0 / 22 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          |  |
| Blood and lymphatic system disorders            |   |                |  |
| Anaemia   | Additional description: Anaemia                               |                |  |
| subjects affected / exposed                     | 0 / 20 (0.00%)  | 2 / 22 (9.09%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 2          |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          |  |
| Coagulopathy                                    | Additional description: Coagulopathy                          |                |  |
| subjects affected / exposed                     | 0 / 20 (0.00%)  | 0 / 22 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          |  |
| Gastrointestinal disorders                      |   |                |  |
| Duodenal ulcer haemorrhage                      | Additional description: Duodenal ulcer haemorrhage            |                |  |
| subjects affected / exposed                     | 0 / 20 (0.00%)  | 0 / 22 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          |  |
| Intestinal haemorrhage                          | Additional description: Intestinal haemorrhage                |                |  |
| subjects affected / exposed                     | 0 / 20 (0.00%)  | 1 / 22 (4.55%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          |  |
| Intestinal ischaemia                            | Additional description: Intestinal ischaemia                  |                |  |
| subjects affected / exposed                     | 0 / 20 (0.00%)  | 0 / 22 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          |  |

|  |  |                |  |
|--|--|----------------|--|
| Upper gastrointestinal haemorrhage<br>subjects affected / exposed<br><br>occurrences causally related to<br>treatment / all<br><br>deaths causally related to<br>treatment / all | Additional description: Upper gastrointestinal haemorrhage |                |  |
|  | 0 / 20 (0.00%)   | 1 / 22 (4.55%) |  |
|  | 0 / 0  | 0 / 1          |  |
|  | 0 / 0  | 0 / 0          |  |
| Hepatobiliary disorders  |  |                |  |
| Hepatic failure<br>subjects affected / exposed<br><br>occurrences causally related to<br>treatment / all<br><br>deaths causally related to<br>treatment / all                    | Additional description: Hepatic failure                    |                |  |
|  | 0 / 20 (0.00%)   | 0 / 22 (0.00%) |  |
|  | 0 / 0  | 0 / 0          |  |
|  | 0 / 0  | 0 / 0          |  |
| Renal and urinary disorders  |  |                |  |
| Acute kidney injury<br>subjects affected / exposed<br><br>occurrences causally related to<br>treatment / all<br><br>deaths causally related to<br>treatment / all                | Additional description: Acute kidney injury                |                |  |
|  | 0 / 20 (0.00%)   | 0 / 22 (0.00%) |  |
|  | 0 / 0  | 0 / 0          |  |
|  | 0 / 0  | 0 / 0          |  |
| End stage renal disease<br>subjects affected / exposed<br><br>occurrences causally related to<br>treatment / all<br><br>deaths causally related to<br>treatment / all            | Additional description: End stage renal disease            |                |  |
|  | 1 / 20 (5.00%)   | 0 / 22 (0.00%) |  |
|  | 0 / 1  | 0 / 0          |  |
|  | 0 / 0  | 0 / 0          |  |
| Renal failure<br>subjects affected / exposed<br><br>occurrences causally related to<br>treatment / all<br><br>deaths causally related to<br>treatment / all                      | Additional description: Renal failure                      |                |  |
|  | 0 / 20 (0.00%)   | 0 / 22 (0.00%) |  |
|  | 0 / 0  | 0 / 0          |  |
|  | 0 / 0  | 0 / 0          |  |
| Urinary bladder varices<br>subjects affected / exposed<br><br>occurrences causally related to<br>treatment / all<br><br>deaths causally related to<br>treatment / all            | Additional description: Urinary bladder varices            |                |  |
|  | 0 / 20 (0.00%)   | 0 / 22 (0.00%) |  |
|  | 0 / 0  | 0 / 0          |  |
|  | 0 / 0  | 0 / 0          |  |
| Infections and infestations  |  |                |  |
| Abdominal abscess<br>subjects affected / exposed<br><br>occurrences causally related to<br>treatment / all<br><br>deaths causally related to<br>treatment / all                  | Additional description: Abdominal abscess                  |                |  |
|  | 0 / 20 (0.00%)   | 1 / 22 (4.55%) |  |
|  | 0 / 0  | 0 / 1          |  |
|  | 0 / 0  | 0 / 0          |  |
| Endocarditis staphylococcal  | Additional description: Endocarditis staphylococcal        |                |  |
|  |  |                |  |



|   |   |                |  |
|---|---|----------------|--|
| subjects affected / exposed                     | 1 / 20 (5.00%)                                    | 0 / 22 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          |  |
| Enterococcal sepsis                             | Additional description: Enterococcal sepsis       |                |  |
| subjects affected / exposed                     | 0 / 20 (0.00%)                                    | 0 / 22 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          |  |
| Gastroenteritis norovirus                       | Additional description: Gastroenteritis norovirus |                |  |
| subjects affected / exposed                     | 1 / 20 (5.00%)                                    | 0 / 22 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          |  |
| Influenza                                       | Additional description: Influenza                 |                |  |
| subjects affected / exposed                     | 1 / 20 (5.00%)                                    | 0 / 22 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          |  |
| Mediastinitis                                   | Additional description: Mediastinitis             |                |  |
| subjects affected / exposed                     | 1 / 20 (5.00%)                                    | 0 / 22 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          |  |
| Nosocomial infection                            | Additional description: Nosocomial infection      |                |  |
| subjects affected / exposed                     | 0 / 20 (0.00%)                                    | 0 / 22 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          |  |
| Pneumonia                                       | Additional description: Pneumonia                 |                |  |
| subjects affected / exposed                     | 0 / 20 (0.00%)                                    | 0 / 22 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          |  |
| Pneumonia haemophilus                           | Additional description: Pneumonia haemophilus     |                |  |
| subjects affected / exposed                     | 0 / 20 (0.00%)                                    | 0 / 22 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          |  |
| Sepsis  | Additional description: Sepsis                    |                |  |

|   |   |                |  |
|---|---|----------------|--|
| subjects affected / exposed                     | 1 / 20 (5.00%)  | 0 / 22 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          |  |
| Severe invasive streptococcal infection         | Additional description: Severe invasive streptococcal infection |                |  |
| subjects affected / exposed                     | 0 / 20 (0.00%)  | 0 / 22 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          |  |
| Urinary tract infection                         | Additional description: Urinary tract infection                 |                |  |
| subjects affected / exposed                     | 0 / 20 (0.00%)  | 0 / 22 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          |  |
| Wound infection                                 | Additional description: Wound infection                         |                |  |
| subjects affected / exposed                     | 1 / 20 (5.00%)  | 0 / 22 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0          |  |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events                            | 1mg/kg bw IFX-1                                  | 2mg/kg bw IFX-1  | 4mg/kg bw IFX-1   |
|---|--|------------------|-------------------|
| Total subjects affected by non-serious adverse events |  |                  |                   |
| subjects affected / exposed                           | 22 / 23 (95.65%)                                 | 17 / 18 (94.44%) | 21 / 21 (100.00%) |
| Vascular disorders                                    |  |                  |                   |
| Haematoma   | Additional description: Haematoma                |                  |                   |
| subjects affected / exposed                           | 0 / 23 (0.00%)                                   | 0 / 18 (0.00%)   | 0 / 21 (0.00%)    |
| occurrences (all)                                     | 0  | 0                | 0                 |
| Haemodynamic instability                              | Additional description: Haemodynamic instability |                  |                   |
| subjects affected / exposed                           | 0 / 23 (0.00%)                                   | 1 / 18 (5.56%)   | 0 / 21 (0.00%)    |
| occurrences (all)                                     | 0  | 1                | 0                 |
| Hypertension  | Additional description: Hypertension             |                  |                   |
| subjects affected / exposed                           | 3 / 23 (13.04%)                                  | 1 / 18 (5.56%)   | 3 / 21 (14.29%)   |
| occurrences (all)                                     | 3  | 1                | 3                 |
| Hypertensive crisis                                   | Additional description: Hypertensive crisis      |                  |                   |
| subjects affected / exposed                           | 0 / 23 (0.00%)                                   | 1 / 18 (5.56%)   | 1 / 21 (4.76%)    |
| occurrences (all)                                     | 0  | 1                | 2                 |

|   |  |                     |                      |
|---|--|---------------------|----------------------|
| Hypotension<br>subjects affected / exposed<br>occurrences (all)   | Additional description: Hypotension            |                     |                      |
|   | 1 / 23 (4.35%)<br>1                            | 1 / 18 (5.56%)<br>1 | 3 / 21 (14.29%)<br>3 |
| Surgical and medical procedures<br>Colectomy<br>subjects affected / exposed<br>occurrences (all)                        | Additional description: Colectomy              |                     |                      |
|   | 1 / 23 (4.35%)<br>1                            | 0 / 18 (0.00%)<br>0 | 0 / 21 (0.00%)<br>0  |
| Explorative laparotomy<br>subjects affected / exposed<br>occurrences (all)  | Additional description: Explorative laparotomy |                     |                      |
|   | 1 / 23 (4.35%)<br>1                            | 0 / 18 (0.00%)<br>0 | 0 / 21 (0.00%)<br>0  |
| General disorders and administration<br>site conditions<br>Asthenia<br>subjects affected / exposed<br>occurrences (all) | Additional description: Asthenia               |                     |                      |
|   | 1 / 23 (4.35%)<br>1                            | 0 / 18 (0.00%)<br>0 | 0 / 21 (0.00%)<br>0  |
| Chest pain<br>subjects affected / exposed<br>occurrences (all)  | Additional description: Chest pain             |                     |                      |
|   | 0 / 23 (0.00%)<br>0                            | 1 / 18 (5.56%)<br>1 | 0 / 21 (0.00%)<br>0  |
| Drug intolerance<br>subjects affected / exposed<br>occurrences (all)  | Additional description: Drug intolerance       |                     |                      |
|   | 0 / 23 (0.00%)<br>0                            | 0 / 18 (0.00%)<br>0 | 0 / 21 (0.00%)<br>0  |
| Gait disturbance<br>subjects affected / exposed<br>occurrences (all)  | Additional description: Gait disturbance       |                     |                      |
|   | 0 / 23 (0.00%)<br>0                            | 0 / 18 (0.00%)<br>0 | 1 / 21 (4.76%)<br>1  |
| Impaired healing<br>subjects affected / exposed<br>occurrences (all)  | Additional description: Impaired healing       |                     |                      |
|   | 1 / 23 (4.35%)<br>1                            | 0 / 18 (0.00%)<br>0 | 0 / 21 (0.00%)<br>0  |
| Malaise<br>subjects affected / exposed<br>occurrences (all)   | Additional description: Malaise                |                     |                      |
|   | 0 / 23 (0.00%)<br>0                            | 0 / 18 (0.00%)<br>0 | 1 / 21 (4.76%)<br>1  |
| Oedema<br>subjects affected / exposed<br>occurrences (all)  | Additional description: Oedema                 |                     |                      |
|   | 1 / 23 (4.35%)<br>1                            | 0 / 18 (0.00%)<br>0 | 1 / 21 (4.76%)<br>1  |
| Oedema peripheral<br>subjects affected / exposed<br>occurrences (all)   | Additional description: Oedema peripheral      |                     |                      |
|   | 4 / 23 (17.39%)<br>4                           | 1 / 18 (5.56%)<br>1 | 4 / 21 (19.05%)<br>5 |
| Peripheral swelling   | Additional description: Peripheral swelling    |                     |                      |
|   |  |                     |                      |

|   |  |                |                 |
|---|--|----------------|-----------------|
| subjects affected / exposed                     | 0 / 23 (0.00%)   | 0 / 18 (0.00%) | 1 / 21 (4.76%)  |
| occurrences (all)                               | 0  | 0              | 1               |
| Pyrexia   | Additional description: Pyrexia                                    |                |                 |
| subjects affected / exposed                     | 2 / 23 (8.70%)   | 0 / 18 (0.00%) | 0 / 21 (0.00%)  |
| occurrences (all)                               | 2  | 0              | 0               |
| Respiratory, thoracic and mediastinal disorders |  |                |                 |
| Acquired diaphragmatic eventration              | Additional description: Acquired diaphragmatic eventration         |                |                 |
| subjects affected / exposed                     | 0 / 23 (0.00%)   | 0 / 18 (0.00%) | 0 / 21 (0.00%)  |
| occurrences (all)                               | 0  | 0              | 0               |
| Acute respiratory failure                       | Additional description: Acute respiratory failure                  |                |                 |
| subjects affected / exposed                     | 0 / 23 (0.00%)   | 0 / 18 (0.00%) | 0 / 21 (0.00%)  |
| occurrences (all)                               | 0  | 0              | 0               |
| Aspiration                                      | Additional description: Aspiration                                 |                |                 |
| subjects affected / exposed                     | 0 / 23 (0.00%)   | 0 / 18 (0.00%) | 1 / 21 (4.76%)  |
| occurrences (all)                               | 0  | 0              | 1               |
| Atelectasis                                     | Additional description: Atelectasis                                |                |                 |
| subjects affected / exposed                     | 0 / 23 (0.00%)   | 1 / 18 (5.56%) | 0 / 21 (0.00%)  |
| occurrences (all)                               | 0  | 1              | 0               |
| Bronchospasm                                    | Additional description: Bronchospasm                               |                |                 |
| subjects affected / exposed                     | 2 / 23 (8.70%)   | 0 / 18 (0.00%) | 1 / 21 (4.76%)  |
| occurrences (all)                               | 2  | 0              | 1               |
| Cough   | Additional description: Cough                                      |                |                 |
| subjects affected / exposed                     | 0 / 23 (0.00%)   | 1 / 18 (5.56%) | 4 / 21 (19.05%) |
| occurrences (all)                               | 0  | 1              | 4               |
| Dyspnoea  | Additional description: Dyspnoea                                   |                |                 |
| subjects affected / exposed                     | 0 / 23 (0.00%)   | 0 / 18 (0.00%) | 0 / 21 (0.00%)  |
| occurrences (all)                               | 0  | 0              | 0               |
| Emphysema                                       | Additional description: Emphysema                                  |                |                 |
| subjects affected / exposed                     | 0 / 23 (0.00%)   | 0 / 18 (0.00%) | 1 / 21 (4.76%)  |
| occurrences (all)                               | 0  | 0              | 1               |
| Epistaxis                                       | Additional description: Epistaxis                                  |                |                 |
| subjects affected / exposed                     | 0 / 23 (0.00%)   | 1 / 18 (5.56%) | 0 / 21 (0.00%)  |
| occurrences (all)                               | 0  | 1              | 0               |
| Increased viscosity of bronchial secretion      | Additional description: Increased viscosity of bronchial secretion |                |                 |

|                             |  |                 |                 |
|-----------------------------|--|-----------------|-----------------|
| subjects affected / exposed | 0 / 23 (0.00%)                               | 0 / 18 (0.00%)  | 1 / 21 (4.76%)  |
| occurrences (all)           | 0  | 0               | 1               |
| Lung disorder               | Additional description: Lung disorder        |                 |                 |
| subjects affected / exposed | 0 / 23 (0.00%)                               | 0 / 18 (0.00%)  | 0 / 21 (0.00%)  |
| occurrences (all)           | 0  | 0               | 0               |
| Lung hypoinflation          | Additional description: Lung hypoinflation   |                 |                 |
| subjects affected / exposed | 0 / 23 (0.00%)                               | 0 / 18 (0.00%)  | 0 / 21 (0.00%)  |
| occurrences (all)           | 0  | 0               | 0               |
| Pleural effusion            | Additional description: Pleural effusion     |                 |                 |
| subjects affected / exposed | 9 / 23 (39.13%)                              | 6 / 18 (33.33%) | 9 / 21 (42.86%) |
| occurrences (all)           | 13   | 6               | 9               |
| Pneumothorax                | Additional description: Pneumothorax         |                 |                 |
| subjects affected / exposed | 2 / 23 (8.70%)                               | 0 / 18 (0.00%)  | 2 / 21 (9.52%)  |
| occurrences (all)           | 2  | 0               | 2               |
| Pulmonary congestion        | Additional description: Pulmonary congestion |                 |                 |
| subjects affected / exposed | 2 / 23 (8.70%)                               | 0 / 18 (0.00%)  | 3 / 21 (14.29%) |
| occurrences (all)           | 2  | 0               | 3               |
| Pulmonary oedema            | Additional description: Pulmonary oedema     |                 |                 |
| subjects affected / exposed | 0 / 23 (0.00%)                               | 1 / 18 (5.56%)  | 0 / 21 (0.00%)  |
| occurrences (all)           | 0  | 1               | 0               |
| Respiratory failure         | Additional description: Respiratory failure  |                 |                 |
| subjects affected / exposed | 1 / 23 (4.35%)                               | 3 / 18 (16.67%) | 2 / 21 (9.52%)  |
| occurrences (all)           | 1  | 3               | 2               |
| Psychiatric disorders       |  |                 |                 |
| Delirium                    | Additional description: Delirium             |                 |                 |
| subjects affected / exposed | 3 / 23 (13.04%)                              | 3 / 18 (16.67%) | 4 / 21 (19.05%) |
| occurrences (all)           | 4  | 3               | 4               |
| Disorientation              | Additional description: Disorientation       |                 |                 |
| subjects affected / exposed | 3 / 23 (13.04%)                              | 0 / 18 (0.00%)  | 1 / 21 (4.76%)  |
| occurrences (all)           | 3  | 0               | 1               |
| Insomnia                    | Additional description: Insomnia             |                 |                 |
| subjects affected / exposed | 0 / 23 (0.00%)                               | 1 / 18 (5.56%)  | 0 / 21 (0.00%)  |
| occurrences (all)           | 0  | 1               | 0               |
| Restlessness                | Additional description: Restlessness         |                 |                 |
| subjects affected / exposed | 0 / 23 (0.00%)                               | 1 / 18 (5.56%)  | 0 / 21 (0.00%)  |
| occurrences (all)           | 0  | 1               | 0               |

|   |   |                 |                 |
|---|---|-----------------|-----------------|
| Sleep disorder<br>subjects affected / exposed<br>occurrences (all)                            | Additional description: Sleep disorder                            |                 |                 |
|   | 1 / 23 (4.35%)  | 2 / 18 (11.11%) | 6 / 21 (28.57%) |
|   | 1   | 2               | 6               |
| Investigations  |   |                 |                 |
| Alanine aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)        | Additional description: Alanine aminotransferase increased        |                 |                 |
|   | 0 / 23 (0.00%)  | 0 / 18 (0.00%)  | 1 / 21 (4.76%)  |
|   | 0   | 0               | 1               |
| Antithrombin III decreased<br>subjects affected / exposed<br>occurrences (all)                | Additional description: Antithrombin III decreased                |                 |                 |
|   | 0 / 23 (0.00%)  | 0 / 18 (0.00%)  | 0 / 21 (0.00%)  |
|   | 0   | 0               | 0               |
| Aspartate aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)      | Additional description: Aspartate aminotransferase increased      |                 |                 |
|   | 0 / 23 (0.00%)  | 0 / 18 (0.00%)  | 1 / 21 (4.76%)  |
|   | 0   | 0               | 1               |
| Blood albumin decreased<br>subjects affected / exposed<br>occurrences (all)                   | Additional description: Blood albumin decreased                   |                 |                 |
|   | 0 / 23 (0.00%)  | 1 / 18 (5.56%)  | 0 / 21 (0.00%)  |
|   | 0   | 1               | 0               |
| Blood alkaline phosphatase increased<br>subjects affected / exposed<br>occurrences (all)      | Additional description: Blood alkaline phosphatase increased      |                 |                 |
|   | 1 / 23 (4.35%)  | 0 / 18 (0.00%)  | 0 / 21 (0.00%)  |
|   | 1   | 0               | 0               |
| Blood bilirubin increased<br>subjects affected / exposed<br>occurrences (all)                 | Additional description: Blood bilirubin increased                 |                 |                 |
|   | 0 / 23 (0.00%)  | 0 / 18 (0.00%)  | 1 / 21 (4.76%)  |
|   | 0   | 0               | 1               |
| Blood calcium decreased<br>subjects affected / exposed<br>occurrences (all)                   | Additional description: Blood calcium decreased                   |                 |                 |
|   | 0 / 23 (0.00%)  | 1 / 18 (5.56%)  | 0 / 21 (0.00%)  |
|   | 0   | 1               | 0               |
| Blood creatine phosphokinase MB increased<br>subjects affected / exposed<br>occurrences (all) | Additional description: Blood creatine phosphokinase MB increased |                 |                 |
|   | 0 / 23 (0.00%)  | 0 / 18 (0.00%)  | 2 / 21 (9.52%)  |
|   | 0   | 0               | 2               |
| Blood creatine phosphokinase increased<br>subjects affected / exposed<br>occurrences (all)    | Additional description: Blood creatine phosphokinase increased    |                 |                 |
|   | 0 / 23 (0.00%)  | 0 / 18 (0.00%)  | 3 / 21 (14.29%) |
|   | 0   | 0               | 3               |
| Blood creatinine increased<br>subjects affected / exposed<br>occurrences (all)                | Additional description: Blood creatinine increased                |                 |                 |
|   | 1 / 23 (4.35%)  | 0 / 18 (0.00%)  | 0 / 21 (0.00%)  |
|   | 1   | 0               | 0               |
| Blood fibrinogen decreased  | Additional description: Blood fibrinogen decreased                |                 |                 |
|   |   |                 |                 |
|   |   |                 |                 |

|                                       |   |                 |                |
|---------------------------------------|---|-----------------|----------------|
| subjects affected / exposed           | 1 / 23 (4.35%)  | 1 / 18 (5.56%)  | 0 / 21 (0.00%) |
| occurrences (all)                     | 1   | 1               | 0              |
| Blood glucose increased               | Additional description: Blood glucose increased               |                 |                |
| subjects affected / exposed           | 1 / 23 (4.35%)  | 2 / 18 (11.11%) | 2 / 21 (9.52%) |
| occurrences (all)                     | 1   | 2               | 2              |
| Blood lactate dehydrogenase increased | Additional description: Blood lactate dehydrogenase increased |                 |                |
| subjects affected / exposed           | 0 / 23 (0.00%)  | 0 / 18 (0.00%)  | 0 / 21 (0.00%) |
| occurrences (all)                     | 0   | 0               | 0              |
| Blood pressure decreased              | Additional description: Blood pressure decreased              |                 |                |
| subjects affected / exposed           | 0 / 23 (0.00%)  | 1 / 18 (5.56%)  | 0 / 21 (0.00%) |
| occurrences (all)                     | 0   | 1               | 0              |
| Blood pressure increased              | Additional description: Blood pressure increased              |                 |                |
| subjects affected / exposed           | 1 / 23 (4.35%)  | 0 / 18 (0.00%)  | 0 / 21 (0.00%) |
| occurrences (all)                     | 1   | 0               | 0              |
| Blood urea increased                  | Additional description: Blood urea increased                  |                 |                |
| subjects affected / exposed           | 1 / 23 (4.35%)  | 0 / 18 (0.00%)  | 0 / 21 (0.00%) |
| occurrences (all)                     | 1   | 0               | 0              |
| Body temperature increased            | Additional description: Body temperature increased            |                 |                |
| subjects affected / exposed           | 1 / 23 (4.35%)  | 2 / 18 (11.11%) | 1 / 21 (4.76%) |
| occurrences (all)                     | 3   | 2               | 1              |
| Breath sounds abnormal                | Additional description: Breath sounds abnormal                |                 |                |
| subjects affected / exposed           | 0 / 23 (0.00%)  | 0 / 18 (0.00%)  | 1 / 21 (4.76%) |
| occurrences (all)                     | 0   | 0               | 1              |
| C-reactive protein increased          | Additional description: C-reactive protein increased          |                 |                |
| subjects affected / exposed           | 0 / 23 (0.00%)  | 0 / 18 (0.00%)  | 0 / 21 (0.00%) |
| occurrences (all)                     | 0   | 0               | 0              |
| Cardiac index decreased               | Additional description: Cardiac index decreased               |                 |                |
| subjects affected / exposed           | 0 / 23 (0.00%)  | 0 / 18 (0.00%)  | 0 / 21 (0.00%) |
| occurrences (all)                     | 0   | 0               | 0              |
| Enterococcus test positive            | Additional description: Enterococcus test positive            |                 |                |
| subjects affected / exposed           | 0 / 23 (0.00%)  | 0 / 18 (0.00%)  | 2 / 21 (9.52%) |
| occurrences (all)                     | 0   | 0               | 2              |
| Escherichia test positive             | Additional description: Escherichia test positive             |                 |                |
| subjects affected / exposed           | 0 / 23 (0.00%)  | 1 / 18 (5.56%)  | 1 / 21 (4.76%) |
| occurrences (all)                     | 0   | 1               | 2              |

|  |  |                 |                 |
|--|--|-----------------|-----------------|
| Gamma-glutamyltransferase increased      | Additional description: Gamma-glutamyltransferase increased      |                 |                 |
| subjects affected / exposed              | 1 / 23 (4.35%)   | 0 / 18 (0.00%)  | 1 / 21 (4.76%)  |
| occurrences (all)                        | 1  | 0               | 1               |
| Glutamate dehydrogenase increased        | Additional description: Glutamate dehydrogenase increased        |                 |                 |
| subjects affected / exposed              | 0 / 23 (0.00%)   | 0 / 18 (0.00%)  | 0 / 21 (0.00%)  |
| occurrences (all)                        | 0  | 0               | 0               |
| Haematocrit decreased                    | Additional description: Haematocrit decreased                    |                 |                 |
| subjects affected / exposed              | 1 / 23 (4.35%)   | 0 / 18 (0.00%)  | 0 / 21 (0.00%)  |
| occurrences (all)                        | 1  | 0               | 0               |
| Haemoglobin decreased                    | Additional description: Haemoglobin decreased                    |                 |                 |
| subjects affected / exposed              | 2 / 23 (8.70%)   | 3 / 18 (16.67%) | 1 / 21 (4.76%)  |
| occurrences (all)                        | 2  | 3               | 1               |
| Heart rate decreased                     | Additional description: Heart rate decreased                     |                 |                 |
| subjects affected / exposed              | 0 / 23 (0.00%)   | 1 / 18 (5.56%)  | 0 / 21 (0.00%)  |
| occurrences (all)                        | 0  | 1               | 0               |
| Hepatic enzyme increased                 | Additional description: Hepatic enzyme increased                 |                 |                 |
| subjects affected / exposed              | 1 / 23 (4.35%)   | 0 / 18 (0.00%)  | 0 / 21 (0.00%)  |
| occurrences (all)                        | 1  | 0               | 0               |
| International normalised ratio increased | Additional description: International normalised ratio increased |                 |                 |
| subjects affected / exposed              | 0 / 23 (0.00%)   | 1 / 18 (5.56%)  | 0 / 21 (0.00%)  |
| occurrences (all)                        | 0  | 1               | 0               |
| Myocardial necrosis marker increased     | Additional description: Myocardial necrosis marker increased     |                 |                 |
| subjects affected / exposed              | 0 / 23 (0.00%)   | 0 / 18 (0.00%)  | 0 / 21 (0.00%)  |
| occurrences (all)                        | 0  | 0               | 0               |
| Oxygen saturation decreased              | Additional description: Oxygen saturation decreased              |                 |                 |
| subjects affected / exposed              | 1 / 23 (4.35%)   | 0 / 18 (0.00%)  | 0 / 21 (0.00%)  |
| occurrences (all)                        | 1  | 0               | 0               |
| Red blood cell count decreased           | Additional description: Red blood cell count decreased           |                 |                 |
| subjects affected / exposed              | 0 / 23 (0.00%)   | 0 / 18 (0.00%)  | 3 / 21 (14.29%) |
| occurrences (all)                        | 0  | 0               | 3               |
| Staphylococcus test positive             | Additional description: Staphylococcus test positive             |                 |                 |
| subjects affected / exposed              | 1 / 23 (4.35%)   | 1 / 18 (5.56%)  | 1 / 21 (4.76%)  |
| occurrences (all)                        | 1  | 1               | 1               |
| Venous oxygen saturation decreased       | Additional description: Venous oxygen saturation decreased       |                 |                 |



|  |  |                 |                |
|--|--|-----------------|----------------|
| subjects affected / exposed                    | 0 / 23 (0.00%)   | 1 / 18 (5.56%)  | 0 / 21 (0.00%) |
| occurrences (all)                              | 0  | 1               | 0              |
| White blood cell count increased               | Additional description: White blood cell count increased   |                 |                |
| subjects affected / exposed                    | 0 / 23 (0.00%)   | 2 / 18 (11.11%) | 1 / 21 (4.76%) |
| occurrences (all)                              | 0  | 2               | 2              |
| Injury, poisoning and procedural complications |  |                 |                |
| Anaemia postoperative                          | Additional description: Anaemia postoperative              |                 |                |
| subjects affected / exposed                    | 0 / 23 (0.00%)   | 0 / 18 (0.00%)  | 0 / 21 (0.00%) |
| occurrences (all)                              | 0  | 0               | 0              |
| Fall   | Additional description: Fall                               |                 |                |
| subjects affected / exposed                    | 1 / 23 (4.35%)   | 0 / 18 (0.00%)  | 1 / 21 (4.76%) |
| occurrences (all)                              | 1  | 0               | 1              |
| Injury   | Additional description: Injury                             |                 |                |
| subjects affected / exposed                    | 0 / 23 (0.00%)   | 0 / 18 (0.00%)  | 1 / 21 (4.76%) |
| occurrences (all)                              | 0  | 0               | 1              |
| Laceration                                     | Additional description: Laceration                         |                 |                |
| subjects affected / exposed                    | 1 / 23 (4.35%)   | 0 / 18 (0.00%)  | 0 / 21 (0.00%) |
| occurrences (all)                              | 1  | 0               | 0              |
| Periorbital haemorrhage                        | Additional description: Periorbital haemorrhage            |                 |                |
| subjects affected / exposed                    | 1 / 23 (4.35%)   | 0 / 18 (0.00%)  | 0 / 21 (0.00%) |
| occurrences (all)                              | 1  | 0               | 0              |
| Post procedural haematoma                      | Additional description: Post procedural haematoma          |                 |                |
| subjects affected / exposed                    | 0 / 23 (0.00%)   | 0 / 18 (0.00%)  | 1 / 21 (4.76%) |
| occurrences (all)                              | 0  | 0               | 1              |
| Post procedural haemorrhage                    | Additional description: Post procedural haemorrhage        |                 |                |
| subjects affected / exposed                    | 0 / 23 (0.00%)   | 1 / 18 (5.56%)  | 2 / 21 (9.52%) |
| occurrences (all)                              | 0  | 1               | 2              |
| Postoperative renal failure                    | Additional description: Postoperative renal failure        |                 |                |
| subjects affected / exposed                    | 0 / 23 (0.00%)   | 1 / 18 (5.56%)  | 0 / 21 (0.00%) |
| occurrences (all)                              | 0  | 1               | 0              |
| Postoperative respiratory distress             | Additional description: Postoperative respiratory distress |                 |                |
| subjects affected / exposed                    | 0 / 23 (0.00%)   | 0 / 18 (0.00%)  | 0 / 21 (0.00%) |
| occurrences (all)                              | 0  | 0               | 0              |
| Postoperative wound complication               | Additional description: Postoperative wound complication   |                 |                |

|                             |   |                 |                 |
|-----------------------------|---|-----------------|-----------------|
| subjects affected / exposed | 1 / 23 (4.35%)                                      | 0 / 18 (0.00%)  | 0 / 21 (0.00%)  |
| occurrences (all)           | 1   | 0               | 0               |
| Procedural haemorrhage      | Additional description: Procedural haemorrhage      |                 |                 |
| subjects affected / exposed | 0 / 23 (0.00%)                                      | 0 / 18 (0.00%)  | 1 / 21 (4.76%)  |
| occurrences (all)           | 0   | 0               | 1               |
| Procedural nausea           | Additional description: Procedural nausea           |                 |                 |
| subjects affected / exposed | 0 / 23 (0.00%)                                      | 0 / 18 (0.00%)  | 1 / 21 (4.76%)  |
| occurrences (all)           | 0   | 0               | 1               |
| Procedural vomiting         | Additional description: Procedural vomiting         |                 |                 |
| subjects affected / exposed | 1 / 23 (4.35%)                                      | 0 / 18 (0.00%)  | 1 / 21 (4.76%)  |
| occurrences (all)           | 1   | 0               | 1               |
| Rib fracture                | Additional description: Rib fracture                |                 |                 |
| subjects affected / exposed | 0 / 23 (0.00%)                                      | 1 / 18 (5.56%)  | 0 / 21 (0.00%)  |
| occurrences (all)           | 0   | 1               | 0               |
| Wound haemorrhage           | Additional description: Wound haemorrhage           |                 |                 |
| subjects affected / exposed | 0 / 23 (0.00%)                                      | 0 / 18 (0.00%)  | 0 / 21 (0.00%)  |
| occurrences (all)           | 0   | 0               | 0               |
| Wound secretion             | Additional description: Wound secretion             |                 |                 |
| subjects affected / exposed | 0 / 23 (0.00%)                                      | 0 / 18 (0.00%)  | 0 / 21 (0.00%)  |
| occurrences (all)           | 0   | 0               | 0               |
| Cardiac disorders           |   |                 |                 |
| Acute myocardial infarction | Additional description: Acute myocardial infarction |                 |                 |
| subjects affected / exposed | 0 / 23 (0.00%)                                      | 0 / 18 (0.00%)  | 0 / 21 (0.00%)  |
| occurrences (all)           | 0   | 0               | 0               |
| Arrhythmia                  | Additional description: Arrhythmia                  |                 |                 |
| subjects affected / exposed | 0 / 23 (0.00%)                                      | 1 / 18 (5.56%)  | 0 / 21 (0.00%)  |
| occurrences (all)           | 0   | 1               | 0               |
| Atrial fibrillation         | Additional description: Atrial fibrillation         |                 |                 |
| subjects affected / exposed | 9 / 23 (39.13%)                                     | 4 / 18 (22.22%) | 9 / 21 (42.86%) |
| occurrences (all)           | 9   | 4               | 9               |
| Atrial flutter              | Additional description: Atrial flutter              |                 |                 |
| subjects affected / exposed | 1 / 23 (4.35%)                                      | 0 / 18 (0.00%)  | 1 / 21 (4.76%)  |
| occurrences (all)           | 1   | 0               | 1               |
| Atrioventricular block      | Additional description: Atrioventricular block      |                 |                 |
| subjects affected / exposed | 2 / 23 (8.70%)                                      | 0 / 18 (0.00%)  | 0 / 21 (0.00%)  |
| occurrences (all)           | 2   | 0               | 0               |

|  |  |                      |                     |
|--|--|----------------------|---------------------|
| Atrioventricular block complete<br>subjects affected / exposed<br>occurrences (all)      | Additional description: Atrioventricular block complete      |                      |                     |
|  | 0 / 23 (0.00%)<br>0  | 3 / 18 (16.67%)<br>3 | 1 / 21 (4.76%)<br>1 |
| Atrioventricular block second degree<br>subjects affected / exposed<br>occurrences (all) | Additional description: Atrioventricular block second degree |                      |                     |
|  | 0 / 23 (0.00%)<br>0  | 0 / 18 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0 |
| Bradyarrhythmia<br>subjects affected / exposed<br>occurrences (all)                      | Additional description: Bradyarrhythmia                      |                      |                     |
|  | 1 / 23 (4.35%)<br>2  | 0 / 18 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0 |
| Bradycardia<br>subjects affected / exposed<br>occurrences (all)                          | Additional description: Bradycardia                          |                      |                     |
|  | 0 / 23 (0.00%)<br>0  | 1 / 18 (5.56%)<br>1  | 1 / 21 (4.76%)<br>1 |
| Bundle branch block left<br>subjects affected / exposed<br>occurrences (all)             | Additional description: Bundle branch block left             |                      |                     |
|  | 1 / 23 (4.35%)<br>1  | 0 / 18 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0 |
| Bundle branch block right<br>subjects affected / exposed<br>occurrences (all)            | Additional description: Bundle branch block right            |                      |                     |
|  | 0 / 23 (0.00%)<br>0  | 0 / 18 (0.00%)<br>0  | 1 / 21 (4.76%)<br>1 |
| Cardiac arrest<br>subjects affected / exposed<br>occurrences (all)                       | Additional description: Cardiac arrest                       |                      |                     |
|  | 1 / 23 (4.35%)<br>1  | 0 / 18 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0 |
| Cardiac failure<br>subjects affected / exposed<br>occurrences (all)                      | Additional description: Cardiac failure                      |                      |                     |
|  | 0 / 23 (0.00%)<br>0  | 0 / 18 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0 |
| Cardiovascular disorder<br>subjects affected / exposed<br>occurrences (all)              | Additional description: Cardiovascular disorder              |                      |                     |
|  | 2 / 23 (8.70%)<br>2  | 1 / 18 (5.56%)<br>1  | 0 / 21 (0.00%)<br>0 |
| Extrasystoles<br>subjects affected / exposed<br>occurrences (all)                        | Additional description: Extrasystoles                        |                      |                     |
|  | 1 / 23 (4.35%)<br>1  | 0 / 18 (0.00%)<br>0  | 1 / 21 (4.76%)<br>1 |
| Left ventricular dysfunction<br>subjects affected / exposed<br>occurrences (all)         | Additional description: Left ventricular dysfunction         |                      |                     |
|  | 0 / 23 (0.00%)<br>0  | 0 / 18 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0 |
| Pericardial effusion<br>subjects affected / exposed<br>occurrences (all)                 | Additional description: Pericardial effusion                 |                      |                     |
|  | 1 / 23 (4.35%)<br>1  | 1 / 18 (5.56%)<br>1  | 1 / 21 (4.76%)<br>1 |

|  |  |                      |                     |
|--|--|----------------------|---------------------|
| Pericardial haemorrhage<br>subjects affected / exposed<br>occurrences (all)      | Additional description: Pericardial haemorrhage      |                      |                     |
|  | 1 / 23 (4.35%)<br>1                                  | 0 / 18 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0 |
| Pulmonary valve incompetence<br>subjects affected / exposed<br>occurrences (all) | Additional description: Pulmonary valve incompetence |                      |                     |
|  | 0 / 23 (0.00%)<br>0                                  | 1 / 18 (5.56%)<br>1  | 0 / 21 (0.00%)<br>0 |
| Sinus arrest<br>subjects affected / exposed<br>occurrences (all)                 | Additional description: Sinus arrest                 |                      |                     |
|  | 0 / 23 (0.00%)<br>0                                  | 0 / 18 (0.00%)<br>0  | 1 / 21 (4.76%)<br>1 |
| Supraventricular tachycardia<br>subjects affected / exposed<br>occurrences (all) | Additional description: Supraventricular tachycardia |                      |                     |
|  | 0 / 23 (0.00%)<br>0                                  | 0 / 18 (0.00%)<br>0  | 1 / 21 (4.76%)<br>1 |
| Tachyarrhythmia<br>subjects affected / exposed<br>occurrences (all)              | Additional description: Tachyarrhythmia              |                      |                     |
|  | 0 / 23 (0.00%)<br>0                                  | 0 / 18 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0 |
| Tachycardia<br>subjects affected / exposed<br>occurrences (all)                  | Additional description: Tachycardia                  |                      |                     |
|  | 1 / 23 (4.35%)<br>1                                  | 2 / 18 (11.11%)<br>2 | 0 / 21 (0.00%)<br>0 |
| Tricuspid valve incompetence<br>subjects affected / exposed<br>occurrences (all) | Additional description: Tricuspid valve incompetence |                      |                     |
|  | 0 / 23 (0.00%)<br>0                                  | 1 / 18 (5.56%)<br>1  | 0 / 21 (0.00%)<br>0 |
| Ventricular extrasystoles<br>subjects affected / exposed<br>occurrences (all)    | Additional description: Ventricular extrasystoles    |                      |                     |
|  | 0 / 23 (0.00%)<br>0                                  | 0 / 18 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0 |
| Ventricular fibrillation<br>subjects affected / exposed<br>occurrences (all)     | Additional description: Ventricular fibrillation     |                      |                     |
|  | 0 / 23 (0.00%)<br>0                                  | 0 / 18 (0.00%)<br>0  | 1 / 21 (4.76%)<br>1 |
| Ventricular hypokinesia<br>subjects affected / exposed<br>occurrences (all)      | Additional description: Ventricular hypokinesia      |                      |                     |
|  | 1 / 23 (4.35%)<br>1                                  | 0 / 18 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0 |
| Ventricular tachycardia<br>subjects affected / exposed<br>occurrences (all)      | Additional description: Ventricular tachycardia      |                      |                     |
|  | 2 / 23 (8.70%)<br>2                                  | 1 / 18 (5.56%)<br>1  | 0 / 21 (0.00%)<br>0 |
| Nervous system disorders<br>Anticholinergic syndrome                             | Additional description: Anticholinergic syndrome     |                      |                     |

|                             |   |                |                |
|-----------------------------|---|----------------|----------------|
| subjects affected / exposed | 0 / 23 (0.00%)                                    | 0 / 18 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all)           | 0   | 0              | 1              |
| Balance disorder            | Additional description: Balance disorder          |                |                |
| subjects affected / exposed | 0 / 23 (0.00%)                                    | 1 / 18 (5.56%) | 0 / 21 (0.00%) |
| occurrences (all)           | 0   | 1              | 0              |
| Brain oedema                | Additional description: Brain oedema              |                |                |
| subjects affected / exposed | 0 / 23 (0.00%)                                    | 1 / 18 (5.56%) | 0 / 21 (0.00%) |
| occurrences (all)           | 0   | 1              | 0              |
| Carotid artery stenosis     | Additional description: Carotid artery stenosis   |                |                |
| subjects affected / exposed | 0 / 23 (0.00%)                                    | 0 / 18 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all)           | 0   | 0              | 1              |
| Cerebral infarction         | Additional description: Cerebral infarction       |                |                |
| subjects affected / exposed | 1 / 23 (4.35%)                                    | 0 / 18 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all)           | 1   | 0              | 0              |
| Disturbance in attention    | Additional description: Disturbance in attention  |                |                |
| subjects affected / exposed | 0 / 23 (0.00%)                                    | 1 / 18 (5.56%) | 0 / 21 (0.00%) |
| occurrences (all)           | 0   | 1              | 0              |
| Headache                    | Additional description: Headache                  |                |                |
| subjects affected / exposed | 0 / 23 (0.00%)                                    | 1 / 18 (5.56%) | 1 / 21 (4.76%) |
| occurrences (all)           | 0   | 1              | 1              |
| Hemiparesis                 | Additional description: Hemiparesis               |                |                |
| subjects affected / exposed | 1 / 23 (4.35%)                                    | 0 / 18 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all)           | 1   | 0              | 1              |
| IIIrd nerve paralysis       | Additional description: IIIrd nerve paralysis     |                |                |
| subjects affected / exposed | 0 / 23 (0.00%)                                    | 0 / 18 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all)           | 0   | 0              | 1              |
| Peripheral nerve lesion     | Additional description: Peripheral nerve lesion   |                |                |
| subjects affected / exposed | 0 / 23 (0.00%)                                    | 1 / 18 (5.56%) | 1 / 21 (4.76%) |
| occurrences (all)           | 0   | 1              | 1              |
| Peripheral nerve paresis    | Additional description: Peripheral nerve paresis  |                |                |
| subjects affected / exposed | 0 / 23 (0.00%)                                    | 0 / 18 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all)           | 0   | 0              | 0              |
| Psychomotor hyperactivity   | Additional description: Psychomotor hyperactivity |                |                |
| subjects affected / exposed | 0 / 23 (0.00%)                                    | 0 / 18 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all)           | 0   | 0              | 0              |
| Seizure                     | Additional description: Seizure                   |                |                |

|  |  |                 |                 |
|--|--|-----------------|-----------------|
| subjects affected / exposed            | 0 / 23 (0.00%)   | 0 / 18 (0.00%)  | 0 / 21 (0.00%)  |
| occurrences (all)                      | 0  | 0               | 0               |
| Syncope                                | Additional description: Syncope                                |                 |                 |
| subjects affected / exposed            | 0 / 23 (0.00%)   | 1 / 18 (5.56%)  | 1 / 21 (4.76%)  |
| occurrences (all)                      | 0  | 2               | 1               |
| Tremor                                 | Additional description: Tremor                                 |                 |                 |
| subjects affected / exposed            | 0 / 23 (0.00%)   | 0 / 18 (0.00%)  | 1 / 21 (4.76%)  |
| occurrences (all)                      | 0  | 0               | 1               |
| Blood and lymphatic system disorders   |  |                 |                 |
| Anaemia                                | Additional description: Anaemia                                |                 |                 |
| subjects affected / exposed            | 5 / 23 (21.74%)  | 1 / 18 (5.56%)  | 6 / 21 (28.57%) |
| occurrences (all)                      | 6  | 1               | 6               |
| Coagulation factor deficiency          | Additional description: Coagulation factor deficiency          |                 |                 |
| subjects affected / exposed            | 0 / 23 (0.00%)   | 0 / 18 (0.00%)  | 1 / 21 (4.76%)  |
| occurrences (all)                      | 0  | 0               | 1               |
| Coagulopathy                           | Additional description: Coagulopathy                           |                 |                 |
| subjects affected / exposed            | 1 / 23 (4.35%)   | 0 / 18 (0.00%)  | 1 / 21 (4.76%)  |
| occurrences (all)                      | 1  | 0               | 1               |
| Disseminated intravascular coagulation | Additional description: Disseminated intravascular coagulation |                 |                 |
| subjects affected / exposed            | 0 / 23 (0.00%)   | 0 / 18 (0.00%)  | 2 / 21 (9.52%)  |
| occurrences (all)                      | 0  | 0               | 2               |
| Erythropenia                           | Additional description: Erythropenia                           |                 |                 |
| subjects affected / exposed            | 0 / 23 (0.00%)   | 0 / 18 (0.00%)  | 0 / 21 (0.00%)  |
| occurrences (all)                      | 0  | 0               | 0               |
| Haemorrhagic anaemia                   | Additional description: Haemorrhagic anaemia                   |                 |                 |
| subjects affected / exposed            | 0 / 23 (0.00%)   | 2 / 18 (11.11%) | 1 / 21 (4.76%)  |
| occurrences (all)                      | 0  | 2               | 1               |
| Heparin-induced thrombocytopenia       | Additional description: Heparin-induced thrombocytopenia       |                 |                 |
| subjects affected / exposed            | 0 / 23 (0.00%)   | 0 / 18 (0.00%)  | 0 / 21 (0.00%)  |
| occurrences (all)                      | 0  | 0               | 0               |
| Leukocytosis                           | Additional description: Leukocytosis                           |                 |                 |
| subjects affected / exposed            | 3 / 23 (13.04%)  | 0 / 18 (0.00%)  | 0 / 21 (0.00%)  |
| occurrences (all)                      | 3  | 0               | 0               |
| Thrombocytopenia                       | Additional description: Thrombocytopenia                       |                 |                 |

|  |  |                      |                      |
|--|--|----------------------|----------------------|
| subjects affected / exposed<br>occurrences (all) | 4 / 23 (17.39%)<br>4                         | 3 / 18 (16.67%)<br>3 | 3 / 21 (14.29%)<br>3 |
| Ear and labyrinth disorders                      |  |                      |                      |
| Hypoacusis                                       | Additional description: Hypoacusis           |                      |                      |
| subjects affected / exposed<br>occurrences (all) | 0 / 23 (0.00%)<br>0                          | 0 / 18 (0.00%)<br>0  | 1 / 21 (4.76%)<br>1  |
| Eye disorders                                    |  |                      |                      |
| Gaze palsy                                       | Additional description: Gaze palsy           |                      |                      |
| subjects affected / exposed<br>occurrences (all) | 0 / 23 (0.00%)<br>0                          | 0 / 18 (0.00%)<br>0  | 1 / 21 (4.76%)<br>1  |
| Pupils unequal                                   | Additional description: Pupils unequal       |                      |                      |
| subjects affected / exposed<br>occurrences (all) | 0 / 23 (0.00%)<br>0                          | 1 / 18 (5.56%)<br>1  | 0 / 21 (0.00%)<br>0  |
| Visual impairment                                | Additional description: Visual impairment    |                      |                      |
| subjects affected / exposed<br>occurrences (all) | 0 / 23 (0.00%)<br>0                          | 0 / 18 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  |
| Gastrointestinal disorders                       |  |                      |                      |
| Abdominal pain                                   | Additional description: Abdominal pain       |                      |                      |
| subjects affected / exposed<br>occurrences (all) | 0 / 23 (0.00%)<br>0                          | 0 / 18 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  |
| Abdominal pain upper                             | Additional description: Abdominal pain upper |                      |                      |
| subjects affected / exposed<br>occurrences (all) | 0 / 23 (0.00%)<br>0                          | 0 / 18 (0.00%)<br>0  | 2 / 21 (9.52%)<br>2  |
| Anal incontinence                                | Additional description: Anal incontinence    |                      |                      |
| subjects affected / exposed<br>occurrences (all) | 0 / 23 (0.00%)<br>0                          | 0 / 18 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  |
| Constipation                                     | Additional description: Constipation         |                      |                      |
| subjects affected / exposed<br>occurrences (all) | 1 / 23 (4.35%)<br>1                          | 0 / 18 (0.00%)<br>0  | 3 / 21 (14.29%)<br>3 |
| Diarrhoea  | Additional description: Diarrhoea            |                      |                      |
| subjects affected / exposed<br>occurrences (all) | 1 / 23 (4.35%)<br>1                          | 2 / 18 (11.11%)<br>2 | 0 / 21 (0.00%)<br>0  |
| Duodenal ulcer                                   | Additional description: Duodenal ulcer       |                      |                      |
| subjects affected / exposed<br>occurrences (all) | 0 / 23 (0.00%)<br>0                          | 0 / 18 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  |
| Dysphagia  | Additional description: Dysphagia            |                      |                      |

|  |  |                 |                 |
|--|--|-----------------|-----------------|
| subjects affected / exposed            | 0 / 23 (0.00%)                                       | 0 / 18 (0.00%)  | 1 / 21 (4.76%)  |
| occurrences (all)                      | 0  | 0               | 1               |
| Flatulence                             | Additional description: Flatulence                   |                 |                 |
| subjects affected / exposed            | 1 / 23 (4.35%)                                       | 1 / 18 (5.56%)  | 0 / 21 (0.00%)  |
| occurrences (all)                      | 1  | 1               | 0               |
| Gastritis                              | Additional description: Gastritis                    |                 |                 |
| subjects affected / exposed            | 0 / 23 (0.00%)                                       | 0 / 18 (0.00%)  | 0 / 21 (0.00%)  |
| occurrences (all)                      | 0  | 0               | 0               |
| Gastrointestinal haemorrhage           | Additional description: Gastrointestinal haemorrhage |                 |                 |
| subjects affected / exposed            | 0 / 23 (0.00%)                                       | 1 / 18 (5.56%)  | 0 / 21 (0.00%)  |
| occurrences (all)                      | 0  | 1               | 0               |
| Large intestinal ulcer                 | Additional description: Large intestinal ulcer       |                 |                 |
| subjects affected / exposed            | 0 / 23 (0.00%)                                       | 0 / 18 (0.00%)  | 0 / 21 (0.00%)  |
| occurrences (all)                      | 0  | 0               | 0               |
| Nausea                                 | Additional description: Nausea                       |                 |                 |
| subjects affected / exposed            | 6 / 23 (26.09%)                                      | 0 / 18 (0.00%)  | 4 / 21 (19.05%) |
| occurrences (all)                      | 6  | 0               | 5               |
| Pancreatitis                           | Additional description: Pancreatitis                 |                 |                 |
| subjects affected / exposed            | 0 / 23 (0.00%)                                       | 0 / 18 (0.00%)  | 1 / 21 (4.76%)  |
| occurrences (all)                      | 0  | 0               | 1               |
| Subileus                               | Additional description: Subileus                     |                 |                 |
| subjects affected / exposed            | 0 / 23 (0.00%)                                       | 1 / 18 (5.56%)  | 0 / 21 (0.00%)  |
| occurrences (all)                      | 0  | 1               | 0               |
| Vomiting                               | Additional description: Vomiting                     |                 |                 |
| subjects affected / exposed            | 1 / 23 (4.35%)                                       | 4 / 18 (22.22%) | 2 / 21 (9.52%)  |
| occurrences (all)                      | 1  | 4               | 2               |
| Skin and subcutaneous tissue disorders |  |                 |                 |
| Decubitus ulcer                        | Additional description: Decubitus ulcer              |                 |                 |
| subjects affected / exposed            | 1 / 23 (4.35%)                                       | 1 / 18 (5.56%)  | 0 / 21 (0.00%)  |
| occurrences (all)                      | 1  | 1               | 0               |
| Erythema                               | Additional description: Erythema                     |                 |                 |
| subjects affected / exposed            | 0 / 23 (0.00%)                                       | 0 / 18 (0.00%)  | 1 / 21 (4.76%)  |
| occurrences (all)                      | 0  | 0               | 1               |
| Rash generalised                       | Additional description: Rash generalised             |                 |                 |
| subjects affected / exposed            | 0 / 23 (0.00%)                                       | 0 / 18 (0.00%)  | 0 / 21 (0.00%)  |
| occurrences (all)                      | 0  | 0               | 0               |



|  |  |                 |                |
|--|--|-----------------|----------------|
| Subcutaneous emphysema<br>subjects affected / exposed<br>occurrences (all) | Additional description: Subcutaneous emphysema |                 |                |
|  | 1 / 23 (4.35%)                                 | 2 / 18 (11.11%) | 0 / 21 (0.00%) |
|  | 1  | 2               | 0              |
| Renal and urinary disorders  |  |                 |                |
|  | Additional description: Acute kidney injury    |                 |                |
|  | 3 / 23 (13.04%)                                | 2 / 18 (11.11%) | 2 / 21 (9.52%) |
|  | 3  | 2               | 2              |
|  | Additional description: Acute prerenal failure |                 |                |
|  | 0 / 23 (0.00%)                                 | 0 / 18 (0.00%)  | 0 / 21 (0.00%) |
|  | 0  | 0               | 0              |
|  | Additional description: Dysuria                |                 |                |
|  | 1 / 23 (4.35%)                                 | 0 / 18 (0.00%)  | 0 / 21 (0.00%) |
|  | 1  | 0               | 0              |
|  | Additional description: Haematuria             |                 |                |
|  | 1 / 23 (4.35%)                                 | 0 / 18 (0.00%)  | 0 / 21 (0.00%) |
|  | 1  | 0               | 0              |
|  | Additional description: Oliguria               |                 |                |
|  | 2 / 23 (8.70%)                                 | 3 / 18 (16.67%) | 2 / 21 (9.52%) |
|  | 2  | 3               | 2              |
|  | Additional description: Renal failure          |                 |                |
|  | 2 / 23 (8.70%)                                 | 1 / 18 (5.56%)  | 0 / 21 (0.00%) |
|  | 2  | 1               | 0              |
|  | Additional description: Urinary incontinence   |                 |                |
|  | 0 / 23 (0.00%)                                 | 1 / 18 (5.56%)  | 2 / 21 (9.52%) |
|  | 0  | 1               | 2              |
|  | Additional description: Urinary retention      |                 |                |
|  | 0 / 23 (0.00%)                                 | 0 / 18 (0.00%)  | 0 / 21 (0.00%) |
|  | 0  | 0               | 0              |
| Musculoskeletal and connective tissue disorders                            |  |                 |                |
|  | Additional description: Back pain              |                 |                |
|  | 2 / 23 (8.70%)                                 | 1 / 18 (5.56%)  | 0 / 21 (0.00%) |
|  | 2  | 1               | 0              |
|  | Additional description: Muscle spasms          |                 |                |
|  | 1 / 23 (4.35%)                                 | 0 / 18 (0.00%)  | 1 / 21 (4.76%) |
|  | 1  | 0               | 1              |
|  | Additional description: Muscular weakness      |                 |                |

|                             |  |                |                |
|-----------------------------|--|----------------|----------------|
| subjects affected / exposed | 0 / 23 (0.00%)                                     | 0 / 18 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all)           | 0  | 0              | 0              |
| Musculoskeletal chest pain  | Additional description: Musculoskeletal chest pain |                |                |
| subjects affected / exposed | 0 / 23 (0.00%)                                     | 1 / 18 (5.56%) | 1 / 21 (4.76%) |
| occurrences (all)           | 0  | 1              | 1              |
| Musculoskeletal pain        | Additional description: Musculoskeletal pain       |                |                |
| subjects affected / exposed | 0 / 23 (0.00%)                                     | 0 / 18 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all)           | 0  | 0              | 1              |
| Infections and infestations |  |                |                |
| Bacterial disease carrier   | Additional description: Bacterial disease carrier  |                |                |
| subjects affected / exposed | 0 / 23 (0.00%)                                     | 0 / 18 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all)           | 0  | 0              | 1              |
| Bronchitis                  | Additional description: Bronchitis                 |                |                |
| subjects affected / exposed | 0 / 23 (0.00%)                                     | 0 / 18 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all)           | 0  | 0              | 0              |
| Clostridial infection       | Additional description: Clostridial infection      |                |                |
| subjects affected / exposed | 0 / 23 (0.00%)                                     | 0 / 18 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all)           | 0  | 0              | 1              |
| Cystitis                    | Additional description: Cystitis                   |                |                |
| subjects affected / exposed | 1 / 23 (4.35%)                                     | 0 / 18 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all)           | 1  | 0              | 1              |
| Device related infection    | Additional description: Device related infection   |                |                |
| subjects affected / exposed | 0 / 23 (0.00%)                                     | 0 / 18 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all)           | 0  | 0              | 1              |
| Enterococcal infection      | Additional description: Enterococcal infection     |                |                |
| subjects affected / exposed | 1 / 23 (4.35%)                                     | 0 / 18 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all)           | 1  | 0              | 0              |
| Infection                   | Additional description: Infection                  |                |                |
| subjects affected / exposed | 0 / 23 (0.00%)                                     | 0 / 18 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all)           | 0  | 0              | 0              |
| Infectious disease carrier  | Additional description: Infectious disease carrier |                |                |
| subjects affected / exposed | 1 / 23 (4.35%)                                     | 0 / 18 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all)           | 1  | 0              | 1              |
| Nasopharyngitis             | Additional description: Nasopharyngitis            |                |                |
| subjects affected / exposed | 0 / 23 (0.00%)                                     | 0 / 18 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all)           | 0  | 0              | 1              |

|   |   |                      |                      |
|---|---|----------------------|----------------------|
| Nosocomial infection<br>subjects affected / exposed<br>occurrences (all)                                  | Additional description: Nosocomial infection    |                      |                      |
|   | 0 / 23 (0.00%)<br>0                             | 0 / 18 (0.00%)<br>0  | 1 / 21 (4.76%)<br>1  |
| Pneumonia<br>subjects affected / exposed<br>occurrences (all)   | Additional description: Pneumonia               |                      |                      |
|   | 0 / 23 (0.00%)<br>0                             | 1 / 18 (5.56%)<br>1  | 2 / 21 (9.52%)<br>2  |
| Pneumonia escherichia<br>subjects affected / exposed<br>occurrences (all)                                 | Additional description: Pneumonia escherichia   |                      |                      |
|   | 0 / 23 (0.00%)<br>0                             | 0 / 18 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  |
| Pneumonia klebsiella<br>subjects affected / exposed<br>occurrences (all)                                  | Additional description: Pneumonia klebsiella    |                      |                      |
|   | 0 / 23 (0.00%)<br>0                             | 0 / 18 (0.00%)<br>0  | 1 / 21 (4.76%)<br>1  |
| Tracheobronchitis<br>subjects affected / exposed<br>occurrences (all)                                     | Additional description: Tracheobronchitis       |                      |                      |
|   | 0 / 23 (0.00%)<br>0                             | 0 / 18 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  |
| Urinary tract infection<br>subjects affected / exposed<br>occurrences (all)                               | Additional description: Urinary tract infection |                      |                      |
|   | 2 / 23 (8.70%)<br>2                             | 1 / 18 (5.56%)<br>1  | 3 / 21 (14.29%)<br>3 |
| Metabolism and nutrition disorders<br>Fluid retention<br>subjects affected / exposed<br>occurrences (all) | Additional description: Fluid retention         |                      |                      |
|   | 0 / 23 (0.00%)<br>0                             | 2 / 18 (11.11%)<br>2 | 0 / 21 (0.00%)<br>0  |
| Gout<br>subjects affected / exposed<br>occurrences (all)  | Additional description: Gout                    |                      |                      |
|   | 1 / 23 (4.35%)<br>1                             | 0 / 18 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  |
| Hyperkalaemia<br>subjects affected / exposed<br>occurrences (all)   | Additional description: Hyperkalaemia           |                      |                      |
|   | 1 / 23 (4.35%)<br>1                             | 0 / 18 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  |
| Hypernatraemia<br>subjects affected / exposed<br>occurrences (all)  | Additional description: Hypernatraemia          |                      |                      |
|   | 0 / 23 (0.00%)<br>0                             | 1 / 18 (5.56%)<br>1  | 1 / 21 (4.76%)<br>1  |
| Hypoalbuminaemia<br>subjects affected / exposed<br>occurrences (all)                                      | Additional description: Hypoalbuminaemia        |                      |                      |
|   | 0 / 23 (0.00%)<br>0                             | 1 / 18 (5.56%)<br>1  | 0 / 21 (0.00%)<br>0  |
| Hyponatraemia   | Additional description: Hyponatraemia           |                      |                      |
|   |   |                      |                      |

|                             |  |                 |                |
|-----------------------------|--|-----------------|----------------|
| subjects affected / exposed | 0 / 23 (0.00%)                             | 0 / 18 (0.00%)  | 0 / 21 (0.00%) |
| occurrences (all)           | 0  | 0               | 0              |
| Hypovolaemia                | Additional description: Hypovolaemia       |                 |                |
| subjects affected / exposed | 2 / 23 (8.70%)                             | 0 / 18 (0.00%)  | 1 / 21 (4.76%) |
| occurrences (all)           | 2  | 0               | 1              |
| Metabolic acidosis          | Additional description: Metabolic acidosis |                 |                |
| subjects affected / exposed | 1 / 23 (4.35%)                             | 2 / 18 (11.11%) | 0 / 21 (0.00%) |
| occurrences (all)           | 2  | 2               | 0              |
| Protein deficiency          | Additional description: Protein deficiency |                 |                |
| subjects affected / exposed | 0 / 23 (0.00%)                             | 1 / 18 (5.56%)  | 2 / 21 (9.52%) |
| occurrences (all)           | 0  | 1               | 2              |

| <b>Non-serious adverse events</b>                     | 8mg/kg bw IFX-1                                  | Placebo          |  |
|---|--|------------------|--|
| Total subjects affected by non-serious adverse events |  |                  |  |
| subjects affected / exposed                           | 19 / 20 (95.00%)                                 | 21 / 22 (95.45%) |  |
| Vascular disorders                                    |  |                  |  |
| Haematoma   | Additional description: Haematoma                |                  |  |
| subjects affected / exposed                           | 2 / 20 (10.00%)                                  | 1 / 22 (4.55%)   |  |
| occurrences (all)                                     | 2  | 1                |  |
| Haemodynamic instability                              | Additional description: Haemodynamic instability |                  |  |
| subjects affected / exposed                           | 0 / 20 (0.00%)                                   | 0 / 22 (0.00%)   |  |
| occurrences (all)                                     | 0  | 0                |  |
| Hypertension  | Additional description: Hypertension             |                  |  |
| subjects affected / exposed                           | 3 / 20 (15.00%)                                  | 4 / 22 (18.18%)  |  |
| occurrences (all)                                     | 3  | 4                |  |
| Hypertensive crisis                                   | Additional description: Hypertensive crisis      |                  |  |
| subjects affected / exposed                           | 0 / 20 (0.00%)                                   | 0 / 22 (0.00%)   |  |
| occurrences (all)                                     | 0  | 0                |  |
| Hypotension   | Additional description: Hypotension              |                  |  |
| subjects affected / exposed                           | 0 / 20 (0.00%)                                   | 0 / 22 (0.00%)   |  |
| occurrences (all)                                     | 0  | 0                |  |
| Surgical and medical procedures                       |  |                  |  |
| Colectomy   | Additional description: Colectomy                |                  |  |
| subjects affected / exposed                           | 0 / 20 (0.00%)                                   | 0 / 22 (0.00%)   |  |
| occurrences (all)                                     | 0  | 0                |  |
| Explorative laparotomy                                | Additional description: Explorative laparotomy   |                  |  |

|   |   |                     |  |
|---|---|---------------------|--|
| subjects affected / exposed<br>occurrences (all)        | 0 / 20 (0.00%)<br>0                         | 0 / 22 (0.00%)<br>0 |  |
| General disorders and administration<br>site conditions |   |                     |  |
| Asthenia  | Additional description: Asthenia            |                     |  |
| subjects affected / exposed<br>occurrences (all)        | 0 / 20 (0.00%)<br>0                         | 0 / 22 (0.00%)<br>0 |  |
| Chest pain  | Additional description: Chest pain          |                     |  |
| subjects affected / exposed<br>occurrences (all)        | 0 / 20 (0.00%)<br>0                         | 0 / 22 (0.00%)<br>0 |  |
| Drug intolerance  | Additional description: Drug intolerance    |                     |  |
| subjects affected / exposed<br>occurrences (all)        | 0 / 20 (0.00%)<br>0                         | 1 / 22 (4.55%)<br>1 |  |
| Gait disturbance  | Additional description: Gait disturbance    |                     |  |
| subjects affected / exposed<br>occurrences (all)        | 0 / 20 (0.00%)<br>0                         | 0 / 22 (0.00%)<br>0 |  |
| Impaired healing  | Additional description: Impaired healing    |                     |  |
| subjects affected / exposed<br>occurrences (all)        | 0 / 20 (0.00%)<br>0                         | 1 / 22 (4.55%)<br>1 |  |
| Malaise   | Additional description: Malaise             |                     |  |
| subjects affected / exposed<br>occurrences (all)        | 0 / 20 (0.00%)<br>0                         | 0 / 22 (0.00%)<br>0 |  |
| Oedema  | Additional description: Oedema              |                     |  |
| subjects affected / exposed<br>occurrences (all)        | 0 / 20 (0.00%)<br>0                         | 2 / 22 (9.09%)<br>2 |  |
| Oedema peripheral                                       | Additional description: Oedema peripheral   |                     |  |
| subjects affected / exposed<br>occurrences (all)        | 3 / 20 (15.00%)<br>3                        | 2 / 22 (9.09%)<br>2 |  |
| Peripheral swelling                                     | Additional description: Peripheral swelling |                     |  |
| subjects affected / exposed<br>occurrences (all)        | 0 / 20 (0.00%)<br>0                         | 0 / 22 (0.00%)<br>0 |  |
| Pyrexia   | Additional description: Pyrexia             |                     |  |
| subjects affected / exposed<br>occurrences (all)        | 1 / 20 (5.00%)<br>1                         | 0 / 22 (0.00%)<br>0 |  |
| Respiratory, thoracic and mediastinal<br>disorders      |   |                     |  |

|   |  |                     |
|---|--|---------------------|
| Acquired diaphragmatic eventration<br>subjects affected / exposed<br>occurrences (all)            | Additional description: Acquired diaphragmatic eventration         |                     |
|   | 0 / 20 (0.00%)<br>0  | 1 / 22 (4.55%)<br>1 |
| Acute respiratory failure<br>subjects affected / exposed<br>occurrences (all)                     | Additional description: Acute respiratory failure                  |                     |
|   | 1 / 20 (5.00%)<br>1  | 0 / 22 (0.00%)<br>0 |
| Aspiration<br>subjects affected / exposed<br>occurrences (all)                                    | Additional description: Aspiration                                 |                     |
|   | 0 / 20 (0.00%)<br>0  | 0 / 22 (0.00%)<br>0 |
| Atelectasis<br>subjects affected / exposed<br>occurrences (all)                                   | Additional description: Atelectasis                                |                     |
|   | 0 / 20 (0.00%)<br>0  | 2 / 22 (9.09%)<br>2 |
| Bronchospasm<br>subjects affected / exposed<br>occurrences (all)                                  | Additional description: Bronchospasm                               |                     |
|   | 0 / 20 (0.00%)<br>0  | 0 / 22 (0.00%)<br>0 |
| Cough<br>subjects affected / exposed<br>occurrences (all)   | Additional description: Cough                                      |                     |
|   | 1 / 20 (5.00%)<br>1  | 0 / 22 (0.00%)<br>0 |
| Dyspnoea<br>subjects affected / exposed<br>occurrences (all)                                      | Additional description: Dyspnoea                                   |                     |
|   | 1 / 20 (5.00%)<br>1  | 0 / 22 (0.00%)<br>0 |
| Emphysema<br>subjects affected / exposed<br>occurrences (all)                                     | Additional description: Emphysema                                  |                     |
|   | 0 / 20 (0.00%)<br>0  | 0 / 22 (0.00%)<br>0 |
| Epistaxis<br>subjects affected / exposed<br>occurrences (all)                                     | Additional description: Epistaxis                                  |                     |
|   | 0 / 20 (0.00%)<br>0  | 1 / 22 (4.55%)<br>1 |
| Increased viscosity of bronchial<br>secretion<br>subjects affected / exposed<br>occurrences (all) | Additional description: Increased viscosity of bronchial secretion |                     |
|   | 0 / 20 (0.00%)<br>0  | 0 / 22 (0.00%)<br>0 |
| Lung disorder<br>subjects affected / exposed<br>occurrences (all)                                 | Additional description: Lung disorder                              |                     |
|   | 1 / 20 (5.00%)<br>1  | 0 / 22 (0.00%)<br>0 |
| Lung hypoinflation  | Additional description: Lung hypoinflation                         |                     |

|                                    |  |                 |  |
|------------------------------------|--|-----------------|--|
| subjects affected / exposed        | 0 / 20 (0.00%)   | 1 / 22 (4.55%)  |  |
| occurrences (all)                  | 0  | 1               |  |
| Pleural effusion                   | Additional description: Pleural effusion                   |                 |  |
| subjects affected / exposed        | 4 / 20 (20.00%)  | 9 / 22 (40.91%) |  |
| occurrences (all)                  | 4  | 9               |  |
| Pneumothorax                       | Additional description: Pneumothorax                       |                 |  |
| subjects affected / exposed        | 0 / 20 (0.00%)   | 1 / 22 (4.55%)  |  |
| occurrences (all)                  | 0  | 1               |  |
| Pulmonary congestion               | Additional description: Pulmonary congestion               |                 |  |
| subjects affected / exposed        | 0 / 20 (0.00%)   | 2 / 22 (9.09%)  |  |
| occurrences (all)                  | 0  | 2               |  |
| Pulmonary oedema                   | Additional description: Pulmonary oedema                   |                 |  |
| subjects affected / exposed        | 0 / 20 (0.00%)   | 0 / 22 (0.00%)  |  |
| occurrences (all)                  | 0  | 0               |  |
| Respiratory failure                | Additional description: Respiratory failure                |                 |  |
| subjects affected / exposed        | 2 / 20 (10.00%)  | 2 / 22 (9.09%)  |  |
| occurrences (all)                  | 2  | 2               |  |
| Psychiatric disorders              |  |                 |  |
| Delirium                           | Additional description: Delirium                           |                 |  |
| subjects affected / exposed        | 6 / 20 (30.00%)  | 6 / 22 (27.27%) |  |
| occurrences (all)                  | 6  | 6               |  |
| Disorientation                     | Additional description: Disorientation                     |                 |  |
| subjects affected / exposed        | 1 / 20 (5.00%)   | 0 / 22 (0.00%)  |  |
| occurrences (all)                  | 1  | 0               |  |
| Insomnia                           | Additional description: Insomnia                           |                 |  |
| subjects affected / exposed        | 0 / 20 (0.00%)   | 0 / 22 (0.00%)  |  |
| occurrences (all)                  | 0  | 0               |  |
| Restlessness                       | Additional description: Restlessness                       |                 |  |
| subjects affected / exposed        | 0 / 20 (0.00%)   | 0 / 22 (0.00%)  |  |
| occurrences (all)                  | 0  | 0               |  |
| Sleep disorder                     | Additional description: Sleep disorder                     |                 |  |
| subjects affected / exposed        | 0 / 20 (0.00%)   | 2 / 22 (9.09%)  |  |
| occurrences (all)                  | 0  | 4               |  |
| Investigations                     |  |                 |  |
| Alanine aminotransferase increased | Additional description: Alanine aminotransferase increased |                 |  |

|   |   |                |  |
|---|---|----------------|--|
| subjects affected / exposed               | 0 / 20 (0.00%)  | 0 / 22 (0.00%) |  |
| occurrences (all)                         | 0   | 0              |  |
| Antithrombin III decreased                | Additional description: Antithrombin III decreased                |                |  |
| subjects affected / exposed               | 0 / 20 (0.00%)  | 1 / 22 (4.55%) |  |
| occurrences (all)                         | 0   | 1              |  |
| Aspartate aminotransferase increased      | Additional description: Aspartate aminotransferase increased      |                |  |
| subjects affected / exposed               | 0 / 20 (0.00%)  | 0 / 22 (0.00%) |  |
| occurrences (all)                         | 0   | 0              |  |
| Blood albumin decreased                   | Additional description: Blood albumin decreased                   |                |  |
| subjects affected / exposed               | 0 / 20 (0.00%)  | 0 / 22 (0.00%) |  |
| occurrences (all)                         | 0   | 0              |  |
| Blood alkaline phosphatase increased      | Additional description: Blood alkaline phosphatase increased      |                |  |
| subjects affected / exposed               | 0 / 20 (0.00%)  | 0 / 22 (0.00%) |  |
| occurrences (all)                         | 0   | 0              |  |
| Blood bilirubin increased                 | Additional description: Blood bilirubin increased                 |                |  |
| subjects affected / exposed               | 0 / 20 (0.00%)  | 0 / 22 (0.00%) |  |
| occurrences (all)                         | 0   | 0              |  |
| Blood calcium decreased                   | Additional description: Blood calcium decreased                   |                |  |
| subjects affected / exposed               | 0 / 20 (0.00%)  | 0 / 22 (0.00%) |  |
| occurrences (all)                         | 0   | 0              |  |
| Blood creatine phosphokinase MB increased | Additional description: Blood creatine phosphokinase MB increased |                |  |
| subjects affected / exposed               | 0 / 20 (0.00%)  | 0 / 22 (0.00%) |  |
| occurrences (all)                         | 0   | 0              |  |
| Blood creatine phosphokinase increased    | Additional description: Blood creatine phosphokinase increased    |                |  |
| subjects affected / exposed               | 0 / 20 (0.00%)  | 0 / 22 (0.00%) |  |
| occurrences (all)                         | 0   | 0              |  |
| Blood creatinine increased                | Additional description: Blood creatinine increased                |                |  |
| subjects affected / exposed               | 0 / 20 (0.00%)  | 0 / 22 (0.00%) |  |
| occurrences (all)                         | 0   | 0              |  |
| Blood fibrinogen decreased                | Additional description: Blood fibrinogen decreased                |                |  |
| subjects affected / exposed               | 0 / 20 (0.00%)  | 0 / 22 (0.00%) |  |
| occurrences (all)                         | 0   | 0              |  |
| Blood glucose increased                   | Additional description: Blood glucose increased                   |                |  |



|                                       |   |                |  |
|---------------------------------------|---|----------------|--|
| subjects affected / exposed           | 0 / 20 (0.00%)  | 1 / 22 (4.55%) |  |
| occurrences (all)                     | 0   | 1              |  |
| Blood lactate dehydrogenase increased | Additional description: Blood lactate dehydrogenase increased |                |  |
| subjects affected / exposed           | 0 / 20 (0.00%)  | 1 / 22 (4.55%) |  |
| occurrences (all)                     | 0   | 1              |  |
| Blood pressure decreased              | Additional description: Blood pressure decreased              |                |  |
| subjects affected / exposed           | 0 / 20 (0.00%)  | 0 / 22 (0.00%) |  |
| occurrences (all)                     | 0   | 0              |  |
| Blood pressure increased              | Additional description: Blood pressure increased              |                |  |
| subjects affected / exposed           | 0 / 20 (0.00%)  | 0 / 22 (0.00%) |  |
| occurrences (all)                     | 0   | 0              |  |
| Blood urea increased                  | Additional description: Blood urea increased                  |                |  |
| subjects affected / exposed           | 0 / 20 (0.00%)  | 0 / 22 (0.00%) |  |
| occurrences (all)                     | 0   | 0              |  |
| Body temperature increased            | Additional description: Body temperature increased            |                |  |
| subjects affected / exposed           | 0 / 20 (0.00%)  | 1 / 22 (4.55%) |  |
| occurrences (all)                     | 0   | 1              |  |
| Breath sounds abnormal                | Additional description: Breath sounds abnormal                |                |  |
| subjects affected / exposed           | 0 / 20 (0.00%)  | 0 / 22 (0.00%) |  |
| occurrences (all)                     | 0   | 0              |  |
| C-reactive protein increased          | Additional description: C-reactive protein increased          |                |  |
| subjects affected / exposed           | 0 / 20 (0.00%)  | 2 / 22 (9.09%) |  |
| occurrences (all)                     | 0   | 2              |  |
| Cardiac index decreased               | Additional description: Cardiac index decreased               |                |  |
| subjects affected / exposed           | 1 / 20 (5.00%)  | 0 / 22 (0.00%) |  |
| occurrences (all)                     | 1   | 0              |  |
| Enterococcus test positive            | Additional description: Enterococcus test positive            |                |  |
| subjects affected / exposed           | 0 / 20 (0.00%)  | 0 / 22 (0.00%) |  |
| occurrences (all)                     | 0   | 0              |  |
| Escherichia test positive             | Additional description: Escherichia test positive             |                |  |
| subjects affected / exposed           | 0 / 20 (0.00%)  | 0 / 22 (0.00%) |  |
| occurrences (all)                     | 0   | 0              |  |
| Gamma-glutamyltransferase increased   | Additional description: Gamma-glutamyltransferase increased   |                |  |

|  |  |                |  |
|--|--|----------------|--|
| subjects affected / exposed              | 0 / 20 (0.00%)   | 0 / 22 (0.00%) |  |
| occurrences (all)                        | 0  | 0              |  |
| Glutamate dehydrogenase increased        | Additional description: Glutamate dehydrogenase increased        |                |  |
| subjects affected / exposed              | 0 / 20 (0.00%)   | 1 / 22 (4.55%) |  |
| occurrences (all)                        | 0  | 1              |  |
| Haematocrit decreased                    | Additional description: Haematocrit decreased                    |                |  |
| subjects affected / exposed              | 0 / 20 (0.00%)   | 0 / 22 (0.00%) |  |
| occurrences (all)                        | 0  | 0              |  |
| Haemoglobin decreased                    | Additional description: Haemoglobin decreased                    |                |  |
| subjects affected / exposed              | 0 / 20 (0.00%)   | 2 / 22 (9.09%) |  |
| occurrences (all)                        | 0  | 2              |  |
| Heart rate decreased                     | Additional description: Heart rate decreased                     |                |  |
| subjects affected / exposed              | 0 / 20 (0.00%)   | 0 / 22 (0.00%) |  |
| occurrences (all)                        | 0  | 0              |  |
| Hepatic enzyme increased                 | Additional description: Hepatic enzyme increased                 |                |  |
| subjects affected / exposed              | 1 / 20 (5.00%)   | 2 / 22 (9.09%) |  |
| occurrences (all)                        | 1  | 2              |  |
| International normalised ratio increased | Additional description: International normalised ratio increased |                |  |
| subjects affected / exposed              | 0 / 20 (0.00%)   | 0 / 22 (0.00%) |  |
| occurrences (all)                        | 0  | 0              |  |
| Myocardial necrosis marker increased     | Additional description: Myocardial necrosis marker increased     |                |  |
| subjects affected / exposed              | 1 / 20 (5.00%)   | 0 / 22 (0.00%) |  |
| occurrences (all)                        | 1  | 0              |  |
| Oxygen saturation decreased              | Additional description: Oxygen saturation decreased              |                |  |
| subjects affected / exposed              | 0 / 20 (0.00%)   | 0 / 22 (0.00%) |  |
| occurrences (all)                        | 0  | 0              |  |
| Red blood cell count decreased           | Additional description: Red blood cell count decreased           |                |  |
| subjects affected / exposed              | 3 / 20 (15.00%)  | 2 / 22 (9.09%) |  |
| occurrences (all)                        | 3  | 2              |  |
| Staphylococcus test positive             | Additional description: Staphylococcus test positive             |                |  |
| subjects affected / exposed              | 0 / 20 (0.00%)   | 0 / 22 (0.00%) |  |
| occurrences (all)                        | 0  | 0              |  |
| Venous oxygen saturation decreased       | Additional description: Venous oxygen saturation decreased       |                |  |

|  |  |                      |  |
|--|--|----------------------|--|
| subjects affected / exposed<br>occurrences (all) | 0 / 20 (0.00%)<br>0  | 0 / 22 (0.00%)<br>0  |  |
| White blood cell count increased                 | Additional description: White blood cell count increased   |                      |  |
| subjects affected / exposed<br>occurrences (all) | 2 / 20 (10.00%)<br>2                                       | 4 / 22 (18.18%)<br>4 |  |
| Injury, poisoning and procedural complications   |  |                      |  |
| Anaemia postoperative                            | Additional description: Anaemia postoperative              |                      |  |
| subjects affected / exposed<br>occurrences (all) | 1 / 20 (5.00%)<br>1  | 2 / 22 (9.09%)<br>2  |  |
| Fall   | Additional description: Fall                               |                      |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 20 (0.00%)<br>0  | 0 / 22 (0.00%)<br>0  |  |
| Injury   | Additional description: Injury                             |                      |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 20 (0.00%)<br>0  | 0 / 22 (0.00%)<br>0  |  |
| Laceration                                       | Additional description: Laceration                         |                      |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 20 (0.00%)<br>0  | 0 / 22 (0.00%)<br>0  |  |
| Periorbital haemorrhage                          | Additional description: Periorbital haemorrhage            |                      |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 20 (0.00%)<br>0  | 0 / 22 (0.00%)<br>0  |  |
| Post procedural haematoma                        | Additional description: Post procedural haematoma          |                      |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 20 (0.00%)<br>0  | 0 / 22 (0.00%)<br>0  |  |
| Post procedural haemorrhage                      | Additional description: Post procedural haemorrhage        |                      |  |
| subjects affected / exposed<br>occurrences (all) | 1 / 20 (5.00%)<br>1  | 0 / 22 (0.00%)<br>0  |  |
| Postoperative renal failure                      | Additional description: Postoperative renal failure        |                      |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 20 (0.00%)<br>0  | 0 / 22 (0.00%)<br>0  |  |
| Postoperative respiratory distress               | Additional description: Postoperative respiratory distress |                      |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 20 (0.00%)<br>0  | 1 / 22 (4.55%)<br>1  |  |
| Postoperative wound complication                 | Additional description: Postoperative wound complication   |                      |  |

|                             |   |                 |  |
|-----------------------------|---|-----------------|--|
| subjects affected / exposed | 0 / 20 (0.00%)                                      | 0 / 22 (0.00%)  |  |
| occurrences (all)           | 0   | 0               |  |
| Procedural haemorrhage      | Additional description: Procedural haemorrhage      |                 |  |
| subjects affected / exposed | 0 / 20 (0.00%)                                      | 0 / 22 (0.00%)  |  |
| occurrences (all)           | 0   | 0               |  |
| Procedural nausea           | Additional description: Procedural nausea           |                 |  |
| subjects affected / exposed | 0 / 20 (0.00%)                                      | 0 / 22 (0.00%)  |  |
| occurrences (all)           | 0   | 0               |  |
| Procedural vomiting         | Additional description: Procedural vomiting         |                 |  |
| subjects affected / exposed | 0 / 20 (0.00%)                                      | 0 / 22 (0.00%)  |  |
| occurrences (all)           | 0   | 0               |  |
| Rib fracture                | Additional description: Rib fracture                |                 |  |
| subjects affected / exposed | 0 / 20 (0.00%)                                      | 0 / 22 (0.00%)  |  |
| occurrences (all)           | 0   | 0               |  |
| Wound haemorrhage           | Additional description: Wound haemorrhage           |                 |  |
| subjects affected / exposed | 0 / 20 (0.00%)                                      | 1 / 22 (4.55%)  |  |
| occurrences (all)           | 0   | 1               |  |
| Wound secretion             | Additional description: Wound secretion             |                 |  |
| subjects affected / exposed | 0 / 20 (0.00%)                                      | 1 / 22 (4.55%)  |  |
| occurrences (all)           | 0   | 1               |  |
| Cardiac disorders           |   |                 |  |
| Acute myocardial infarction | Additional description: Acute myocardial infarction |                 |  |
| subjects affected / exposed | 0 / 20 (0.00%)                                      | 1 / 22 (4.55%)  |  |
| occurrences (all)           | 0   | 1               |  |
| Arrhythmia                  | Additional description: Arrhythmia                  |                 |  |
| subjects affected / exposed | 0 / 20 (0.00%)                                      | 1 / 22 (4.55%)  |  |
| occurrences (all)           | 0   | 1               |  |
| Atrial fibrillation         | Additional description: Atrial fibrillation         |                 |  |
| subjects affected / exposed | 9 / 20 (45.00%)                                     | 8 / 22 (36.36%) |  |
| occurrences (all)           | 11  | 10              |  |
| Atrial flutter              | Additional description: Atrial flutter              |                 |  |
| subjects affected / exposed | 0 / 20 (0.00%)                                      | 0 / 22 (0.00%)  |  |
| occurrences (all)           | 0   | 0               |  |
| Atrioventricular block      | Additional description: Atrioventricular block      |                 |  |
| subjects affected / exposed | 0 / 20 (0.00%)                                      | 0 / 22 (0.00%)  |  |
| occurrences (all)           | 0   | 0               |  |

|  |  |                      |
|--|--|----------------------|
| Atrioventricular block complete<br>subjects affected / exposed<br>occurrences (all)      | Additional description: Atrioventricular block complete      |                      |
|  | 1 / 20 (5.00%)<br>1  | 2 / 22 (9.09%)<br>2  |
| Atrioventricular block second degree<br>subjects affected / exposed<br>occurrences (all) | Additional description: Atrioventricular block second degree |                      |
|  | 1 / 20 (5.00%)<br>1  | 0 / 22 (0.00%)<br>0  |
| Bradyarrhythmia<br>subjects affected / exposed<br>occurrences (all)                      | Additional description: Bradyarrhythmia                      |                      |
|  | 0 / 20 (0.00%)<br>0  | 0 / 22 (0.00%)<br>0  |
| Bradycardia<br>subjects affected / exposed<br>occurrences (all)                          | Additional description: Bradycardia                          |                      |
|  | 3 / 20 (15.00%)<br>3   | 1 / 22 (4.55%)<br>1  |
| Bundle branch block left<br>subjects affected / exposed<br>occurrences (all)             | Additional description: Bundle branch block left             |                      |
|  | 0 / 20 (0.00%)<br>0  | 2 / 22 (9.09%)<br>2  |
| Bundle branch block right<br>subjects affected / exposed<br>occurrences (all)            | Additional description: Bundle branch block right            |                      |
|  | 1 / 20 (5.00%)<br>1  | 0 / 22 (0.00%)<br>0  |
| Cardiac arrest<br>subjects affected / exposed<br>occurrences (all)                       | Additional description: Cardiac arrest                       |                      |
|  | 0 / 20 (0.00%)<br>0  | 0 / 22 (0.00%)<br>0  |
| Cardiac failure<br>subjects affected / exposed<br>occurrences (all)                      | Additional description: Cardiac failure                      |                      |
|  | 1 / 20 (5.00%)<br>1  | 0 / 22 (0.00%)<br>0  |
| Cardiovascular disorder<br>subjects affected / exposed<br>occurrences (all)              | Additional description: Cardiovascular disorder              |                      |
|  | 3 / 20 (15.00%)<br>3   | 4 / 22 (18.18%)<br>4 |
| Extrasystoles<br>subjects affected / exposed<br>occurrences (all)                        | Additional description: Extrasystoles                        |                      |
|  | 0 / 20 (0.00%)<br>0  | 1 / 22 (4.55%)<br>1  |
| Left ventricular dysfunction<br>subjects affected / exposed<br>occurrences (all)         | Additional description: Left ventricular dysfunction         |                      |
|  | 1 / 20 (5.00%)<br>1  | 0 / 22 (0.00%)<br>0  |
| Pericardial effusion<br>subjects affected / exposed<br>occurrences (all)                 | Additional description: Pericardial effusion                 |                      |
|  | 1 / 20 (5.00%)<br>1  | 1 / 22 (4.55%)<br>1  |

|  |   |                     |  |
|--|---|---------------------|--|
| Pericardial haemorrhage<br>subjects affected / exposed<br>occurrences (all)      | Additional description: Pericardial haemorrhage<br>0 / 20 (0.00%)<br>0      | 0 / 22 (0.00%)<br>0 |  |
| Pulmonary valve incompetence<br>subjects affected / exposed<br>occurrences (all) | Additional description: Pulmonary valve incompetence<br>0 / 20 (0.00%)<br>0 | 0 / 22 (0.00%)<br>0 |  |
| Sinus arrest<br>subjects affected / exposed<br>occurrences (all)                 | Additional description: Sinus arrest<br>0 / 20 (0.00%)<br>0                 | 0 / 22 (0.00%)<br>0 |  |
| Supraventricular tachycardia<br>subjects affected / exposed<br>occurrences (all) | Additional description: Supraventricular tachycardia<br>0 / 20 (0.00%)<br>0 | 0 / 22 (0.00%)<br>0 |  |
| Tachyarrhythmia<br>subjects affected / exposed<br>occurrences (all)              | Additional description: Tachyarrhythmia<br>1 / 20 (5.00%)<br>1              | 0 / 22 (0.00%)<br>0 |  |
| Tachycardia<br>subjects affected / exposed<br>occurrences (all)                  | Additional description: Tachycardia<br>0 / 20 (0.00%)<br>0                  | 0 / 22 (0.00%)<br>0 |  |
| Tricuspid valve incompetence<br>subjects affected / exposed<br>occurrences (all) | Additional description: Tricuspid valve incompetence<br>0 / 20 (0.00%)<br>0 | 0 / 22 (0.00%)<br>0 |  |
| Ventricular extrasystoles<br>subjects affected / exposed<br>occurrences (all)    | Additional description: Ventricular extrasystoles<br>2 / 20 (10.00%)<br>2   | 2 / 22 (9.09%)<br>2 |  |
| Ventricular fibrillation<br>subjects affected / exposed<br>occurrences (all)     | Additional description: Ventricular fibrillation<br>0 / 20 (0.00%)<br>0     | 0 / 22 (0.00%)<br>0 |  |
| Ventricular hypokinesia<br>subjects affected / exposed<br>occurrences (all)      | Additional description: Ventricular hypokinesia<br>0 / 20 (0.00%)<br>0      | 0 / 22 (0.00%)<br>0 |  |
| Ventricular tachycardia<br>subjects affected / exposed<br>occurrences (all)      | Additional description: Ventricular tachycardia<br>2 / 20 (10.00%)<br>2     | 1 / 22 (4.55%)<br>1 |  |
| Nervous system disorders<br>Anticholinergic syndrome                             | Additional description: Anticholinergic syndrome                            |                     |  |

|                             |   |                |  |
|-----------------------------|---|----------------|--|
| subjects affected / exposed | 0 / 20 (0.00%)                                    | 0 / 22 (0.00%) |  |
| occurrences (all)           | 0   | 0              |  |
| Balance disorder            | Additional description: Balance disorder          |                |  |
| subjects affected / exposed | 0 / 20 (0.00%)                                    | 0 / 22 (0.00%) |  |
| occurrences (all)           | 0   | 0              |  |
| Brain oedema                | Additional description: Brain oedema              |                |  |
| subjects affected / exposed | 0 / 20 (0.00%)                                    | 0 / 22 (0.00%) |  |
| occurrences (all)           | 0   | 0              |  |
| Carotid artery stenosis     | Additional description: Carotid artery stenosis   |                |  |
| subjects affected / exposed | 0 / 20 (0.00%)                                    | 0 / 22 (0.00%) |  |
| occurrences (all)           | 0   | 0              |  |
| Cerebral infarction         | Additional description: Cerebral infarction       |                |  |
| subjects affected / exposed | 0 / 20 (0.00%)                                    | 0 / 22 (0.00%) |  |
| occurrences (all)           | 0   | 0              |  |
| Disturbance in attention    | Additional description: Disturbance in attention  |                |  |
| subjects affected / exposed | 0 / 20 (0.00%)                                    | 0 / 22 (0.00%) |  |
| occurrences (all)           | 0   | 0              |  |
| Headache                    | Additional description: Headache                  |                |  |
| subjects affected / exposed | 0 / 20 (0.00%)                                    | 0 / 22 (0.00%) |  |
| occurrences (all)           | 0   | 0              |  |
| Hemiparesis                 | Additional description: Hemiparesis               |                |  |
| subjects affected / exposed | 0 / 20 (0.00%)                                    | 0 / 22 (0.00%) |  |
| occurrences (all)           | 0   | 0              |  |
| IIIrd nerve paralysis       | Additional description: IIIrd nerve paralysis     |                |  |
| subjects affected / exposed | 0 / 20 (0.00%)                                    | 0 / 22 (0.00%) |  |
| occurrences (all)           | 0   | 0              |  |
| Peripheral nerve lesion     | Additional description: Peripheral nerve lesion   |                |  |
| subjects affected / exposed | 0 / 20 (0.00%)                                    | 0 / 22 (0.00%) |  |
| occurrences (all)           | 0   | 0              |  |
| Peripheral nerve paresis    | Additional description: Peripheral nerve paresis  |                |  |
| subjects affected / exposed | 1 / 20 (5.00%)                                    | 0 / 22 (0.00%) |  |
| occurrences (all)           | 1   | 0              |  |
| Psychomotor hyperactivity   | Additional description: Psychomotor hyperactivity |                |  |
| subjects affected / exposed | 1 / 20 (5.00%)                                    | 0 / 22 (0.00%) |  |
| occurrences (all)           | 1   | 0              |  |
| Seizure                     | Additional description: Seizure                   |                |  |

|  |  |                 |  |
|--|--|-----------------|--|
| subjects affected / exposed            | 0 / 20 (0.00%)   | 1 / 22 (4.55%)  |  |
| occurrences (all)                      | 0  | 1               |  |
| Syncope                                | Additional description: Syncope                                |                 |  |
| subjects affected / exposed            | 0 / 20 (0.00%)   | 0 / 22 (0.00%)  |  |
| occurrences (all)                      | 0  | 0               |  |
| Tremor                                 | Additional description: Tremor                                 |                 |  |
| subjects affected / exposed            | 0 / 20 (0.00%)   | 0 / 22 (0.00%)  |  |
| occurrences (all)                      | 0  | 0               |  |
| Blood and lymphatic system disorders   |  |                 |  |
| Anaemia                                | Additional description: Anaemia                                |                 |  |
| subjects affected / exposed            | 3 / 20 (15.00%)  | 6 / 22 (27.27%) |  |
| occurrences (all)                      | 3  | 6               |  |
| Coagulation factor deficiency          | Additional description: Coagulation factor deficiency          |                 |  |
| subjects affected / exposed            | 0 / 20 (0.00%)   | 0 / 22 (0.00%)  |  |
| occurrences (all)                      | 0  | 0               |  |
| Coagulopathy                           | Additional description: Coagulopathy                           |                 |  |
| subjects affected / exposed            | 1 / 20 (5.00%)   | 2 / 22 (9.09%)  |  |
| occurrences (all)                      | 1  | 2               |  |
| Disseminated intravascular coagulation | Additional description: Disseminated intravascular coagulation |                 |  |
| subjects affected / exposed            | 2 / 20 (10.00%)  | 1 / 22 (4.55%)  |  |
| occurrences (all)                      | 2  | 1               |  |
| Erythropenia                           | Additional description: Erythropenia                           |                 |  |
| subjects affected / exposed            | 0 / 20 (0.00%)   | 1 / 22 (4.55%)  |  |
| occurrences (all)                      | 0  | 1               |  |
| Haemorrhagic anaemia                   | Additional description: Haemorrhagic anaemia                   |                 |  |
| subjects affected / exposed            | 1 / 20 (5.00%)   | 0 / 22 (0.00%)  |  |
| occurrences (all)                      | 1  | 0               |  |
| Heparin-induced thrombocytopenia       | Additional description: Heparin-induced thrombocytopenia       |                 |  |
| subjects affected / exposed            | 0 / 20 (0.00%)   | 1 / 22 (4.55%)  |  |
| occurrences (all)                      | 0  | 1               |  |
| Leukocytosis                           | Additional description: Leukocytosis                           |                 |  |
| subjects affected / exposed            | 0 / 20 (0.00%)   | 0 / 22 (0.00%)  |  |
| occurrences (all)                      | 0  | 0               |  |
| Thrombocytopenia                       | Additional description: Thrombocytopenia                       |                 |  |



|  |  |                     |  |
|--|--|---------------------|--|
| subjects affected / exposed<br>occurrences (all) | 0 / 20 (0.00%)<br>0                          | 2 / 22 (9.09%)<br>2 |  |
| Ear and labyrinth disorders                      |  |                     |  |
| Hypoacusis                                       | Additional description: Hypoacusis           |                     |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 20 (0.00%)<br>0                          | 0 / 22 (0.00%)<br>0 |  |
| Eye disorders                                    |  |                     |  |
| Gaze palsy                                       | Additional description: Gaze palsy           |                     |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 20 (0.00%)<br>0                          | 0 / 22 (0.00%)<br>0 |  |
| Pupils unequal                                   | Additional description: Pupils unequal       |                     |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 20 (0.00%)<br>0                          | 0 / 22 (0.00%)<br>0 |  |
| Visual impairment                                | Additional description: Visual impairment    |                     |  |
| subjects affected / exposed<br>occurrences (all) | 1 / 20 (5.00%)<br>1                          | 0 / 22 (0.00%)<br>0 |  |
| Gastrointestinal disorders                       |  |                     |  |
| Abdominal pain                                   | Additional description: Abdominal pain       |                     |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 20 (0.00%)<br>0                          | 1 / 22 (4.55%)<br>1 |  |
| Abdominal pain upper                             | Additional description: Abdominal pain upper |                     |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 20 (0.00%)<br>0                          | 0 / 22 (0.00%)<br>0 |  |
| Anal incontinence                                | Additional description: Anal incontinence    |                     |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 20 (0.00%)<br>0                          | 1 / 22 (4.55%)<br>1 |  |
| Constipation                                     | Additional description: Constipation         |                     |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 20 (0.00%)<br>0                          | 0 / 22 (0.00%)<br>0 |  |
| Diarrhoea  | Additional description: Diarrhoea            |                     |  |
| subjects affected / exposed<br>occurrences (all) | 1 / 20 (5.00%)<br>1                          | 2 / 22 (9.09%)<br>2 |  |
| Duodenal ulcer                                   | Additional description: Duodenal ulcer       |                     |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 20 (0.00%)<br>0                          | 1 / 22 (4.55%)<br>1 |  |
| Dysphagia  | Additional description: Dysphagia            |                     |  |

|  |  |                |  |
|--|--|----------------|--|
| subjects affected / exposed            | 0 / 20 (0.00%)                                       | 0 / 22 (0.00%) |  |
| occurrences (all)                      | 0  | 0              |  |
| Flatulence                             | Additional description: Flatulence                   |                |  |
| subjects affected / exposed            | 0 / 20 (0.00%)                                       | 0 / 22 (0.00%) |  |
| occurrences (all)                      | 0  | 0              |  |
| Gastritis                              | Additional description: Gastritis                    |                |  |
| subjects affected / exposed            | 1 / 20 (5.00%)                                       | 0 / 22 (0.00%) |  |
| occurrences (all)                      | 1  | 0              |  |
| Gastrointestinal haemorrhage           | Additional description: Gastrointestinal haemorrhage |                |  |
| subjects affected / exposed            | 0 / 20 (0.00%)                                       | 0 / 22 (0.00%) |  |
| occurrences (all)                      | 0  | 0              |  |
| Large intestinal ulcer                 | Additional description: Large intestinal ulcer       |                |  |
| subjects affected / exposed            | 0 / 20 (0.00%)                                       | 1 / 22 (4.55%) |  |
| occurrences (all)                      | 0  | 1              |  |
| Nausea                                 | Additional description: Nausea                       |                |  |
| subjects affected / exposed            | 2 / 20 (10.00%)                                      | 2 / 22 (9.09%) |  |
| occurrences (all)                      | 2  | 2              |  |
| Pancreatitis                           | Additional description: Pancreatitis                 |                |  |
| subjects affected / exposed            | 0 / 20 (0.00%)                                       | 0 / 22 (0.00%) |  |
| occurrences (all)                      | 0  | 0              |  |
| Subileus                               | Additional description: Subileus                     |                |  |
| subjects affected / exposed            | 0 / 20 (0.00%)                                       | 1 / 22 (4.55%) |  |
| occurrences (all)                      | 0  | 1              |  |
| Vomiting                               | Additional description: Vomiting                     |                |  |
| subjects affected / exposed            | 1 / 20 (5.00%)                                       | 0 / 22 (0.00%) |  |
| occurrences (all)                      | 1  | 0              |  |
| Skin and subcutaneous tissue disorders |  |                |  |
| Decubitus ulcer                        | Additional description: Decubitus ulcer              |                |  |
| subjects affected / exposed            | 0 / 20 (0.00%)                                       | 0 / 22 (0.00%) |  |
| occurrences (all)                      | 0  | 0              |  |
| Erythema                               | Additional description: Erythema                     |                |  |
| subjects affected / exposed            | 1 / 20 (5.00%)                                       | 0 / 22 (0.00%) |  |
| occurrences (all)                      | 1  | 0              |  |
| Rash generalised                       | Additional description: Rash generalised             |                |  |
| subjects affected / exposed            | 0 / 20 (0.00%)                                       | 1 / 22 (4.55%) |  |
| occurrences (all)                      | 0  | 1              |  |

|  |  |                 |  |
|--|--|-----------------|--|
| Subcutaneous emphysema<br>subjects affected / exposed<br>occurrences (all) | Additional description: Subcutaneous emphysema |                 |  |
|  | 0 / 20 (0.00%)                                 | 0 / 22 (0.00%)  |  |
|  | 0  | 0               |  |
| Renal and urinary disorders  | Additional description: Acute kidney injury    |                 |  |
|  | 5 / 20 (25.00%)                                | 6 / 22 (27.27%) |  |
|  | 5  | 6               |  |
|  | Additional description: Acute prerenal failure |                 |  |
|  | 1 / 20 (5.00%)                                 | 0 / 22 (0.00%)  |  |
|  | 1  | 0               |  |
|  | Additional description: Dysuria                |                 |  |
|  | 0 / 20 (0.00%)                                 | 0 / 22 (0.00%)  |  |
|  | 0  | 0               |  |
|  | Additional description: Haematuria             |                 |  |
|  | 1 / 20 (5.00%)                                 | 0 / 22 (0.00%)  |  |
|  | 1  | 0               |  |
|  | Additional description: Oliguria               |                 |  |
|  | 0 / 20 (0.00%)                                 | 2 / 22 (9.09%)  |  |
|  | 0  | 2               |  |
|  | Additional description: Renal failure          |                 |  |
|  | 0 / 20 (0.00%)                                 | 0 / 22 (0.00%)  |  |
|  | 0  | 0               |  |
|  | Additional description: Urinary incontinence   |                 |  |
|  | 0 / 20 (0.00%)                                 | 0 / 22 (0.00%)  |  |
|  | 0  | 0               |  |
|  | Additional description: Urinary retention      |                 |  |
|  | 1 / 20 (5.00%)                                 | 1 / 22 (4.55%)  |  |
|  | 1  | 1               |  |
| Musculoskeletal and connective tissue disorders                            | Additional description: Back pain              |                 |  |
|  | 0 / 20 (0.00%)                                 | 1 / 22 (4.55%)  |  |
|  | 0  | 1               |  |
|  | Additional description: Muscle spasms          |                 |  |
|  | 0 / 20 (0.00%)                                 | 0 / 22 (0.00%)  |  |
|  | 0  | 0               |  |
|  | Additional description: Muscular weakness      |                 |  |

|                             |  |                |  |
|-----------------------------|--|----------------|--|
| subjects affected / exposed | 1 / 20 (5.00%)                                     | 0 / 22 (0.00%) |  |
| occurrences (all)           | 1  | 0              |  |
| Musculoskeletal chest pain  | Additional description: Musculoskeletal chest pain |                |  |
| subjects affected / exposed | 0 / 20 (0.00%)                                     | 1 / 22 (4.55%) |  |
| occurrences (all)           | 0  | 2              |  |
| Musculoskeletal pain        | Additional description: Musculoskeletal pain       |                |  |
| subjects affected / exposed | 0 / 20 (0.00%)                                     | 0 / 22 (0.00%) |  |
| occurrences (all)           | 0  | 0              |  |
| Infections and infestations |  |                |  |
| Bacterial disease carrier   | Additional description: Bacterial disease carrier  |                |  |
| subjects affected / exposed | 0 / 20 (0.00%)                                     | 0 / 22 (0.00%) |  |
| occurrences (all)           | 0  | 0              |  |
| Bronchitis                  | Additional description: Bronchitis                 |                |  |
| subjects affected / exposed | 1 / 20 (5.00%)                                     | 1 / 22 (4.55%) |  |
| occurrences (all)           | 1  | 1              |  |
| Clostridial infection       | Additional description: Clostridial infection      |                |  |
| subjects affected / exposed | 0 / 20 (0.00%)                                     | 0 / 22 (0.00%) |  |
| occurrences (all)           | 0  | 0              |  |
| Cystitis                    | Additional description: Cystitis                   |                |  |
| subjects affected / exposed | 0 / 20 (0.00%)                                     | 1 / 22 (4.55%) |  |
| occurrences (all)           | 0  | 1              |  |
| Device related infection    | Additional description: Device related infection   |                |  |
| subjects affected / exposed | 0 / 20 (0.00%)                                     | 0 / 22 (0.00%) |  |
| occurrences (all)           | 0  | 0              |  |
| Enterococcal infection      | Additional description: Enterococcal infection     |                |  |
| subjects affected / exposed | 0 / 20 (0.00%)                                     | 0 / 22 (0.00%) |  |
| occurrences (all)           | 0  | 0              |  |
| Infection                   | Additional description: Infection                  |                |  |
| subjects affected / exposed | 0 / 20 (0.00%)                                     | 1 / 22 (4.55%) |  |
| occurrences (all)           | 0  | 1              |  |
| Infectious disease carrier  | Additional description: Infectious disease carrier |                |  |
| subjects affected / exposed | 0 / 20 (0.00%)                                     | 0 / 22 (0.00%) |  |
| occurrences (all)           | 0  | 0              |  |
| Nasopharyngitis             | Additional description: Nasopharyngitis            |                |  |
| subjects affected / exposed | 0 / 20 (0.00%)                                     | 0 / 22 (0.00%) |  |
| occurrences (all)           | 0  | 0              |  |

|   |   |                |  |
|---|---|----------------|--|
| <p>Nosocomial infection</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pneumonia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pneumonia escherichia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pneumonia klebsiella</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Tracheobronchitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Urinary tract infection</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | Additional description: Nosocomial infection    |                |  |
|   | 0 / 20 (0.00%)                                  | 0 / 22 (0.00%) |  |
|   | 0   | 0              |  |
|   | Additional description: Pneumonia               |                |  |
|   | 1 / 20 (5.00%)                                  | 2 / 22 (9.09%) |  |
|   | 1   | 2              |  |
|   | Additional description: Pneumonia escherichia   |                |  |
|   | 1 / 20 (5.00%)                                  | 0 / 22 (0.00%) |  |
|   | 1   | 0              |  |
|   | Additional description: Pneumonia klebsiella    |                |  |
|   | 1 / 20 (5.00%)                                  | 0 / 22 (0.00%) |  |
|   | 1   | 0              |  |
|   | Additional description: Tracheobronchitis       |                |  |
|   | 1 / 20 (5.00%)                                  | 0 / 22 (0.00%) |  |
|   | 1   | 0              |  |
|   | Additional description: Urinary tract infection |                |  |
|   | 0 / 20 (0.00%)                                  | 1 / 22 (4.55%) |  |
|   | 0   | 1              |  |
| <p>Metabolism and nutrition disorders</p> <p>Fluid retention</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Gout</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Hyperkalaemia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Hypernatraemia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Hypoalbuminaemia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Hyponatraemia</p>  |   |                |  |
|   | Additional description: Fluid retention         |                |  |
|   | 0 / 20 (0.00%)                                  | 0 / 22 (0.00%) |  |
|   | 0   | 0              |  |
|   | Additional description: Gout                    |                |  |
|   | 0 / 20 (0.00%)                                  | 0 / 22 (0.00%) |  |
|   | 0   | 0              |  |
|   | Additional description: Hyperkalaemia           |                |  |
|   | 0 / 20 (0.00%)                                  | 0 / 22 (0.00%) |  |
|   | 0   | 0              |  |
|   | Additional description: Hypernatraemia          |                |  |
|   | 0 / 20 (0.00%)                                  | 0 / 22 (0.00%) |  |
|   | 0   | 0              |  |
|   | Additional description: Hypoalbuminaemia        |                |  |
|   | 0 / 20 (0.00%)                                  | 1 / 22 (4.55%) |  |
|   | 0   | 1              |  |
|   | Additional description: Hyponatraemia           |                |  |

|                             |  |                |  |
|-----------------------------|--|----------------|--|
| subjects affected / exposed | 1 / 20 (5.00%)                             | 1 / 22 (4.55%) |  |
| occurrences (all)           | 1  | 1              |  |
| Hypovolaemia                | Additional description: Hypovolaemia       |                |  |
| subjects affected / exposed | 0 / 20 (0.00%)                             | 1 / 22 (4.55%) |  |
| occurrences (all)           | 0  | 1              |  |
| Metabolic acidosis          | Additional description: Metabolic acidosis |                |  |
| subjects affected / exposed | 0 / 20 (0.00%)                             | 2 / 22 (9.09%) |  |
| occurrences (all)           | 0  | 2              |  |
| Protein deficiency          | Additional description: Protein deficiency |                |  |
| subjects affected / exposed | 0 / 20 (0.00%)                             | 0 / 22 (0.00%) |  |
| occurrences (all)           | 0  | 0              |  |

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported