Clinical trial results:
A multi-center, non-blinded, randomized cross-over study to compare the acute tolerability and pharmacokinetics of BAYQ6256 (iloprost; Ventavis) inhalation using the I-Neb nebulizer and the FOX nebulizer in subjects with pulmonary arterial hypertension

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

Summary

EudraCT number	2013-002783-12
Trial protocol	DE AT
Global end of trial date	29 September 2017

Results information

Result version number	v1 (current)
This version publication date	21 July 2016
First version publication date	21 July 2016

Trial information

Trial identification

Sponsor protocol code	BAYQ006256/16483

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02032836
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bayer AG
Sponsor organisation address	Kaiser-Wilhelm-Allee, D-51368 Leverkusen, Germany,
Public contact	Therapeutic Area Head, Bayer AG, clinical-trials-contact@bayer.com
Scientific contact	Therapeutic Area Head, Bayer AG, clinical-trials-contact@bayer.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	29 September 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 September 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to assess, in subjects with pulmonary arterial hypertension, the acute tolerability of 5 microgram (mcg) iloprost inhaled as Ventavis 20 microgram per milliliter (mcg/mL) solution through a FOX nebulizer* with that of 5 mcg iloprost inhaled as Ventavis 10 mcg/mL solution through the I-Neb nebulizer.
* FOX or FOX Bavent nebuliser used for Ventavis® meanwhile carries the product name Breelib™

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the International Conference on Harmonization guideline E6: Good Clinical Practice. Before entering the study, the informed consent form was read by and explained to all subjects. Participating subjects signed informed consent for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy:

Individual therapy of underlying pulmonary arterial hypertension (PAH) and other comorbidities. Inhalative therapy with 5 mcg iloprost using the I-Neb nebulizer until Day 2 (before first cross-over dosing).

Evidence for comparator: -

Actual start date of recruitment	10 March 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Ethical reason
Long term follow-up duration	39 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 1
Country: Number of subjects enrolled	Germany: 27
Worldwide total number of subjects	28
EEA total number of subjects	28

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0

Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	18
From 65 to 84 years	10
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at five study centers in Germany and one in Austria in healthy male and female subjects between 10 March 2014 (first subject first visit) and 27 July 2017 (last subject last visit for study part 4).

Pre-assignment

Screening details:

Overall, 28 subjects were screened and randomized into the study, of which 1 subject never received study drug. Of 27 subjects, 26 received iloprost using I-Neb nebulizer and 27 received iloprost using FOX nebulizer in a cross-over fashion during Part 2 and Part 3 of the study. Of these subjects, 25 entered Part 4 and were included in the analysis.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	I-Neb – FOX

Arm description:

Part 1: Subjects received single inhalation of 1.25 mcg iloprost using 10 mcg/ml iloprost solution (Ventavis 10) and then 2.5 mcg iloprost using Ventavis 10, both using the FOX nebulizer on Day 1. Part 2: On Day 2, subjects received single inhalation of 5 mcg iloprost using Ventavis 10 with the I-Neb nebulizer; followed by single inhalation of 5 mcg iloprost using 20 mcg/ml iloprost solution (Ventavis 20) with the FOX nebulizer in a cross-over fashion. A washout period of at least 2 hours was maintained between treatments in Part 1 and Part 2. Part 3: Continued on Day 2, and through until Day 30, subjects received multiple inhalations (approximately 6 to 9 inhalations per day) of 5 mcg iloprost using Ventavis 10 with the I-Neb nebulizer for 2 weeks; followed by multiple inhalations (approximately 6 to 9 inhalations per day) of 5 mcg iloprost using Ventavis 20 with the FOX nebulizer for 2 weeks in a cross-over fashion.

Arm type	Experimental
Investigational medicinal product name	Iloprost 1.25 mcg via Iloprost 10 mcg/mL with FOX nebulizer (Experimental)
Investigational medicinal product code	BAYQ6256
Other name	Ventavis
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Subjects received single inhalation of 1.25 mcg iloprost using 10 mcg/ml iloprost solution (Ventavis 10) with the FOX nebulizer in Part 1.

Investigational medicinal product name	Iloprost 2.5 mcg via Iloprost 10 mcg/mL with FOX nebulizer (Experimental)
Investigational medicinal product code	BAYQ6256
Other name	Ventavis
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Subjects received single inhalation of 2.5 mcg iloprost using Ventavis 10 with the FOX nebulizer in Part 1.

Investigational medicinal product name	Iloprost 5 mcg via Iloprost 10 mcg/mL with I-neb nebulizer (Active comparator)
Investigational medicinal product code	BAYQ6256

	Ventavis
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Subjects received single inhalation of 5 mcg iloprost using Ventavis 10 with the I-Neb nebulizer in Part 2.

Investigational medicinal product name	Iloprost 5 mcg via Iloprost 20 mcg/mL with FOX nebulizer (Experimental)
Investigational medicinal product code	BAYQ6256
Other name	Ventavis
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Subjects received single inhalation of 5 mcg iloprost using 20 mcg/ml iloprost solution (Ventavis 20) with the FOX nebulizer in Part 2.

Investigational medicinal product name	Iloprost 5 mcg via Iloprost 10 mcg/mL with I-Neb nebulizer (Active comparator)
Investigational medicinal product code	BAYQ6256
Other name	Ventavis
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Subjects received multiple inhalations (approximately 6 to 9 inhalations per day) of 5 mcg iloprost using Ventavis 10 with the I-Neb nebulizer for 2 weeks in Part 3.

Investigational medicinal product name	Iloprost 5 mcg via Iloprost 20 mcg/mL with FOX nebulizer (Experimental)
Investigational medicinal product code	BAYQ6256
Other name	Ventavis
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Subjects received multiple inhalations (approximately 6 to 9 inhalations per day) of 5 mcg iloprost using Ventavis 20 with the FOX nebulizer for 2 weeks in Part 3.

Arm title	FOX - I-Neb

Arm description:

Part 1: Subjects received single inhalation of 1.25 mcg iloprost using 10 mcg/ml iloprost solution (Ventavis 10) and then 2.5 mcg iloprost using Ventavis 10, both using the FOX nebulizer on Day 1. Part 2: On Day 2, subjects received single inhalation of 5 mcg iloprost using 20 mcg/ml iloprost solution (Ventavis 20) with the FOX nebulizer; followed by single inhalation of 5 mcg iloprost using Ventavis 10 with the I-Neb nebulizer in a cross-over fashion. A wash-out period of at least 2 hours was maintained between treatments in Part 1 and Part 2. Part 3: Continued on Day 2, and through until Day 30, subjects received multiple inhalations (approximately 6 to 9 inhalations per day) of 5 mcg iloprost using Ventavis 20 with the FOX nebulizer for 2 weeks; followed by multiple inhalations (approximately 6 to 9 inhalations per day) of 5 mcg iloprost using Ventavis 10 with the I-Neb nebulizer for 2 weeks in a cross-over fashion.

Arm type	Experimental
Investigational medicinal product name	Iloprost 1.25 mcg via Iloprost 10 mcg/mL with FOX nebulizer (Experimental)
Investigational medicinal product code	BAYQ6256
Other name	Ventavis
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Subjects received single inhalation of 1.25 mcg iloprost using 10 mcg/ml iloprost solution (Ventavis 10) with the FOX nebulizer in Part 1.

Investigational medicinal product name	Iloprost 2.5 mcg via Iloprost 10 mcg/mL with FOX nebulizer (Experimental)
Investigational medicinal product code	BAYQ6256
Other name	Ventavis
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Subjects received single inhalation of 2.5 mcg iloprost using Ventavis 10 with the FOX nebulizer in Part 1.

Investigational medicinal product name	Iloprost 5 mcg via Iloprost 10 mcg/mL with I-neb nebulizer (Active comparator)
Investigational medicinal product code	BAYQ6256
Other name	Ventavis
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Subjects received single inhalation of 5 mcg iloprost using Ventavis 10 with the I-Neb nebulizer in Part 2.

Investigational medicinal product name	Iloprost 5 mcg via Iloprost 20 mcg/mL with FOX nebulizer (Experimental)
Investigational medicinal product code	BAYQ6256
Other name	Ventavis
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Subjects received single inhalation of 5 mcg iloprost using 20 mcg/ml iloprost solution (Ventavis 20) with the FOX nebulizer in Part 2.

Investigational medicinal product name	Iloprost 5 mcg via Iloprost 10 mcg/mL with I-Neb nebulizer (Active comparator)
Investigational medicinal product code	BAYQ6256
Other name	Ventavis
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Subjects received multiple inhalations (approximately 6 to 9 inhalations per day) of 5 mcg iloprost using Ventavis 10 with the I-Neb nebulizer for 2 weeks in Part 3.

Investigational medicinal product name	Iloprost 5 mcg via Iloprost 20 mcg/mL with FOX nebulizer (Experimental)
Investigational medicinal product code	BAYQ6256
Other name	Ventavis
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Subjects received multiple inhalations (approximately 6 to 9 inhalations per day) of 5 mcg iloprost using Ventavis 20 with the FOX nebulizer for 2 weeks in Part 3.

Number of subjects in period 1[1]	I-Neb – FOX	FOX - I-Neb
Started	13	14
Completed	13	13
Not completed	0	1
Non-compliance with study drug	-	1

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: Not all the enrolled subjects were treated with study drugs. As baseline only included treated subjects, the worldwide number enrolled in the trial differs with the number of subjects reported in the baseline period.

Baseline characteristics

Reporting groups	
Reporting group title	I-Neb – FOX

Reporting group description:

Part 1: Subjects received single inhalation of 1.25 mcg iloprost using 10 mcg/ml iloprost solution (Ventavis 10) and then 2.5 mcg iloprost using Ventavis 10, both using the FOX nebulizer on Day 1. Part 2: On Day 2, subjects received single inhalation of 5 mcg iloprost using Ventavis 10 with the I-Neb nebulizer; followed by single inhalation of 5 mcg iloprost using 20 mcg/ml iloprost solution (Ventavis 20) with the FOX nebulizer in a cross-over fashion. A washout period of at least 2 hours was maintained between treatments in Part 1 and Part 2. Part 3: Continued on Day 2, and through until Day 30, subjects received multiple inhalations (approximately 6 to 9 inhalations per day) of 5 mcg iloprost using Ventavis 10 with the I-Neb nebulizer for 2 weeks; followed by multiple inhalations (approximately 6 to 9 inhalations per day) of 5 mcg iloprost using Ventavis 20 with the FOX nebulizer for 2 weeks in a cross-over fashion.

Reporting group title	FOX - I-Neb

Reporting group description:

Part 1: Subjects received single inhalation of 1.25 mcg iloprost using 10 mcg/ml iloprost solution (Ventavis 10) and then 2.5 mcg iloprost using Ventavis 10, both using the FOX nebulizer on Day 1. Part 2: On Day 2, subjects received single inhalation of 5 mcg iloprost using 20 mcg/ml iloprost solution (Ventavis 20) with the FOX nebulizer; followed by single inhalation of 5 mcg iloprost using Ventavis 10 with the I-Neb nebulizer in a cross-over fashion. A wash-out period of at least 2 hours was maintained between treatments in Part 1 and Part 2. Part 3: Continued on Day 2, and through until Day 30, subjects received multiple inhalations (approximately 6 to 9 inhalations per day) of 5 mcg iloprost using Ventavis 20 with the FOX nebulizer for 2 weeks; followed by multiple inhalations (approximately 6 to 9 inhalations per day) of 5 mcg iloprost using Ventavis 10 with the I-Neb nebulizer for 2 weeks in a cross-over fashion.

Reporting group values	I-Neb – FOX	FOX - I-Neb	Total
Number of subjects	13	14	27
Age Categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	59.8	56.4	
standard deviation	± 17.1	± 14.5	-
Gender Categorical Units: Subjects			
Female	10	11	21
Male	3	3	6

End points

End points reporting groups

Reporting group title	I-Neb – FOX

Reporting group description:

Part 1: Subjects received single inhalation of 1.25 mcg iloprost using 10 mcg/ml iloprost solution (Ventavis 10) and then 2.5 mcg iloprost using Ventavis 10, both using the FOX nebulizer on Day 1. Part 2: On Day 2, subjects received single inhalation of 5 mcg iloprost using Ventavis 10 with the I-Neb nebulizer; followed by single inhalation of 5 mcg iloprost using 20 mcg/ml iloprost solution (Ventavis 20) with the FOX nebulizer in a cross-over fashion. A washout period of at least 2 hours was maintained between treatments in Part 1 and Part 2. Part 3: Continued on Day 2, and through until Day 30, subjects received multiple inhalations (approximately 6 to 9 inhalations per day) of 5 mcg iloprost using Ventavis 10 with the I-Neb nebulizer for 2 weeks; followed by multiple inhalations (approximately 6 to 9 inhalations per day) of 5 mcg iloprost using Ventavis 20 with the FOX nebulizer for 2 weeks in a cross-over fashion.

Reporting group title	FOX - I-Neb

Reporting group description:

Part 1: Subjects received single inhalation of 1.25 mcg iloprost using 10 mcg/ml iloprost solution (Ventavis 10) and then 2.5 mcg iloprost using Ventavis 10, both using the FOX nebulizer on Day 1. Part 2: On Day 2, subjects received single inhalation of 5 mcg iloprost using 20 mcg/ml iloprost solution (Ventavis 20) with the FOX nebulizer; followed by single inhalation of 5 mcg iloprost using Ventavis 10 with the I-Neb nebulizer in a cross-over fashion. A wash-out period of at least 2 hours was maintained between treatments in Part 1 and Part 2. Part 3: Continued on Day 2, and through until Day 30, subjects received multiple inhalations (approximately 6 to 9 inhalations per day) of 5 mcg iloprost using Ventavis 20 with the FOX nebulizer for 2 weeks; followed by multiple inhalations (approximately 6 to 9 inhalations per day) of 5 mcg iloprost using Ventavis 10 with the I-Neb nebulizer for 2 weeks in a cross-over fashion.

Subject analysis set title	Safety Analysis Set (SAF)
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects who received any treatment with the study medication (with the I-Neb or the FOX nebulizer, or with both) were included.

Subject analysis set title	Hemodynamic Set (HDS-1)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All subjects who were treated in both treatment periods at Visit 2 (Part 2), for whom no major deviations from protocol were recorded, who had any quantifiable iloprost plasma concentrations in both periods and for whom pre-inhalation blood-pressure and heart rate measurement and at least one post-inhalation blood-pressure and heart rate measurement were available for both periods were included.

Subject analysis set title	Hemodynamic Set (HDS-2)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All subjects valid for HDS-1 and who had no shift in basic heart rhythm during Visit 2 (Part 2), and who did not have a heart rhythm that was primarily driven by a pacemaker, were included.

Subject analysis set title	Pharmacokinetic Set for dose-linearity analysis (PKS-1)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All subjects who completed Visit 1 (Part 1) and who had two valid pharmacokinetic (PK) profiles (as judged by the responsible PK expert) using the FOX nebulizer (2.5 mcg in Part 1 and 5 mcg in Part 2) were included.

Subject analysis set title	Pharmacokinetic Set for Visit 2 (PKS-2)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All subjects who completed Visit 2 (Part 2) and who had valid pharmacokinetic profiles In both treatment periods were included.

Subject analysis set title	Iloprost 5 mcg, I-Neb nebulizer – HDS-1
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received single inhalation of 5 mcg iloprost using Ventavis 10 with the I-Neb nebulizer in Part 2.

Subject analysis set title	Iloprost 5 mcg, FOX nebulizer – HDS-1
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received single inhalation of 5 mcg iloprost using 20 mcg/ml iloprost solution (Ventavis 20) with the FOX nebulizer in Part 2.

Subject analysis set title	Iloprost 2.5 mcg, FOX nebulizer – PKS-1
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received single inhalation of 2.5 mcg iloprost using Ventavis 10 with the FOX nebulizer on Day 1.

Subject analysis set title	Iloprost 5 mcg, FOX nebulizer – PKS-1
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received single inhalation of 5 mcg iloprost using Ventavis 20 with the FOX nebulizer in Part 2.

Subject analysis set title	Iloprost 5 mcg, I-Neb nebulizer – PKS-2
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received single inhalation of 5 mcg iloprost using Ventavis 10 with the I-Neb nebulizer in Part 2.

Subject analysis set title	Iloprost 5 mcg, FOX nebulizer – PKS-2
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received single inhalation of 5 mcg iloprost using Ventavis 20 with the FOX nebulizer in Part 2.

Primary: Percentage of subjects with a meaningful maximum increase (i.e. >=25%) in heart rate and/or a meaningful maximum decrease (i.e. >=20%) in systolic blood pressure within the 30 minutes after the completion of inhalation

End point title	Percentage of subjects with a meaningful maximum increase (i.e. >=25%) in heart rate and/or a meaningful maximum decrease (i.e. >=20%) in systolic blood pressure within the 30 minutes after the completion of inhalation[1]

End point description:

Maximum increase in heart rate between post-inhalation and pre-inhalation measurements within the 30 minutes after inhalation. Relative change (% change) were calculated as ΔHR = 100 * ΔHR / HR pre inhalation. Maximum decrease in systolic blood pressure between post-inhalation and pre-inhalation measurements within the 30 minutes after inhalation. Relative change (% change) were calculated as ΔSBP = 100 * ΔSBP / SBP pre inhalation. Percentage of subjects with relative increase in "all QRS" heart rate > 25% OR relative decrease in systolic blood pressure > 20% were reported.

End point type	Primary

End point timeframe:

Within the 30 minutes after the completion of inhalation

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Iloprost 5 mcg, I-Neb nebulizer – HDS-1	Iloprost 5 mcg, FOX nebulizer – HDS-1		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24[2]	24[3]		
Units: Percentage of subjects				
number (not applicable)	4.2	16.7		

Notes:

[2] - HDS-1

[3] - HDS-1

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute decrease in systolic blood pressure within 30 minutes after end of inhalation

End point title	Absolute decrease in systolic blood pressure within 30 minutes after end of inhalation

End point description:

Systolic blood pressures (SBP) were measured over a two-hour interval after inhalation of iloprost using either the FOX inhaler or in randomized order the I-Neb nebulizer. Changes in the systolic blood pressure as decreases are shown. (i.e., a positive number means a decrease in blood pressure.)

End point type	Secondary

End point timeframe:

Up to 2 hours after start of each inhalation

End point values	Iloprost 5 mcg, I-Neb nebulizer – HDS-1	Iloprost 5 mcg, FOX nebulizer – HDS-1		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24[4]	24[5]		
Units: millimeter of mercury (mmHg)				
arithmetic mean (standard deviation)	10.125 (± 9.1429)	12.7917 (± 9.8289)		

Notes:

[4] - HDS-1

[5] - HDS-1

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute decrease in diastolic blood pressure within 30 minutes after end of inhalation

End point title	Absolute decrease in diastolic blood pressure within 30 minutes after end of inhalation

End point description:

Diastolic blood pressures (DBP) were measured over a two-hour interval after inhalation of iloprost using either the FOX inhaler or in randomized order the I-Neb nebulizer. Changes in the diastolic blood pressure as decreases are shown. (i.e., a positive number means a decrease in blood pressure.)

End point type	Secondary

End point timeframe:

Up to 2 hours after start of each inhalation

End point values	Iloprost 5 mcg, I-Neb nebulizer – HDS-1	Iloprost 5 mcg, FOX nebulizer – HDS-1		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24[6]	24[7]		
Units: mmHg				
arithmetic mean (standard deviation)	9.5833 (± 5.9411)	10.3333 (± 7.8997)		

Notes:

[6] - HDS-1

[7] - HDS-1

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute decrease in mean arterial blood pressure within 30 minutes after end of inhalation

End point title	Absolute decrease in mean arterial blood pressure within 30 minutes after end of inhalation

End point description:

Mean arterial blood pressure was calculated as a linear combination of systolic and diastolic blood pressures. Changes in the mean arterial blood pressure as decreases are shown. (i.e., a positive number means a decrease in blood pressure.)

End point type	Secondary

End point timeframe:

Up to 2 hours after start of each inhalation

End point values	Iloprost 5 mcg, I-Neb nebulizer – HDS-1	Iloprost 5 mcg, FOX nebulizer – HDS-1		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24[8]	24[9]		
Units: mmHg				
arithmetic mean (standard deviation)	8.75 (± 4.9395)	10.1111 (± 8.4308)		

Notes:

[8] - HDS-1

[9] - HDS-1

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute increase in heart rate (all QRS) within 30 minutes after end of inhalation

End point title	Absolute increase in heart rate (all QRS) within 30 minutes after end of inhalation

End point description:

The subjects' heart rate was measured over a two-hour interval after inhalation of iloprost using either the FOX inhaler or in randomized order the I-Neb nebulizer. Changes in the heart rate as increases are shown. (i.e., a positive number means an increase in heart rate.)

End point type	Secondary

End point timeframe:

Up to 2 hours after start of each inhalation

End point values	Iloprost 5 mcg, I-Neb nebulizer – HDS-1	Iloprost 5 mcg, FOX nebulizer – HDS-1		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24[10]	24[11]		
Units: beats/minute				
arithmetic mean (standard deviation)	2.3333 (± 3.9636)	6.5417 (± 4.5871)		

Notes:

[10] - HDS-1

[11] - HDS-1

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute decrease in oxygen saturation within 30 minutes after end of inhalation

End point title	Absolute decrease in oxygen saturation within 30 minutes after end of inhalation

End point description:

During visit 2, peripheral arterial oxygen saturation will be monitored by finger pulse oxymetry (locally available devices).

End point type	Secondary

End point timeframe:

Up to 2 hours after start of each inhalation

End point values	Iloprost 5 mcg, I-Neb nebulizer – HDS-1	Iloprost 5 mcg, FOX nebulizer – HDS-1		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24[12]	24[13]		
Units: percentage of oxygen saturation				
arithmetic mean (standard deviation)	2.2917 (± 3.445)	2.375 (± 1.3772)		

Notes:

[12] - HDS-1

[13] - HDS-1

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the plasma concentration versus time curve from zero to infinity [AUC] of iloprost in plasma

End point title	Area under the plasma concentration versus time curve from zero to infinity [AUC] of iloprost in plasma

End point description:

Area under the concentration versus time curve from zero to infinity after single (first) dose. Geometric mean and percentage geometric coefficient of variation (%CV) were reported.

End point type	Secondary

End point timeframe:

0, 2, 5, 10, 20, 30 and 45 minutes after inhalation on Day 1 and 0, 2, 5, 10, 20, 30, 45 and 60 minutes after inhalation on Day 2

End point values	Iloprost 2.5 mcg, FOX nebulizer – PKS-1	Iloprost 5 mcg, FOX nebulizer – PKS-1	Iloprost 5 mcg, I-Neb nebulizer – PKS-2	Iloprost 5 mcg, FOX nebulizer – PKS-2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	7[14]	8[15]	5[16]	7[17]
Units: ng·h/L				
geometric mean (geometric coefficient of variation)	44.975 (± 11.88)	63.057 (± 42.44)	44.564 (± 27.11)	61.848 (± 45.7)

Notes:

[14] - PKS-1

[15] - PKS-1

[16] - PKS-2

[17] - PKS-2

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The relative bioavailability of iloprost administered through the I-Neb and FOX nebulizers devices was investigated by comparing AUC for each subject in turn. Thereafter, the geometric least-squares mean for these ratios was derived.

Comparison groups	Iloprost 5 mcg, FOX nebulizer – PKS-2 v Iloprost 5 mcg, I-Neb nebulizer – PKS-2
Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Least squares mean
Point estimate	2.3048
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.5053
upper limit	10.513

Secondary: Area under the plasma concentration versus time curve from zero to the last data point [AUC(0-tlast)] of iloprost in plasma

End point title	Area under the plasma concentration versus time curve from zero to the last data point [AUC(0-tlast)] of iloprost in plasma

End point description:

As AUC could be determined reliably only for a minority of subjects, owing to the rapid decrease of plasma concentrations below lower limit of quantification (LLOQ) after the end of inhalation. Therefore, according to the rules set out prospectively, AUC(0–tlast) was used as primary PK arameter instead. Area under the plasma concentration versus time curve from zero to the last data point. Geometric mean and percentage geometric coefficient of variation (%CV) were reported.

End point type	Secondary

End point timeframe:

0, 2, 5, 10, 20, 30 and 45 minutes after inhalation on Day 1 and 0, 2, 5, 10, 20, 30, 45 and 60 minutes after inhalation on Day 2

End point values	Iloprost 2.5 mcg, FOX nebulizer – PKS-1	Iloprost 5 mcg, FOX nebulizer – PKS-1	Iloprost 5 mcg, I-Neb nebulizer – PKS-2	Iloprost 5 mcg, FOX nebulizer – PKS-2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	24[18]	24[19]	24[20]	24[21]
Units: ng·h/L				
geometric mean (geometric coefficient of variation)	23.487 (± 76.51)	46.6096 (± 77.84)	29.0543 (± 67.4)	40.9102 (± 81.45)

Notes:

[18] - PKS-1

[19] - PKS-1

[20] - PKS-2

[21] - PKS-2

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The relative bioavailability of iloprost administered through the I-Neb and FOX nebulizers devices was investigated by comparing AUC(0–tlast) for each subject in turn. Thereafter, the geometric least-squares mean for these ratios was derived.

Comparison groups	Iloprost 5 mcg, FOX nebulizer – PKS-2 v Iloprost 5 mcg, I-Neb nebulizer – PKS-2
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Least squares mean
Point estimate	1.4239
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.0441
upper limit	1.9417

Secondary: Half-life associated with the terminal slope [t1/2] of iloprost in plasma

End point title	Half-life associated with the terminal slope [t1/2] of iloprost in plasma

End point description:

Half-life associated with the terminal slope. Geometric mean and percentage geometric coefficient of variation (%CV) were reported.

End point type	Secondary

End point timeframe:

0, 2, 5, 10, 20, 30 and 45 minutes after inhalation on Day 1 and 0, 2, 5, 10, 20, 30, 45 and 60 minutes after inhalation on Day 2

End point values	Iloprost 2.5 mcg, FOX nebulizer – PKS-1	Iloprost 5 mcg, FOX nebulizer – PKS-1	Iloprost 5 mcg, I-Neb nebulizer – PKS-2	Iloprost 5 mcg, FOX nebulizer – PKS-2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11[22]	10[23]	5[24]	9[25]
Units: hour				
geometric mean (geometric coefficient of variation)	0.2041 (± 27.32)	0.1746 (± 23.93)	0.1482 (± 27.73)	0.1697 (± 23.48)

Notes:

[22] - PKS-1

[23] - PKS-1

[24] - PKS-2

[25] - PKS-2

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the plasma concentration versus time curve from start to end of inhalation [AUC(0-t1)] of iloprost in plasma

End point title	Area under the plasma concentration versus time curve from start to end of inhalation [AUC(0-t1)] of iloprost in plasma

End point description:

Area under the plasma concentration versus time curve from start to end of inhalation. Geometric mean and percentage geometric coefficient of variation (%CV) were reported.

End point type	Secondary

End point timeframe:

0, 2, 5, 10, 20, 30 and 45 minutes after inhalation on Day 1 and 0, 2, 5, 10, 20, 30, 45 and 60 minutes after inhalation on Day 2

End point values	Iloprost 2.5 mcg, FOX nebulizer – PKS-1	Iloprost 5 mcg, FOX nebulizer – PKS-1	Iloprost 5 mcg, I-Neb nebulizer – PKS-2	Iloprost 5 mcg, FOX nebulizer – PKS-2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	24[26]	24[27]	24[28]	24[29]
Units: ng·h/L				
geometric mean (geometric coefficient	1.1122 (±	1.6375 (±	6.8297 (±	1.4627 (±

of variation)	94.96)	84.77)	66.03)	87.91)

Notes:

[26] - PKS-1

[27] - PKS-1

[28] - PKS-2

[29] - PKS-2

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum observed drug concentration in plasma [Cmax] after single dose administration of iloprost

End point title	Maximum observed drug concentration in plasma [Cmax] after single dose administration of iloprost

End point description:

Maximum observed drug concentration in plasma. Geometric mean and percentage geometric coefficient of variation (%CV) were reported.

End point type	Secondary

End point timeframe:

0, 2, 5, 10, 20, 30 and 45 minutes after inhalation on Day 1 and 0, 2, 5, 10, 20, 30, 45 and 60 minutes after inhalation on Day 2

End point values	Iloprost 2.5 mcg, FOX nebulizer – PKS-1	Iloprost 5 mcg, FOX nebulizer – PKS-1	Iloprost 5 mcg, I-Neb nebulizer – PKS-2	Iloprost 5 mcg, FOX nebulizer – PKS-2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	24[30]	24[31]	24[32]	24[33]
Units: ng/L				
geometric mean (geometric coefficient of variation)	89.1 (± 47.21)	176.27 (± 58.49)	90.23 (± 54.54)	158.7 (± 59.7)

Notes:

[30] - PKS-1

[31] - PKS-1

[32] - PKS-2

[33] - PKS-2

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The relative bioavailability of iloprost administered through the I-Neb and FOX nebulizers devices was investigated by comparing Cmax for each subject in turn. Thereafter, the geometric least-squares mean for these ratios was derived.

Comparison groups	Iloprost 5 mcg, FOX nebulizer – PKS-2 v Iloprost 5 mcg, I-Neb nebulizer – PKS-2

Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Least squares mean
Point estimate	1.7723
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.3647
upper limit	2.3018

Secondary: Time to reach maximum drug observed concentration in plasma [tmax] after single dose of iloprost

End point title	Time to reach maximum drug observed concentration in plasma [tmax] after single dose of iloprost

End point description:

Time to reach maximum drug observed concentration in plasma. Median and full range were reported.

End point type	Secondary

End point timeframe:

0, 2, 5, 10, 20, 30 and 45 minutes after inhalation on Day 1 and 0, 2, 5, 10, 20, 30, 45 and 60 minutes after inhalation on Day 2

End point values	Iloprost 2.5 mcg, FOX nebulizer – PKS-1	Iloprost 5 mcg, FOX nebulizer – PKS-1	Iloprost 5 mcg, I-Neb nebulizer – PKS-2	Iloprost 5 mcg, FOX nebulizer – PKS-2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	24[34]	24[35]	24[36]	24[37]
Units: hour				
median (full range (min-max))	0.11667 (0.0667 to 0.1833)	0.11667 (0.0667 to 0.15)	0.21667 (0.1167 to 0.4)	0.1 (0.0667 to 0.15)

Notes:

[34] - PKS-1

[35] - PKS-1

[36] - PKS-2

[37] - PKS-2

Statistical analyses

No statistical analyses for this end point

Secondary: Time to reach maximum observed drug concentration in plasma at steady state [tmax,end] after single dose administration of iloprost

End point title	Time to reach maximum observed drug concentration in plasma at steady state [tmax,end] after single dose administration of iloprost

End point description:

Time to reach maximum observed drug concentration in plasma at steady state. Median and full range were reported.

End point type	Secondary

End point timeframe:

0, 2, 5, 10, 20, 30 and 45 minutes after inhalation on Day 1 and 0, 2, 5, 10, 20, 30, 45 and 60 minutes after inhalation on Day 2

End point values	Iloprost 2.5 mcg, FOX nebulizer – PKS-1	Iloprost 5 mcg, FOX nebulizer – PKS-1	Iloprost 5 mcg, I-Neb nebulizer – PKS-2	Iloprost 5 mcg, FOX nebulizer – PKS-2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	24[38]	24[39]	24[40]	24[41]
Units: hour				
median (full range (min-max))	0.0614 (0.0252 to 0.1108)	0.07065 (0.0406 to 0.1111)	0.03735 (0.0056 to 0.0986)	0.06365 (0.0406 to 0.1072)

Notes:

[38] - PKS-1

[39] - PKS-1

[40] - PKS-2

[41] - PKS-2

Statistical analyses

No statistical analyses for this end point

Secondary: Time of last concentration above lower limit of quantification (LLOQ), directly taken from analytical data [tlast] after single dose administration of iloprost

End point title	Time of last concentration above lower limit of quantification (LLOQ), directly taken from analytical data [tlast] after single dose administration of iloprost

End point description:

Time of last concentration above lower limit of quantification (LLOQ), directly taken from analytical data. Median and full range were reported.

End point type	Secondary

End point timeframe:

0, 2, 5, 10, 20, 30 and 45 minutes after inhalation on Day 1 and 0, 2, 5, 10, 20, 30, 45 and 60 minutes after inhalation on Day 2

End point values	Iloprost 2.5 mcg, FOX nebulizer – PKS-1	Iloprost 5 mcg, FOX nebulizer – PKS-1	Iloprost 5 mcg, I-Neb nebulizer – PKS-2	Iloprost 5 mcg, FOX nebulizer – PKS-2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	24[42]	24[43]	24[44]	24[45]
Units: hour				
median (full range (min-max))	0.56667 (0.2167 to 0.8333)	0.68333 (0.2 to 1.1)	0.6 (0.2667 to 1.2833)	0.56667 (0.2 to 1.0667)

Notes:

[42] - PKS-1

[43] - PKS-1

[44] - PKS-2

[45] - PKS-2

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of area under the plasma concentration versus time curve from the last data point to infinity [%AUC(tlast-inf)] after single dose administration of iloprost

End point title	Percentage of area under the plasma concentration versus time curve from the last data point to infinity [%AUC(tlast-inf)] after single dose administration of iloprost

End point description:

Percentage of AUC from the last data point above LLOQ to infinity. Geometric mean and percentage geometric coefficient of variation (%CV) were reported.

End point type	Secondary

End point timeframe:

0, 2, 5, 10, 20, 30 and 45 minutes after inhalation on Day 1 and 0, 2, 5, 10, 20, 30, 45 and 60 minutes after inhalation on Day 2

End point values	Iloprost 2.5 mcg, FOX nebulizer – PKS-1	Iloprost 5 mcg, FOX nebulizer – PKS-1	Iloprost 5 mcg, I-Neb nebulizer – PKS-2	Iloprost 5 mcg, FOX nebulizer – PKS-2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	7[46]	8[47]	5[48]	7[49]
Units: percentage of AUC				
geometric mean (geometric coefficient of variation)	15.1 (± 22.9)	8.84 (± 32.5)	12.5 (± 49.3)	8.82 (± 35.3)

Notes:

[46] - PKS-1

[47] - PKS-1

[48] - PKS-2

[49] - PKS-2

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From the start of study treatment until end of study Part 4, over a period up to 3 years	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.0
Reporting groups	
Reporting group title	1.25 UG FOX
Reporting group description: Iloprost 1.25 mcg, FOX nebulizer - Part 1	
Reporting group title	2.5 UG FOX
Reporting group description: Iloprost 2.5 mcg, FOX nebulizer - Part 1	
Reporting group title	5 UG I-NEB SD
Reporting group description: Iloprost 5 mcg Single Dose (SD), I-Neb nebulizer - Part 2	
Reporting group title	5 UG FOX SD
Reporting group description: Iloprost 5 mcg Single Dose (SD), FOX nebulizer - Part 2	
Reporting group title	5 UG I-NEB MD
Reporting group description: Iloprost 5 mcg Multiple Dose (MD), I-Neb nebulizer - Part 3	
Reporting group title	5 UG FOX MD PART 3
Reporting group description: Iloprost 5 mcg Multiple Dose (MD), FOX nebulizer - Part 3	
Reporting group title	5 UG FOX MD PART 4
Reporting group description: Iloprost 5 mcg, MD, FOX nebulizer - Part 4	

Serious adverse events	1.25 UG FOX	2.5 UG FOX	5 UG I-NEB SD
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			

Lung transplant			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Therapy change			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary artery aneurysm			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary congestion			

subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary hypertension			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary arterial hypertension			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
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			
Catheterisation cardiac			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colonoscopy			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transplant evaluation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Rib fracture			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Lumbar vertebral fracture			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device use error			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
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 failure			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Right ventricular failure			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iron deficiency anaemia			

subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal tear			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Visual acuity reduced			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastrointestinal disorder			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Melaena			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine polyp			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			

Renal failure			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Flank pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Abscess jaw			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	5 UG FOX SD	5 UG I-NEB MD	5 UG FOX MD PART 3
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 27 (0.00%)	2 / 26 (7.69%)	2 / 27 (7.41%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Lung transplant			

subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Therapy change			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary artery aneurysm			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary congestion			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pulmonary hypertension			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary arterial hypertension			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
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			
Catheterisation cardiac			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colonoscopy			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	0 / 27 (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
Transplant evaluation			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Rib fracture			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar vertebral fracture			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Device use error			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
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 failure			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Right ventricular failure			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	1 / 27 (3.70%)
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			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iron deficiency anaemia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Cataract			

subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal tear			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Visual acuity reduced			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastrointestinal disorder			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Melaena			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine polyp			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			

subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Flank pain			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal infection			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess jaw			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory tract infection			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	0 / 27 (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
Hyperglycaemia			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	0 / 27 (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
Hypokalaemia			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	5 UG FOX MD PART 4		
Total subjects affected by serious adverse events			
subjects affected / exposed	20 / 25 (80.00%)		
number of deaths (all causes)	5		
number of deaths resulting from adverse events	5		
Vascular disorders			
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Surgical and medical procedures			
Lung transplant			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Therapy change			

subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Oedema peripheral			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Haemoptysis			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary artery aneurysm			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary congestion			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary hypertension			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Pulmonary arterial hypertension				
subjects affected / exposed	5 / 25 (20.00%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 0			
Investigations				
Catheterisation cardiac				
subjects affected / exposed	2 / 25 (8.00%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Colonoscopy				
subjects affected / exposed	0 / 25 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Transplant evaluation				
subjects affected / exposed	2 / 25 (8.00%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Rib fracture				
subjects affected / exposed	1 / 25 (4.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Spinal compression fracture				
subjects affected / exposed	1 / 25 (4.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lumbar vertebral fracture				
subjects affected / exposed	1 / 25 (4.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Device use error				
subjects affected / exposed	1 / 25 (4.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Cardiac failure			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Right ventricular failure			
subjects affected / exposed	5 / 25 (20.00%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 2		
Nervous system disorders			
Syncope			
subjects affected / exposed	5 / 25 (20.00%)		
occurrences causally related to treatment / all	0 / 17		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Iron deficiency anaemia			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Cataract			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Retinal tear			

subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Visual acuity reduced			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastrointestinal disorder			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal haemorrhage			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Melaena			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Large intestine polyp			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Acute kidney injury			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue			

disorders			
Flank pain			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal infection			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abscess jaw			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection			
subjects affected / exposed	3 / 25 (12.00%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		

Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperglycaemia			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	1.25 UG FOX	2.5 UG FOX	5 UG I-NEB SD
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 11 (27.27%)	6 / 27 (22.22%)	3 / 26 (11.54%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenoma benign			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Tracheal neoplasm			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Blood pressure fluctuation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Flushing			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Haematoma			

subjects affected / exposed	0 / 11 (0.00%)	1 / 27 (3.70%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Hypertension			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Hypertensive crisis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Hypotension			
subjects affected / exposed	2 / 11 (18.18%)	3 / 27 (11.11%)	1 / 26 (3.85%)
occurrences (all)	2	3	1
Phlebitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Hot flush			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
Endodontic procedure			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Intestinal polypectomy			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Cataract operation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Oxygen therapy			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			

subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Extravasation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Feeling abnormal			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Gait disturbance			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
General physical health deterioration			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Exercise tolerance decreased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Medical device site reaction			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Puncture site pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			

Hypersensitivity			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Seasonal allergy			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Mite allergy			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Social circumstances			
Postmenopause			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Nipple pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 11 (0.00%)	1 / 27 (3.70%)	1 / 26 (3.85%)
occurrences (all)	0	1	1
Dysphonia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0

Pleural effusion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Pleurisy			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Pulmonary artery aneurysm			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Pulmonary hypertension			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Pulmonary oedema			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Throat irritation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Nocturnal dyspnoea			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Pulmonary arterial hypertension			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Restlessness			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Sleep disorder			

subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Stereotypy			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Stress			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Hepatic steatosis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Blood potassium decreased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Blood sodium abnormal			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			

subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Catheterisation cardiac			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
International normalised ratio increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
PCO2 increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Pulmonary arterial pressure increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Serum ferritin decreased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Brain natriuretic peptide increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Neurological examination abnormal			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Hepatic enzyme increased			

subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Walking distance test abnormal			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
N-terminal prohormone brain natriuretic peptide increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Myocardial necrosis marker increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Head injury			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Laceration			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Rib fracture			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Spinal compression fracture			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Post procedural haemorrhage			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Limb injury			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Procedural nausea			

subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Congenital, familial and genetic disorders			
Atrial septal defect			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Hereditary haemorrhagic telangiectasia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 11 (0.00%)	1 / 27 (3.70%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Atrioventricular block first degree			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Atrioventricular block second degree			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Bradycardia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Bundle branch block right			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Cardiac failure			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Cardiovascular disorder			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Cyanosis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Extrasystoles			

subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Pericardial effusion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Sinus bradycardia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Bradyarrhythmia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 11 (0.00%)	1 / 27 (3.70%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Dizziness exertional			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Head discomfort			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	1 / 11 (9.09%)	1 / 27 (3.70%)	0 / 26 (0.00%)
occurrences (all)	1	1	0
Memory impairment			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0

Paraesthesia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Polyneuropathy			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Iron deficiency anaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Hypoacusis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
External ear pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Periorbital oedema			

subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Visual acuity reduced			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Visual impairment			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Eyelid haematoma			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Anorectal disorder			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Ascites			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Dental caries			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Diverticulum			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0

Diverticulum intestinal			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Gastritis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorder			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Melaena			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0

Large intestine polyp			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Bowel movement irregularity			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Reactive gastropathy			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Hirsutism			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Milia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Petechiae			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Dermatosis			

subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Acute prerenal failure			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Incontinence			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Nocturia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Renal failure			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Urinary incontinence			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Renal impairment			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Acute kidney injury			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Arthritis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Back pain			

subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Bursitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Osteoarthritis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Pain in jaw			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Tendonitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal discomfort			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Tendon calcification			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Spinal pain			

subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Fungal infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Periodontitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Subcutaneous abscess			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0

Urinary tract infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 11 (0.00%)	1 / 27 (3.70%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal fungal infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Abscess jaw			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Lung infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Herpes dermatitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Infective glossitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Diabetes mellitus			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Gout			

subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Hyperuricaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Iron deficiency			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Metabolic alkalosis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Vitamin D deficiency			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Hyperlipidaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	5 UG FOX SD	5 UG I-NEB MD	5 UG FOX MD PART 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 27 (14.81%)	6 / 26 (23.08%)	12 / 27 (44.44%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenoma benign			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Tracheal neoplasm			

subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Blood pressure fluctuation			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Flushing			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Haematoma			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Hypertensive crisis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	4 / 27 (14.81%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	4	0	0
Phlebitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Hot flush			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	2 / 27 (7.41%)
occurrences (all)	0	0	2
Surgical and medical procedures			
Endodontic procedure			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Intestinal polypectomy			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Cataract operation			

subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Oxygen therapy			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Chills			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Extravasation			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Feeling abnormal			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
Gait disturbance			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Oedema peripheral			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
General physical health deterioration			

subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Exercise tolerance decreased			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Medical device site reaction			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Puncture site pain			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Seasonal allergy			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Mite allergy			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Social circumstances			
Postmenopause			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Nipple pain			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	3 / 27 (11.11%)
occurrences (all)	0	0	3

Dysphonia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Dyspnoea			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Pleural effusion			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Pleurisy			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Pulmonary artery aneurysm			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Pulmonary hypertension			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Pulmonary oedema			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Throat irritation			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Nocturnal dyspnoea			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Pulmonary arterial hypertension			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0

Oropharyngeal pain			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Restlessness			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Sleep disorder			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Stereotypy			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Stress			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Hepatic steatosis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0

Blood creatinine increased			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Blood potassium decreased			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Blood sodium abnormal			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Catheterisation cardiac			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
International normalised ratio increased			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
PCO2 increased			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Pulmonary arterial pressure increased			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Serum ferritin decreased			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Brain natriuretic peptide increased			

subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Neurological examination abnormal			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Walking distance test abnormal			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
N-terminal prohormone brain natriuretic peptide increased			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Myocardial necrosis marker increased			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Head injury			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Laceration			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Rib fracture			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Spinal compression fracture			

subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Post procedural haemorrhage			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Limb injury			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Procedural nausea			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Congenital, familial and genetic disorders			
Atrial septal defect			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Hereditary haemorrhagic telangiectasia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Atrioventricular block first degree			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	2 / 27 (7.41%)
occurrences (all)	0	0	2
Atrioventricular block second degree			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Bradycardia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Bundle branch block right			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Cardiac failure			

subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Cardiovascular disorder			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Cyanosis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Extrasystoles			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	2 / 27 (7.41%)
occurrences (all)	0	0	2
Pericardial effusion			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Sinus bradycardia			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Tachycardia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Bradyarrhythmia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 27 (3.70%)	1 / 26 (3.85%)	0 / 27 (0.00%)
occurrences (all)	1	1	0
Dizziness exertional			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Head discomfort			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0

Headache			
subjects affected / exposed	0 / 27 (0.00%)	2 / 26 (7.69%)	4 / 27 (14.81%)
occurrences (all)	0	2	4
Memory impairment			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	1 / 27 (3.70%)
occurrences (all)	0	1	1
Paraesthesia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Polyneuropathy			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Iron deficiency anaemia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Hypoacusis			

subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
External ear pain			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Periorbital oedema			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Visual acuity reduced			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Visual impairment			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Eyelid haematoma			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Anorectal disorder			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Ascites			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Constipation			

subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Dental caries			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Diverticulum			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Diverticulum intestinal			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Gastritis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorder			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal pain			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			

subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Melaena			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Large intestine polyp			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Bowel movement irregularity			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Reactive gastropathy			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Hirsutism			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1

Milia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Petechiae			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Dermatosis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Acute prerenal failure			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Incontinence			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Nocturia			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Renal failure			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Urinary incontinence			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Renal impairment			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Acute kidney injury			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			

Hyperthyroidism			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Arthritis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Bursitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Osteoarthritis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Pain in jaw			

subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Tendonitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal discomfort			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Tendon calcification			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Spinal pain			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Conjunctivitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Fungal infection			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal infection			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Periodontitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0

Rhinitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Subcutaneous abscess			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal fungal infection			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Abscess jaw			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Lung infection			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	1 / 27 (3.70%)
occurrences (all)	0	1	1
Herpes dermatitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0

Infective glossitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Diabetes mellitus			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Gout			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Hyperuricaemia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Iron deficiency			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Metabolic alkalosis			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Vitamin D deficiency			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Hyperlipidaemia			

subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	5 UG FOX MD PART 4		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 25 (96.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenoma benign			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Tracheal neoplasm			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Vascular disorders			
Blood pressure fluctuation			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Flushing			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	3		
Haematoma			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Hypertension			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Hypertensive crisis			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Hypotension			
subjects affected / exposed	3 / 25 (12.00%)		
occurrences (all)	4		
Phlebitis			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Hot flush			

subjects affected / exposed	0 / 25 (0.00%)		
occurrences (all)	0		
Surgical and medical procedures			
Endodontic procedure			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	2		
Intestinal polypectomy			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Cataract operation			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Oxygen therapy			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Chest discomfort			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	3		
Chills			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Extravasation			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	3 / 25 (12.00%)		
occurrences (all)	3		
Feeling abnormal			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences (all)	0		
Gait disturbance			

subjects affected / exposed	0 / 25 (0.00%)		
occurrences (all)	0		
Oedema peripheral			
subjects affected / exposed	11 / 25 (44.00%)		
occurrences (all)	13		
Pyrexia			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
General physical health deterioration			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Exercise tolerance decreased			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Medical device site reaction			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Puncture site pain			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Seasonal allergy			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Mite allergy			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Social circumstances			
Postmenopause			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Reproductive system and breast disorders			

Nipple pain			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Cough			
subjects affected / exposed	6 / 25 (24.00%)		
occurrences (all)	10		
Dysphonia			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences (all)	0		
Dyspnoea			
subjects affected / exposed	9 / 25 (36.00%)		
occurrences (all)	15		
Epistaxis			
subjects affected / exposed	6 / 25 (24.00%)		
occurrences (all)	11		
Nasal congestion			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences (all)	0		
Pleural effusion			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Pleurisy			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Pulmonary artery aneurysm			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Pulmonary hypertension			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Pulmonary oedema			

subjects affected / exposed occurrences (all)	2 / 25 (8.00%) 2		
Throat irritation subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1		
Nocturnal dyspnoea subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 2		
Pulmonary arterial hypertension subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1		
Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0		
Psychiatric disorders			
Depression subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1		
Restlessness subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1		
Sleep disorder subjects affected / exposed occurrences (all)	3 / 25 (12.00%) 3		
Stereotypy subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1		
Stress subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 2		
Hepatobiliary disorders			
Cholelithiasis subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1		
Hepatic steatosis			

subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	2		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Blood creatinine increased			
subjects affected / exposed	3 / 25 (12.00%)		
occurrences (all)	3		
Blood potassium decreased			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Blood sodium abnormal			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
C-reactive protein increased			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	3		
Catheterisation cardiac			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	3		
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
International normalised ratio increased			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
PCO2 increased			

subjects affected / exposed	0 / 25 (0.00%)		
occurrences (all)	0		
Pulmonary arterial pressure increased			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Serum ferritin decreased			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Weight decreased			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Brain natriuretic peptide increased			
subjects affected / exposed	4 / 25 (16.00%)		
occurrences (all)	5		
Neurological examination abnormal			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences (all)	0		
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Hepatic enzyme increased			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Walking distance test abnormal			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
N-terminal prohormone brain natriuretic peptide increased			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Myocardial necrosis marker increased			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			

Fall subjects affected / exposed occurrences (all)	2 / 25 (8.00%) 2		
Head injury subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 2		
Laceration subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1		
Rib fracture subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1		
Spinal compression fracture subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1		
Post procedural haemorrhage subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1		
Limb injury subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 2		
Procedural nausea subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1		
Congenital, familial and genetic disorders			
Atrial septal defect subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 2		
Hereditary haemorrhagic telangiectasia subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1		
Cardiac disorders			
Angina pectoris subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0		
Atrioventricular block first degree			

subjects affected / exposed	1 / 25 (4.00%)			
occurrences (all)	1			
Atrioventricular block second degree				
subjects affected / exposed	1 / 25 (4.00%)			
occurrences (all)	1			
Bradycardia				
subjects affected / exposed	0 / 25 (0.00%)			
occurrences (all)	0			
Bundle branch block right				
subjects affected / exposed	1 / 25 (4.00%)			
occurrences (all)	1			
Cardiac failure				
subjects affected / exposed	1 / 25 (4.00%)			
occurrences (all)	1			
Cardiovascular disorder				
subjects affected / exposed	0 / 25 (0.00%)			
occurrences (all)	0			
Cyanosis				
subjects affected / exposed	1 / 25 (4.00%)			
occurrences (all)	1			
Extrasystoles				
subjects affected / exposed	1 / 25 (4.00%)			
occurrences (all)	1			
Palpitations				
subjects affected / exposed	6 / 25 (24.00%)			
occurrences (all)	6			
Pericardial effusion				
subjects affected / exposed	1 / 25 (4.00%)			
occurrences (all)	1			
Sinus bradycardia				
subjects affected / exposed	0 / 25 (0.00%)			
occurrences (all)	0			
Tachycardia				
subjects affected / exposed	8 / 25 (32.00%)			
occurrences (all)	10			
Bradyarrhythmia				

subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Nervous system disorders			
Dizziness			
subjects affected / exposed	7 / 25 (28.00%)		
occurrences (all)	9		
Dizziness exertional			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Head discomfort			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	6 / 25 (24.00%)		
occurrences (all)	7		
Memory impairment			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	2		
Migraine			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	11		
Paraesthesia			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	3		
Polyneuropathy			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Syncope			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Tremor			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	7 / 25 (28.00%)		
occurrences (all)	11		
Iron deficiency anaemia			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	3		
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Vertigo			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences (all)	0		
Hypoacusis			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
External ear pain			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Eye disorders			
Cataract			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Periorbital oedema			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Visual acuity reduced			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Visual impairment			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	3		
Eyelid haematoma			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Gastrointestinal disorders			

Abdominal pain				
subjects affected / exposed	1 / 25 (4.00%)			
occurrences (all)	1			
Abdominal pain upper				
subjects affected / exposed	1 / 25 (4.00%)			
occurrences (all)	2			
Anorectal disorder				
subjects affected / exposed	0 / 25 (0.00%)			
occurrences (all)	0			
Ascites				
subjects affected / exposed	1 / 25 (4.00%)			
occurrences (all)	1			
Constipation				
subjects affected / exposed	5 / 25 (20.00%)			
occurrences (all)	6			
Dental caries				
subjects affected / exposed	1 / 25 (4.00%)			
occurrences (all)	1			
Diarrhoea				
subjects affected / exposed	5 / 25 (20.00%)			
occurrences (all)	9			
Diverticulum				
subjects affected / exposed	1 / 25 (4.00%)			
occurrences (all)	1			
Diverticulum intestinal				
subjects affected / exposed	1 / 25 (4.00%)			
occurrences (all)	1			
Dry mouth				
subjects affected / exposed	1 / 25 (4.00%)			
occurrences (all)	1			
Dyspepsia				
subjects affected / exposed	1 / 25 (4.00%)			
occurrences (all)	1			
Flatulence				
subjects affected / exposed	2 / 25 (8.00%)			
occurrences (all)	2			

Gastritis subjects affected / exposed occurrences (all)	2 / 25 (8.00%) 2		
Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	2 / 25 (8.00%) 2		
Gastrointestinal disorder subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1		
Gastrointestinal pain subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1		
Haemorrhoids subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1		
Melaena subjects affected / exposed occurrences (all)	3 / 25 (12.00%) 3		
Nausea subjects affected / exposed occurrences (all)	9 / 25 (36.00%) 15		
Vomiting subjects affected / exposed occurrences (all)	3 / 25 (12.00%) 6		
Large intestine polyp subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1		
Bowel movement irregularity subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1		
Reactive gastropathy subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1		
Skin and subcutaneous tissue disorders Dermatitis			

subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Eczema			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Erythema			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Hirsutism			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Hyperhidrosis			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences (all)	0		
Milia			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Petechiae			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Dermatosis			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Renal and urinary disorders			
Acute prerenal failure			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Incontinence			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Nocturia			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		

Renal failure			
subjects affected / exposed	3 / 25 (12.00%)		
occurrences (all)	5		
Urinary incontinence			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Renal impairment			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Acute kidney injury			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences (all)	0		
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Arthritis			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Back pain			
subjects affected / exposed	4 / 25 (16.00%)		
occurrences (all)	5		
Bursitis			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Muscle spasms			
subjects affected / exposed	3 / 25 (12.00%)		
occurrences (all)	5		
Musculoskeletal pain			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Myalgia			

subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Neck pain			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	2		
Osteoarthritis			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Pain in jaw			
subjects affected / exposed	4 / 25 (16.00%)		
occurrences (all)	4		
Tendonitis			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Musculoskeletal discomfort			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Tendon calcification			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Spinal pain			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	6		
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	3		
Conjunctivitis			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Fungal infection			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		

Gastroenteritis				
subjects affected / exposed	2 / 25 (8.00%)			
occurrences (all)	2			
Gastrointestinal infection				
subjects affected / exposed	4 / 25 (16.00%)			
occurrences (all)	4			
Periodontitis				
subjects affected / exposed	1 / 25 (4.00%)			
occurrences (all)	1			
Pneumonia				
subjects affected / exposed	3 / 25 (12.00%)			
occurrences (all)	4			
Rhinitis				
subjects affected / exposed	1 / 25 (4.00%)			
occurrences (all)	1			
Sinusitis				
subjects affected / exposed	1 / 25 (4.00%)			
occurrences (all)	1			
Subcutaneous abscess				
subjects affected / exposed	1 / 25 (4.00%)			
occurrences (all)	1			
Upper respiratory tract infection				
subjects affected / exposed	2 / 25 (8.00%)			
occurrences (all)	2			
Urinary tract infection				
subjects affected / exposed	4 / 25 (16.00%)			
occurrences (all)	6			
Viral infection				
subjects affected / exposed	1 / 25 (4.00%)			
occurrences (all)	1			
Viral upper respiratory tract infection				
subjects affected / exposed	9 / 25 (36.00%)			
occurrences (all)	15			
Gastrointestinal fungal infection				
subjects affected / exposed	1 / 25 (4.00%)			
occurrences (all)	1			

Abscess jaw subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1			
Lung infection subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1			
Respiratory tract infection subjects affected / exposed occurrences (all)	10 / 25 (40.00%) 19			
Herpes dermatitis subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1			
Infective glossitis subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1			
Metabolism and nutrition disorders Acidosis subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1			
Diabetes mellitus subjects affected / exposed occurrences (all)	3 / 25 (12.00%) 3			
Gout subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 4			
Hyperuricaemia subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1			
Hypoglycaemia subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1			
Hypokalaemia subjects affected / exposed occurrences (all)	8 / 25 (32.00%) 16			
Hyponatraemia				

subjects affected / exposed	3 / 25 (12.00%)		
occurrences (all)	3		
Iron deficiency			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Metabolic alkalosis			
subjects affected / exposed	0 / 25 (0.00%)		
occurrences (all)	0		
Vitamin D deficiency			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Hyperlipidaemia			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 December 2013	The German Competent Authority BfArM requested that the method of contraception for women of child-bearing potential shall be highly-effective and follow the "Note for guidance on non-clinical safety studies for the conduct of human clinical trials for pharmaceuticals (CPMP/ICH/286/95, modification)".
21 July 2014	Modification 1: Clarification of measurements of heart rate and blood pressure at Visit 1 and Visit 2. Modification 2: Clarification that multiple heart-rate and blood-pressure measurements were to be performed starting at the end of the inhalation. Modification 3: Minor adaptations.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Occurrence of "±" in relation with geometric CV is auto-generated and cannot be deleted. Decimal places were automatically truncated if last decimal equals zero.

Notes: