



## Clinical trial results:

### A Dose-Ranging Study of the Efficacy and Safety of Bardoxolone Methyl in Patients with Pulmonary Hypertension (PH) - LARIAT

#### Summary

EudraCT number	2016-004793-17
Trial protocol	DE GB ES
Global end of trial date	16 May 2018

#### Results information

Result version number	v1 (current)
This version publication date	01 December 2021
First version publication date	01 December 2021

#### Trial information

##### Trial identification

Sponsor protocol code	402-C-1302
-----------------------	------------

##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02036970
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	Reata Pharmaceuticals, Inc.
Sponsor organisation address	5320 Legacy Drive, Plano, United States, 75024
Public contact	Kris Loerwald, Reata Pharmaceuticals, Inc., 972 865-2219, MedicalAffairs-Team@reatapharma.com
Scientific contact	Kris Loerwald, Reata Pharmaceuticals, Inc., 972 865-2219, MedicalAffairs-Team@reatapharma.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	17 December 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 January 2018
Global end of trial reached?	Yes
Global end of trial date	16 May 2018
Was the trial ended prematurely?	No

Notes:

---

**General information about the trial**

---

Main objective of the trial:

This study assesses the safety and efficacy of bardoxolone methyl relative to placebo in patients with pulmonary hypertension to determine the recommended dose range, evaluate the change from baseline in 6-minute walk distance (6MWD) and determine the effect of Bardoxolone methyl in pulmonary hypertension associated with connective tissue disease, interstitial lung disease, and idiopathic etiologies, including subsets of patients with WHO Group III or WHO Group V PH following 16 weeks of study participation.

Protection of trial subjects:

A Protocol Safety Review Committee (PSRC) assessed the starting dose and each new dose level of bardoxolone methyl for safety and tolerability based on review of all available data for this study at the time of each review. PSRC reviews occurred after the Week 4 data are available for the first eight patients enrolled at each new dose level combined across Cohorts 1 and 2 (i.e., the 6MWD  $\leq$  450 m and 6MWD > 450 m cohorts). Upon completion of the dose ranging portion of the study, the PSRC continued to meet at regular intervals (approximately quarterly) to monitor safety of all patients, including those enrolled in Cohorts 3 and 4. The PSRC included at a minimum a Sponsor representative, a cardiologist, and a statistician. PSRC also assessed for general safety and specific signs and symptoms of fluid overload. The PSRC assessment included a dose level recommendation based on clinical evaluation of protocol specified assessments for subsequent cohorts to escalate to a higher dose, proceed to a lower dose, or maintain the current dose. The PSRC also could recommend stopping dosing in current cohorts.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 June 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

---

**Population of trial subjects**

---

**Subjects enrolled per country**

Country: Number of subjects enrolled	United States: 164
Country: Number of subjects enrolled	Germany: 2
Worldwide total number of subjects	166
EEA total number of subjects	2

Notes:

<b>Subjects enrolled per age group</b>	
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)	124
From 65 to 84 years	42
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Part 1: 16-week double-blind, randomized, placebo-controlled treatment period (Day 1 to Week 16).  
Part 2: Open-label extension period (Week 16 onwards). Part 2 is the extension period and patients were to stay until study drug became available through extended access program [Study 402-C-1602]. Each participant in Part 2 was also in Part 1.

### Period 1

Period 1 title	Part 1: Day 1 Through Week 16
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Part 1:Dose Ranging Bardoxolone Methyl 2.5mg

Arm description:

Participants received bardoxolone methyl 2.5 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 2.5 mg once-daily in Part 2 (Week 16 and onwards)

Arm type	Experimental
Investigational medicinal product name	Bardoxolone methyl capsules 2.5mg
Investigational medicinal product code	RTA 402
Other name	RTA 402 capsules
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received bardoxolone methyl 2.5 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 2.5 mg once-daily in Part 2 (Week 16 and onwards)

<b>Arm title</b>	Part 1:Dose-Ranging Bardoxolone Methyl 5mg
------------------	--

Arm description:

Participants received bardoxolone methyl 5 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 5 mg once-daily in Part 2 (Week 16 and onwards)

Arm type	Experimental
Investigational medicinal product name	Bardoxolone methyl capsules 5mg
Investigational medicinal product code	RTA 402
Other name	RTA 402 capsules
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received bardoxolone methyl 5 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 5 mg once-daily in Part 2 (Week 16 and onwards)

<b>Arm title</b>	Part 1:Dose-Ranging Bardoxolone Methyl 10mg
------------------	---

Arm description:

Participants received bardoxolone methyl 10 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 10 mg once-daily in Part 2

(Week 16 and onwards)

Arm type	Experimental
Investigational medicinal product name	Bardoxolone methyl capsules 10mg
Investigational medicinal product code	RTA 402
Other name	RTA 402 capsules
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received bardoxolone methyl 10 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 10 mg once-daily in Part 2 (Week 16 and onwards)

<b>Arm title</b>	Part 1:Dose-Ranging Bardoxolone Methyl 20mg
------------------	---

Arm description:

Participants received bardoxolone methyl 20 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 20 mg once-daily in Part 2 (Week 16 and onwards)

Arm type	Experimental
Investigational medicinal product name	Bardoxolone methyl capsules 20mg
Investigational medicinal product code	RTA 402
Other name	RTA 402 capsules
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received bardoxolone methyl 20 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 20 mg once-daily in Part 2 (Week 16 and onwards)

<b>Arm title</b>	Part 1:Dose-Ranging Placebo 2.5mg
------------------	-----------------------------------

Arm description:

Participants received bardoxolone methyl 2.5 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 2.5 mg once-daily in Part 2 (Week 16 and onwards)

Arm type	Placebo
Investigational medicinal product name	Placebo Capsules
Investigational medicinal product code	Placebo
Other name	Placebo
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received bardoxolone methyl 2.5 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 2.5 mg once-daily in Part 2 (Week 16 and onwards)

<b>Arm title</b>	Part 1: Dose-Ranging Placebo 5 mg
------------------	-----------------------------------

Arm description:

Participants received bardoxolone methyl 5 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 5 mg once-daily in Part 2 (Week 16 and onwards)

Arm type	Placebo
Investigational medicinal product name	Placebo Capsules 5mg
Investigational medicinal product code	Placebo
Other name	Placebo
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received bardoxolone methyl 5 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 5 mg once-daily in Part 2

<b>Arm title</b>	Part 1: Dose-Ranging Placebo 10 mg
Arm description: Participants received bardoxolone methyl 10 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 10 mg once-daily in Part 2 (Week 16 and onwards)	
Arm type	Placebo
Investigational medicinal product name	Placebo Capsules 10mg
Investigational medicinal product code	Placebo
Other name	Placebo
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: Participants received bardoxolone methyl 10 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 10 mg once-daily in Part 2 (Week 16 and onwards)	
<b>Arm title</b>	Part 1: Dose-Ranging Placebo 20 mg
Arm description: Participants received bardoxolone methyl 20 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 20 mg once-daily in Part 2 (Week 16 and onwards)	
Arm type	Placebo
Investigational medicinal product name	Placebo Capsules 20mg
Investigational medicinal product code	Placebo
Other name	Placebo
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: Participants received bardoxolone methyl 20 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 20 mg once-daily in Part 2 (Week 16 and onwards)	
<b>Arm title</b>	Part 1: Dose Titration: Bardoxolone Methyl 10 mg
Arm description: Participants in Part 1 started with bardoxolone methyl 5 mg once-daily from Day 1 and escalated to bardoxolone methyl 10 mg once-daily starting at Week 4 thru Week 16. Participants who continued to Part 2 continued to receive the same bardoxolone methyl dose once-daily in Part 2 (Week 16 and onwards)	
Arm type	Experimental
Investigational medicinal product name	Bardoxolone methyl capsules 10mg
Investigational medicinal product code	RTA 402
Other name	RTA 402 capsules
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: Participants in Part 1 started with bardoxolone methyl 5 mg once-daily from Day 1 and escalated to bardoxolone methyl 10 mg once-daily starting at Week 4 thru Week 16. Participants who continued to Part 2 continued to receive the same bardoxolone methyl dose once-daily in Part 2 (Week 16 and onwards)	
<b>Arm title</b>	Part 1: Dose Titration: Placebo 10 mg

Arm description:

Participants in Part 1 received Placebo once-daily from Day 1 thru Week 16. Participants who continued to Part 2 initially received bardoxolone methyl 5 mg once-daily from Week 16 thru Week 20 and bardoxolone methyl 10 mg from week 20 onwards

Arm type	Placebo
Investigational medicinal product name	Placebo Capsules 10mg
Investigational medicinal product code	Placebo
Other name	Placebo
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants in Part 1 received Placebo once-daily from Day 1 thru Week 16. Participants who continued to Part 2 initially received bardoxolone methyl 5 mg once-daily from Week 16 thru Week 20 and bardoxolone methyl 10 mg from week 20 onwards

Number of subjects in period 1	Part 1:Dose Ranging Bardoxolone Methyl 2.5mg	Part 1:Dose-Ranging Bardoxolone Methyl 5mg	Part 1:Dose-Ranging Bardoxolone Methyl 10mg
Started	6	12	11
Completed	5	12	7
Not completed	1	0	4
Consent withdrawn by subject	-	-	-
Adverse event, non-fatal	-	-	3
Death	-	-	-
Progressive Disease	-	-	-
Protocol deviation	1	-	1

Number of subjects in period 1	Part 1:Dose-Ranging Bardoxolone Methyl 20mg	Part 1:Dose-Ranging Placebo 2.5mg	Part 1: Dose- Ranging Placebo 5 mg
Started	12	2	4
Completed	9	1	3
Not completed	3	1	1
Consent withdrawn by subject	-	1	-
Adverse event, non-fatal	2	-	1
Death	-	-	-
Progressive Disease	1	-	-
Protocol deviation	-	-	-

Number of subjects in period 1	Part 1: Dose- Ranging Placebo 10 mg	Part 1: Dose- Ranging Placebo 20 mg	Part 1: Dose Titration: Bardoxolone Methyl 10 mg
Started	3	4	74
Completed	3	3	66
Not completed	0	1	8
Consent withdrawn by subject	-	-	2
Adverse event, non-fatal	-	1	3

Death	-	-	1
Progressive Disease	-	-	-
Protocol deviation	-	-	2

Number of subjects in period 1	Part 1: Dose Titration: Placebo 10 mg
Started	38
Completed	33
Not completed	5
Consent withdrawn by subject	4
Adverse event, non-fatal	1
Death	-
Progressive Disease	-
Protocol deviation	-

## Period 2

Period 2 title	Part 2 Open-label extension: Week 16 On
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

## Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Part 2: Open-Label Bardoxolone Methyl 2.5 mg

### Arm description:

Participants received bardoxolone methyl 2.5 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 2.5 mg once-daily in Part 2 (Week 16 and onwards)

Arm type	Experimental
Investigational medicinal product name	Bardoxolone methyl capsules 2.5mg
Investigational medicinal product code	RTA 402
Other name	RTA 402 capsules
Pharmaceutical forms	Capsule
Routes of administration	Oral use

### Dosage and administration details:

Participants received bardoxolone methyl 2.5 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 2.5 mg once-daily in Part 2 (Week 16 and onwards)

<b>Arm title</b>	Part 2: Open-Label Bardoxolone Methyl 5 mg
------------------	--

### Arm description:

Participants received bardoxolone methyl 5 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 5 mg once-daily in Part 2 (Week 16 and onwards)

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



Investigational medicinal product name	Bardoxolone methyl capsules 5mg
Investigational medicinal product code	RTA 402
Other name	RTA 402 capsules
Pharmaceutical forms	Capsule
Routes of administration	Oral use

**Dosage and administration details:**

Participants received bardoxolone methyl 5 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 5 mg once-daily in Part 2 (Week 16 and onwards)

<b>Arm title</b>	Part 2: Open-Label Bardoxolone Methyl 10 mg
------------------	---

**Arm description:**

Participants received bardoxolone methyl 10 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 10 mg once-daily in Part 2 (Week 16 and onwards)

Arm type	Experimental
Investigational medicinal product name	Bardoxolone methyl capsules 10mg
Investigational medicinal product code	RTA 402
Other name	RTA 402 capsules
Pharmaceutical forms	Capsule
Routes of administration	Oral use

**Dosage and administration details:**

Participants received bardoxolone methyl 10 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 10 mg once-daily in Part 2 (Week 16 and onwards)

<b>Arm title</b>	Part 2: Open-Label Bardoxolone Methyl 20 mg
------------------	---

**Arm description:**

Participants received bardoxolone methyl 20 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 20 mg once-daily in Part 2 (Week 16 and onwards)

Arm type	Experimental
Investigational medicinal product name	Bardoxolone methyl capsules 20 mg
Investigational medicinal product code	RTA 402
Other name	RTA 402 capsules
Pharmaceutical forms	Capsule
Routes of administration	Oral use

**Dosage and administration details:**

Participants received bardoxolone methyl 20 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 20 mg once-daily in Part 2 (Week 16 and onwards)

<b>Arm title</b>	Part 2: Bardoxolone Methyl 2.5 mg
------------------	-----------------------------------

**Arm description:**

Participants received bardoxolone methyl 2.5 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 2.5 mg once-daily in Part 2 (Week 16 and onwards)

Arm type	Experimental
Investigational medicinal product name	Bardoxolone methyl capsules 2.5mg
Investigational medicinal product code	RTA 402
Other name	RTA 402 capsules
Pharmaceutical forms	Capsule
Routes of administration	Oral use

**Dosage and administration details:**

Participants received bardoxolone methyl 2.5 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 2.5 mg once-daily in Part 2 (Week 16 and onwards)

<b>Arm title</b>	Part 2: Bardoxolone Methyl 5 mg
------------------	---------------------------------

**Arm description:**

Participants received bardoxolone methyl 5 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 5 mg once-daily in Part 2 (Week 16 and onwards)

Arm type	Experimental
Investigational medicinal product name	Bardoxolone methyl capsules 5mg
Investigational medicinal product code	RTA 402
Other name	RTA 402 capsules
Pharmaceutical forms	Capsule
Routes of administration	Oral use

**Dosage and administration details:**

Participants received bardoxolone methyl 5 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 5 mg once-daily in Part 2 (Week 16 and onwards)

<b>Arm title</b>	Part 2: Bardoxolone Methyl 10 mg
------------------	----------------------------------

**Arm description:**

Participants received bardoxolone methyl 10 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 10 mg once-daily in Part 2 (Week 16 and onwards)

Arm type	Experimental
Investigational medicinal product name	Bardoxolone methyl capsules 10mg
Investigational medicinal product code	RTA 402
Other name	RTA 402 capsules
Pharmaceutical forms	Capsule
Routes of administration	Oral use

**Dosage and administration details:**

Participants received bardoxolone methyl 10 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 10 mg once-daily in Part 2 (Week 16 and onwards)

<b>Arm title</b>	Part 2: Bardoxolone Methyl 20 mg
------------------	----------------------------------

**Arm description:**

Participants received bardoxolone methyl 20 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 20 mg once-daily in Part 2 (Week 16 and onwards)

Arm type	Experimental
Investigational medicinal product name	Bardoxolone methyl capsules 20mg
Investigational medicinal product code	RTA 402
Other name	RTA 402 capsules
Pharmaceutical forms	Capsule
Routes of administration	Oral use

**Dosage and administration details:**

Participants received bardoxolone methyl 20 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 20 mg once-daily in Part 2 (Week 16 and onwards)

<b>Arm title</b>	Part 2: Bardoxolone Methyl 10 mg
------------------	----------------------------------

**Arm description:**

Participants in Part 1 started with bardoxolone methyl 5 mg once-daily from Day 1 and escalated to bardoxolone methyl 10 mg once-daily starting at Week 4 thru Week 16. Participants who continued to Part 2 continued to receive the same bardoxolone methyl dose once-daily in Part 2 (Week 16 and onwards)

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

Investigational medicinal product name	Bardoxolone methyl capsules 10mg
Investigational medicinal product code	RTA 402
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Bardoxolone methyl capsules 10mg taken orally once daily in Part 2 Open label.

Investigational medicinal product name	Bardoxolone methyl capsules 10mg
Investigational medicinal product code	RTA 402
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Bardoxolone methyl capsules 10mg taken orally once daily in Part 2 (Open label)

<b>Arm title</b>	Part 2: Bardoxolone methyl capsules 10mg
------------------	--

Arm description:

Participants in Part 1 received Placebo once-daily from Day 1 thru Week 16. Participants who continued to Part 2 initially received bardoxolone methyl 5 mg once-daily from Week 16 thru Week 20 and bardoxolone methyl 10 mg from week 20 onwards

Arm type	Experimental
Investigational medicinal product name	Bardoxolone Methyl 10 mg
Investigational medicinal product code	RTA 402
Other name	RTA 402 capsules
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants in Part 1 received Placebo once-daily from Day 1 thru Week 16. Participants who continued to Part 2 initially received bardoxolone methyl 5 mg once-daily from Week 16 thru Week 20 and bardoxolone methyl 10 mg from week 20 onwards

<b>Number of subjects in period 2<sup>[1]</sup></b>	Part 2: Open-Label Bardoxolone Methyl 2.5 mg	Part 2: Open-Label Bardoxolone Methyl 5 mg	Part 2: Open-Label Bardoxolone Methyl 10 mg
Started	5	11	6
Completed	5	6	3
Not completed	0	5	3
Consent withdrawn by subject	-	1	1
Adverse event, non-fatal	-	2	1
Progressive Disease	-	2	1
Protocol deviation	-	-	-

<b>Number of subjects in period 2<sup>[1]</sup></b>	Part 2: Open-Label Bardoxolone Methyl 20 mg	Part 2: Bardoxolone Methyl 2.5 mg	Part 2: Bardoxolone Methyl 5 mg
Started	9	1	3
Completed	7	0	3
Not completed	2	1	0
Consent withdrawn by subject	-	-	-
Adverse event, non-fatal	1	1	-

Progressive Disease	1	-	-
Protocol deviation	-	-	-

Number of subjects in period 2 <sup>[1]</sup>	Part 2: Bardoxolone Methyl 10 mg	Part 2: Bardoxolone Methyl 20 mg	Part 2: Bardoxolone Methyl 10 mg
Started	3	3	63
Completed	2	2	54
Not completed	1	1	9
Consent withdrawn by subject	-	-	3
Adverse event, non-fatal	1	-	6
Progressive Disease	-	-	-
Protocol deviation	-	1	-

Number of subjects in period 2 <sup>[1]</sup>	Part 2: Bardoxolone methyl capsules 10mg
Started	33
Completed	28
Not completed	5
Consent withdrawn by subject	-
Adverse event, non-fatal	3
Progressive Disease	2
Protocol deviation	-

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: 4 Patients total that completed Part 1 of the trial, elected not to continue into Part 2 of the trial therefore, the number of subjects starting the period will not be consistent with the number completing the preceding period.

## Baseline characteristics

### Reporting groups

Reporting group title	Part 1:Dose Ranging Bardoxolone Methyl 2.5mg
Reporting group description: Participants received bardoxolone methyl 2.5 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 2.5 mg once-daily in Part 2 (Week 16 and onwards)	
Reporting group title	Part 1:Dose-Ranging Bardoxolone Methyl 5mg
Reporting group description: Participants received bardoxolone methyl 5 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 5 mg once-daily in Part 2 (Week 16 and onwards)	
Reporting group title	Part 1:Dose-Ranging Bardoxolone Methyl 10mg
Reporting group description: Participants received bardoxolone methyl 10 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 10 mg once-daily in Part 2 (Week 16 and onwards)	
Reporting group title	Part 1:Dose-Ranging Bardoxolone Methyl 20mg
Reporting group description: Participants received bardoxolone methyl 20 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 20 mg once-daily in Part 2 (Week 16 and onwards)	
Reporting group title	Part 1:Dose-Ranging Placebo 2.5mg
Reporting group description: Participants received bardoxolone methyl 2.5 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 2.5 mg once-daily in Part 2 (Week 16 and onwards)	
Reporting group title	Part 1: Dose-Ranging Placebo 5 mg
Reporting group description: Participants received bardoxolone methyl 5 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 5 mg once-daily in Part 2 (Week 16 and onwards)	
Reporting group title	Part 1: Dose-Ranging Placebo 10 mg
Reporting group description: Participants received bardoxolone methyl 10 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 10 mg once-daily in Part 2 (Week 16 and onwards)	
Reporting group title	Part 1: Dose-Ranging Placebo 20 mg
Reporting group description: Participants received bardoxolone methyl 20 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 20 mg once-daily in Part 2 (Week 16 and onwards)	
Reporting group title	Part 1: Dose Titration: Bardoxolone Methyl 10 mg
Reporting group description: Participants in Part 1 started with bardoxolone methyl 5 mg once-daily from Day 1 and escalated to bardoxolone methyl 10 mg once-daily starting at Week 4 thru Week 16. Participants who continued to Part 2 continued to receive the same bardoxolone methyl dose once-daily in Part 2 (Week 16 and onwards)	
Reporting group title	Part 1: Dose Titration: Placebo 10 mg
Reporting group description: Participants in Part 1 received Placebo once-daily from Day 1 thru Week 16. Participants who continued to Part 2 initially received bardoxolone methyl 5 mg once-daily from Week 16 thru Week 20 and bardoxolone methyl 10 mg from week 20 onwards	

Reporting group values	Part 1:Dose Ranging Bardoxolone Methyl 2.5mg	Part 1:Dose-Ranging Bardoxolone Methyl 5mg	Part 1:Dose-Ranging Bardoxolone Methyl 10mg
Number of subjects	6	12	11
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous			
Part 1: 16-week double-blind, randomized, placebo-controlled treatment period (Day 1 to Week 16) Part 2: Open-label extension period (Week 16 and onwards)			
Units: years			
arithmetic mean standard deviation	52.5 ± 7.15	52.8 ± 14.84	50.6 ± 16.33
Gender categorical Units: Subjects			
Female Male	4 2	10 2	8 3
Ethnicity Units: Subjects			
Hispanic or Latino Not Hispanic or Latino Unknown or Not Reported	2 4 0	3 9 0	0 11 0
Race Units: Subjects			
American Indian or Alaskan Native Asia Native Hawaiian or Pacific Islander Black or African American White More than one Race Unknown or Not Reported	0 0 0 0 6 0 0	0 0 0 1 11 0 0	0 0 0 1 9 0 1
6-Minute Walk Test (6MWT)[1]			
[1] Measure Analysis Population Description: Modified Intent-to-treat (mITT) population, which included all randomized patients who received at least 28 doses of study treatment, did not undergo heart or lung transplantation during the treatment period, and performed at least one-post baseline 6MWT assessment. Only Part 1 patients are included since the primary outcome is the change from baseline in 6MWD through Week 16			
Units: Meters			
arithmetic mean standard deviation	412 ± 19.7	425.8 ± 81	385.7 ± 55.45
Reporting group values	Part 1:Dose-Ranging Bardoxolone Methyl 20mg	Part 1:Dose-Ranging Placebo 2.5mg	Part 1: Dose-Ranging Placebo 5 mg
Number of subjects	12	2	4

Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous			
Part 1: 16-week double-blind, randomized, placebo-controlled treatment period (Day 1 to Week 16) Part 2: Open-label extension period (Week 16 and onwards)			
Units: years			
arithmetic mean	49.6	53	39.5
standard deviation	± 13.06	± 15.56	± 11.27
Gender categorical Units: Subjects			
Female	11	1	4
Male	1	1	0
Ethnicity Units: Subjects			
Hispanic or Latino	1	0	1
Not Hispanic or Latino	11	2	3
Unknown or Not Reported	0	0	0
Race Units: Subjects			
American Indian or Alaskan Native	0	0	0
Asia	0	0	0
Native Hawaiian or Pacific Islander	0	0	0
Black or African American	0	0	3
White	12	2	1
More than one Race	0	0	0
Unknown or Not Reported	0	0	0
6-Minute Walk Test (6MWT)[1]			
[1] Measure Analysis Population Description: Modified Intent-to-treat (mITT) population, which included all randomized patients who received at least 28 doses of study treatment, did not undergo heart or lung transplantation during the treatment period, and performed at least one-post baseline 6MWT assessment. Only Part 1 patients are included since the primary outcome is the change from baseline in 6MWD through Week 16			
Units: Meters			
arithmetic mean	454.5	358	418.9
standard deviation	± 93.01	± 96.17	± 71.18
<b>Reporting group values</b>	Part 1: Dose-Ranging Placebo 10 mg	Part 1: Dose-Ranging Placebo 20 mg	Part 1: Dose Titration: Bardoxolone Methyl 10 mg
Number of subjects	3	4	74

Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous			
Part 1: 16-week double-blind, randomized, placebo-controlled treatment period (Day 1 to Week 16) Part 2: Open-label extension period (Week 16 and onwards)			
Units: years			
arithmetic mean	54.7	51.3	56.4
standard deviation	± .58	± 8.54	± 12.41
Gender categorical Units: Subjects			
Female	2	3	54
Male	1	1	20
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	12
Not Hispanic or Latino	3	4	62
Unknown or Not Reported	0	0	0
Race Units: Subjects			
American Indian or Alaskan Native	0	0	0
Asia	0	0	2
Native Hawaiian or Pacific Islander	0	0	0
Black or African American	0	0	17
White	3	4	54
More than one Race	0	0	0
Unknown or Not Reported	0	0	1
6-Minute Walk Test (6MWT)[1]			
[1] Measure Analysis Population Description: Modified Intent-to-treat (mITT) population, which included all randomized patients who received at least 28 doses of study treatment, did not undergo heart or lung transplantation during the treatment period, and performed at least one-post baseline 6MWT assessment. Only Part 1 patients are included since the primary outcome is the change from baseline in 6MWD through Week 16			
Units: Meters			
arithmetic mean	367	449.3	380.8
standard deviation	± 46.02	± 84.64	± 96.46
<b>Reporting group values</b>	Part 1: Dose Titration: Placebo 10 mg	Total	
Number of subjects	38	166	
Age categorical Units: Subjects			
In utero		0	



Preterm newborn infants (gestational age < 37 wks)		0	
Newborns (0-27 days)		0	
Infants and toddlers (28 days-23 months)		0	
Children (2-11 years)		0	
Adolescents (12-17 years)		0	
Adults (18-64 years)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous			
Part 1: 16-week double-blind, randomized, placebo-controlled treatment period (Day 1 to Week 16) Part 2: Open-label extension period (Week 16 and onwards)			
Units: years			
arithmetic mean	55.6		
standard deviation	± 12.7	-	
Gender categorical			
Units: Subjects			
Female	27	124	
Male	11	42	
Ethnicity			
Units: Subjects			
Hispanic or Latino	7	26	
Not Hispanic or Latino	31	140	
Unknown or Not Reported	0	0	
Race			
Units: Subjects			
American Indian or Alaskan Native	0	0	
Asia	0	2	
Native Hawaiian or Pacific Islander	1	1	
Black or African American	9	31	
White	28	130	
More than one Race	0	0	
Unknown or Not Reported	0	2	
6-Minute Walk Test (6MWT)[1]			
[1] Measure Analysis Population Description: Modified Intent-to-treat (mITT) population, which included all randomized patients who received at least 28 doses of study treatment, did not undergo heart or lung transplantation during the treatment period, and performed at least one-post baseline 6MWT assessment. Only Part 1 patients are included since the primary outcome is the change from baseline in 6MWD through Week 16			
Units: Meters			
arithmetic mean	395.2		
standard deviation	± 84.99	-	

## Subject analysis sets

Subject analysis set title	Part 2: Open-Label Bardoxolone Methyl 2.5 mg
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Part 2: Participants who completed treatment in Part 1 were eligible to continue to the extension Part 2 and continued to receive the same bardoxolone methyl 2.5 mg once-daily from Week 16 onwards.	
Subject analysis set title	Part 2: Open-Label Bardoxolone Methyl 5mg
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Part 2: Participants who completed treatment in Part 1 were eligible to continue to the extension Part 2 and continued to receive the same bardoxolone methyl 5 mg once-daily from Week 16 onwards.

Subject analysis set title	Part 2: Open-Label Bardoxolone Methyl 10 mg
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Part 2: Participants who completed treatment in Part 1 were eligible to continue to the extension Part 2 and continued to receive the same bardoxolone methyl 10 mg once-daily from Week 16 onwards.

Subject analysis set title	Part 2: Open-Label Bardoxolone Methyl 20 mg
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Part 2: Participants who completed treatment in Part 1 were eligible to continue to the extension Part 2 and continued to receive the same bardoxolone methyl 20 mg once-daily from Week 16 onwards.

Subject analysis set title	Part 2: Bardoxolone Methyl 2.5 mg
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Part 2: Participants who completed treatment in Part 1 were eligible to continue to the extension Part 2 and received bardoxolone methyl 2.5 mg once-daily from Week 16 and onwards.

Subject analysis set title	Part 2: Bardoxolone Methyl 5 mg
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Part 2: Participants who completed treatment in Part 1 were eligible to continue to the extension Part 2 and received bardoxolone methyl 5 mg once-daily from Week 16 and onwards.

Subject analysis set title	Part 2: Bardoxolone Methyl 10 mg
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Part 2: Participants who completed treatment in Part 1 were eligible to continue to the extension Part 2 and received bardoxolone methyl 10 mg once-daily from Week 16 and onwards.

Subject analysis set title	Part 2: Bardoxolone Methyl 20 mg
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Part 2: Participants who completed treatment in Part 1 were eligible to continue to the extension Part 2 and received bardoxolone methyl 20 mg once-daily from Week 16 and onwards.

Subject analysis set title	Part 2: Bardoxolone Methyl 10 mg
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Part 2: Participants who completed treatment in Part 1 were eligible to continue to the extension Part 2 and received the same bardoxolone methyl dose once-daily from Week 16 and onwards.

Subject analysis set title	Part 2: Bardoxolone Methyl 10 mg
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Part 2: Participants who completed treatment in Part 1 were eligible to continue to the extension Part 2 and initially received bardoxolone methyl 5 mg once-daily from Week 16 thru Week 20 and bardoxolone methyl 10 mg from Week 20 and onwards.

Subject analysis set title	Part 2: Total
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Part 2: Open-label extension period (Week 16 and onwards)

Subject analysis set title	Change from Baseline through Week 16 for participants with PH
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Part 1: Dose Titration: Bardoxolone Methyl 10 mg

Participants were randomized to receive bardoxolone methyl 10 mg capsules. Participants initially started with bardoxolone methyl 5 mg once-daily from Day 1 and titrated to bardoxolone methyl 10 mg once-daily starting at Week 4 up to Week 16.

Subject analysis set title	Change from Baseline though Week 16 for participants with PH
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Part 1: Dose Titration: Placebo 10 mg

<b>Reporting group values</b>	Part 2: Open-Label Bardoxolone Methyl 2.5 mg	Part 2: Open-Label Bardoxolone Methyl 5mg	Part 2: Open-Label Bardoxolone Methyl 10 mg
Number of subjects	5	11	6
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous			
Part 1: 16-week double-blind, randomized, placebo-controlled treatment period (Day 1 to Week 16) Part 2: Open-label extension period (Week 16 and onwards)			
Units: years			
arithmetic mean standard deviation	54.6 ± 5.55	53.4 ± 14.4	59.2 ± 10.26
Gender categorical Units: Subjects			
Female Male	4 1	9 2	4 2
Ethnicity Units: Subjects			
Hispanic or Latino Not Hispanic or Latino Unknown or Not Reported	2 3 0	2 9 0	0 6 0
Race Units: Subjects			
American Indian or Alaskan Native Asia Native Hawaiian or Pacific Islander Black or African American White More than one Race Unknown or Not Reported	0 0 0 0 5 0 0	0 0 0 1 10 0 0	0 0 0 0 5 0 1
6-Minute Walk Test (6MWT)[1]			
[1] Measure Analysis Population Description: Modified Intent-to-treat (mITT) population, which included all randomized patients who received at least 28 doses of study treatment, did not undergo heart or lung transplantation during the treatment period, and performed at least one-post baseline 6MWT assessment. Only Part 1 patients are included since the primary outcome is the change from baseline in 6MWD through Week 16			
Units: Meters			
arithmetic mean			

standard deviation	±	±	±
--------------------	---	---	---

Reporting group values	Part 2: Open-Label Bardoxolone Methyl 20 mg	Part 2: Bardoxolone Methyl 2.5 mg	Part 2: Bardoxolone Methyl 5 mg
Number of subjects	9	1	3
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous			
Part 1: 16-week double-blind, randomized, placebo-controlled treatment period (Day 1 to Week 16) Part 2: Open-label extension period (Week 16 and onwards)			
Units: years			
arithmetic mean	51	64	40
standard deviation	± 14.76	± 0	± 13.75
Gender categorical Units: Subjects			
Female	9	1	3
Male	0	0	0
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	9	1	3
Unknown or Not Reported	0	0	0
Race Units: Subjects			
American Indian or Alaskan Native	0	0	0
Asia	0	0	0
Native Hawaiian or Pacific Islander	0	0	0
Black or African American	0	0	3
White	9	1	0
More than one Race	0	0	0
Unknown or Not Reported	0	0	0
6-Minute Walk Test (6MWT)[1]			
[1] Measure Analysis Population Description: Modified Intent-to-treat (mITT) population, which included all randomized patients who received at least 28 doses of study treatment, did not undergo heart or lung transplantation during the treatment period, and performed at least one-post baseline 6MWT assessment. Only Part 1 patients are included since the primary outcome is the change from baseline in 6MWD through Week 16			
Units: Meters			
arithmetic mean			
standard deviation	±	±	±

Reporting group values	Part 2: Bardoxolone Methyl 10 mg	Part 2: Bardoxolone Methyl 20 mg	Part 2: Bardoxolone Methyl 10 mg
Number of subjects	3	3	63
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous			
Part 1: 16-week double-blind, randomized, placebo-controlled treatment period (Day 1 to Week 16) Part 2: Open-label extension period (Week 16 and onwards)			
Units: years			
arithmetic mean standard deviation	54.7 ± .58	47.7 ± 5.69	56.5 ± 12.23
Gender categorical Units: Subjects			
Female Male	2 1	3 0	47 16
Ethnicity Units: Subjects			
Hispanic or Latino Not Hispanic or Latino Unknown or Not Reported	0 3 0	0 3 0	10 53 0
Race Units: Subjects			
American Indian or Alaskan Native Asia Native Hawaiian or Pacific Islander Black or African American White More than one Race Unknown or Not Reported	0 0 0 0 3 0 0	0 0 0 0 3 0 0	0 1 0 14 47 0 1
6-Minute Walk Test (6MWT)[1]			
[1] Measure Analysis Population Description: Modified Intent-to-treat (mITT) population, which included all randomized patients who received at least 28 doses of study treatment, did not undergo heart or lung transplantation during the treatment period, and performed at least one-post baseline 6MWT assessment. Only Part 1 patients are included since the primary outcome is the change from baseline in 6MWD through Week 16			
Units: Meters			
arithmetic mean standard deviation	±	±	±
Reporting group values	Part 2: Bardoxolone Methyl 10 mg	Part 2: Total	Change from Baseline though Week 16 for participants with PH

Number of subjects	33	137	70
Age categorical			
Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous			
Part 1: 16-week double-blind, randomized, placebo-controlled treatment period (Day 1 to Week 16) Part 2: Open-label extension period (Week 16 and onwards)			
Units: years			
arithmetic mean	56.7	55.5	
standard deviation	± 12.44	± 12.38	±
Gender categorical			
Units: Subjects			
Female	24	106	
Male	9	31	
Ethnicity			
Units: Subjects			
Hispanic or Latino	7	21	
Not Hispanic or Latino	26	116	
Unknown or Not Reported	0	0	
Race			
Units: Subjects			
American Indian or Alaskan Native	0	0	
Asia	0	1	
Native Hawaiian or Pacific Islander	0	0	
Black or African American	5	23	
White	28	111	
More than one Race	0	0	
Unknown or Not Reported	0	2	
6-Minute Walk Test (6MWT)[1]			
[1] Measure Analysis Population Description: Modified Intent-to-treat (mITT) population, which included all randomized patients who received at least 28 doses of study treatment, did not undergo heart or lung transplantation during the treatment period, and performed at least one-post baseline 6MWT assessment. Only Part 1 patients are included since the primary outcome is the change from baseline in 6MWD through Week 16			
Units: Meters			
arithmetic mean			
standard deviation	±	±	±
<b>Reporting group values</b>	Change from Baseline though Week 16 for participants with PH		
Number of subjects	70		

Age categorical			
Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous			
Part 1: 16-week double-blind, randomized, placebo-controlled treatment period (Day 1 to Week 16) Part 2: Open-label extension period (Week 16 and onwards)			
Units: years			
arithmetic mean standard deviation	±		
Gender categorical			
Units: Subjects			
Female Male			
Ethnicity			
Units: Subjects			
Hispanic or Latino Not Hispanic or Latino Unknown or Not Reported			
Race			
Units: Subjects			
American Indian or Alaskan Native Asia Native Hawaiian or Pacific Islander Black or African American White More than one Race Unknown or Not Reported			
6-Minute Walk Test (6MWT)[1]			
[1] Measure Analysis Population Description: Modified Intent-to-treat (mITT) population, which included all randomized patients who received at least 28 doses of study treatment, did not undergo heart or lung transplantation during the treatment period, and performed at least one-post baseline 6MWT assessment. Only Part 1 patients are included since the primary outcome is the change from baseline in 6MWD through Week 16			
Units: Meters			
arithmetic mean standard deviation	±		

## End points

### End points reporting groups

Reporting group title	Part 1:Dose Ranging Bardoxolone Methyl 2.5mg
Reporting group description: Participants received bardoxolone methyl 2.5 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 2.5 mg once-daily in Part 2 (Week 16 and onwards)	
Reporting group title	Part 1:Dose-Ranging Bardoxolone Methyl 5mg
Reporting group description: Participants received bardoxolone methyl 5 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 5 mg once-daily in Part 2 (Week 16 and onwards)	
Reporting group title	Part 1:Dose-Ranging Bardoxolone Methyl 10mg
Reporting group description: Participants received bardoxolone methyl 10 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 10 mg once-daily in Part 2 (Week 16 and onwards)	
Reporting group title	Part 1:Dose-Ranging Bardoxolone Methyl 20mg
Reporting group description: Participants received bardoxolone methyl 20 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 20 mg once-daily in Part 2 (Week 16 and onwards)	
Reporting group title	Part 1:Dose-Ranging Placebo 2.5mg
Reporting group description: Participants received bardoxolone methyl 2.5 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 2.5 mg once-daily in Part 2 (Week 16 and onwards)	
Reporting group title	Part 1: Dose-Ranging Placebo 5 mg
Reporting group description: Participants received bardoxolone methyl 5 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 5 mg once-daily in Part 2 (Week 16 and onwards)	
Reporting group title	Part 1: Dose-Ranging Placebo 10 mg
Reporting group description: Participants received bardoxolone methyl 10 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 10 mg once-daily in Part 2 (Week 16 and onwards)	
Reporting group title	Part 1: Dose-Ranging Placebo 20 mg
Reporting group description: Participants received bardoxolone methyl 20 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 20 mg once-daily in Part 2 (Week 16 and onwards)	
Reporting group title	Part 1: Dose Titration: Bardoxolone Methyl 10 mg
Reporting group description: Participants in Part 1 started with bardoxolone methyl 5 mg once-daily from Day 1 and escalated to bardoxolone methyl 10 mg once-daily starting at Week 4 thru Week 16. Participants who continued to Part 2 continued to receive the same bardoxolone methyl dose once-daily in Part 2 (Week 16 and onwards)	
Reporting group title	Part 1: Dose Titration: Placebo 10 mg
Reporting group description: Participants in Part 1 received Placebo once-daily from Day 1 thru Week 16. Participants who continued to Part 2 initially received bardoxolone methyl 5 mg once-daily from Week 16 thru Week 20 and bardoxolone methyl 10 mg from week 20 onwards	
Reporting group title	Part 2: Open-Label Bardoxolone Methyl 2.5 mg
Reporting group description: Participants received bardoxolone methyl 2.5 mg once-daily in Part 1 (Day 1 to Week 16). Participants	



who continued to Part 2 continued to receive the same bardoxolone methyl 2.5 mg once-daily in Part 2 (Week 16 and onwards)

Reporting group title	Part 2: Open-Label Bardoxolone Methyl 5 mg
-----------------------	--

Reporting group description:

Participants received bardoxolone methyl 5 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 5 mg once-daily in Part 2 (Week 16 and onwards)

Reporting group title	Part 2: Open-Label Bardoxolone Methyl 10 mg
-----------------------	---

Reporting group description:

Participants received bardoxolone methyl 10 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 10 mg once-daily in Part 2 (Week 16 and onwards)

Reporting group title	Part 2: Open-Label Bardoxolone Methyl 20 mg
-----------------------	---

Reporting group description:

Participants received bardoxolone methyl 20 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 20 mg once-daily in Part 2 (Week 16 and onwards)

Reporting group title	Part 2: Bardoxolone Methyl 2.5 mg
-----------------------	-----------------------------------

Reporting group description:

Participants received bardoxolone methyl 2.5 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 2.5 mg once-daily in Part 2 (Week 16 and onwards)

Reporting group title	Part 2: Bardoxolone Methyl 5 mg
-----------------------	---------------------------------

Reporting group description:

Participants received bardoxolone methyl 5 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 5 mg once-daily in Part 2 (Week 16 and onwards)

Reporting group title	Part 2: Bardoxolone Methyl 10 mg
-----------------------	----------------------------------

Reporting group description:

Participants received bardoxolone methyl 10 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 10 mg once-daily in Part 2 (Week 16 and onwards)

Reporting group title	Part 2: Bardoxolone Methyl 20 mg
-----------------------	----------------------------------

Reporting group description:

Participants received bardoxolone methyl 20 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 20 mg once-daily in Part 2 (Week 16 and onwards)

Reporting group title	Part 2: Bardoxolone Methyl 10 mg
-----------------------	----------------------------------

Reporting group description:

Participants in Part 1 started with bardoxolone methyl 5 mg once-daily from Day 1 and escalated to bardoxolone methyl 10 mg once-daily starting at Week 4 thru Week 16. Participants who continued to Part 2 continued to receive the same bardoxolone methyl dose once-daily in Part 2 (Week 16 and onwards)

Reporting group title	Part 2: Bardoxolone methyl capsules 10mg
-----------------------	--

Reporting group description:

Participants in Part 1 received Placebo once-daily from Day 1 thru Week 16. Participants who continued to Part 2 initially received bardoxolone methyl 5 mg once-daily from Week 16 thru Week 20 and bardoxolone methyl 10 mg from week 20 onwards

Subject analysis set title	Part 2: Open-Label Bardoxolone Methyl 2.5 mg
----------------------------	--

Subject analysis set type	Intention-to-treat
---------------------------	--------------------

Subject analysis set description:

Part 2: Participants who completed treatment in Part 1 were eligible to continue to the extension Part 2 and continued to receive the same bardoxolone methyl 2.5 mg once-daily from Week 16 onwards.

Subject analysis set title	Part 2: Open-Label Bardoxolone Methyl 5mg
----------------------------	---

Subject analysis set type	Intention-to-treat
---------------------------	--------------------

Subject analysis set description:

Part 2: Participants who completed treatment in Part 1 were eligible to continue to the extension Part 2 and continued to receive the same bardoxolone methyl 5 mg once-daily from Week 16 onwards.

Subject analysis set title	Part 2: Open-Label Bardoxolone Methyl 10 mg
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Part 2: Participants who completed treatment in Part 1 were eligible to continue to the extension Part 2 and continued to receive the same bardoxolone methyl 10 mg once-daily from Week 16 onwards.	
Subject analysis set title	Part 2: Open-Label Bardoxolone Methyl 20 mg
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Part 2: Participants who completed treatment in Part 1 were eligible to continue to the extension Part 2 and continued to receive the same bardoxolone methyl 20 mg once-daily from Week 16 onwards.	
Subject analysis set title	Part 2: Bardoxolone Methyl 2.5 mg
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Part 2: Participants who completed treatment in Part 1 were eligible to continue to the extension Part 2 and received bardoxolone methyl 2.5 mg once-daily from Week 16 and onwards.	
Subject analysis set title	Part 2: Bardoxolone Methyl 5 mg
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Part 2: Participants who completed treatment in Part 1 were eligible to continue to the extension Part 2 and received bardoxolone methyl 5 mg once-daily from Week 16 and onwards.	
Subject analysis set title	Part 2: Bardoxolone Methyl 10 mg
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Part 2: Participants who completed treatment in Part 1 were eligible to continue to the extension Part 2 and received bardoxolone methyl 10 mg once-daily from Week 16 and onwards.	
Subject analysis set title	Part 2: Bardoxolone Methyl 20 mg
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Part 2: Participants who completed treatment in Part 1 were eligible to continue to the extension Part 2 and received bardoxolone methyl 20 mg once-daily from Week 16 and onwards.	
Subject analysis set title	Part 2: Bardoxolone Methyl 10 mg
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Part 2: Participants who completed treatment in Part 1 were eligible to continue to the extension Part 2 and received the same bardoxolone methyl dose once-daily from Week 16 and onwards.	
Subject analysis set title	Part 2: Bardoxolone Methyl 10 mg
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Part 2: Participants who completed treatment in Part 1 were eligible to continue to the extension Part 2 and initially received bardoxolone methyl 5 mg once-daily from Week 16 thru Week 20 and bardoxolone methyl 10 mg from Week 20 and onwards.	
Subject analysis set title	Part 2: Total
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Part 2: Open-label extension period (Week 16 and onwards)	
Subject analysis set title	Change from Baseline though Week 16 for participants with PH
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Part 1: Dose Titration: Bardoxolone Methyl 10 mg	
Participants were randomized to receive bardoxolone methyl 10 mg capsules. Participants initially started with bardoxolone methyl 5 mg once-daily from Day 1 and titrated to bardoxolone methyl 10 mg once-daily starting at Week 4 up to Week 16.	
Subject analysis set title	Change from Baseline though Week 16 for participants with PH
Subject analysis set type	Intention-to-treat

**Primary: Change From Baseline Though Week 16 in 6-Minute Walk Distance (6MWD) for Bardoxolone Methyl Compared to Placebo**

End point title	Change From Baseline Though Week 16 in 6-Minute Walk Distance (6MWD) for Bardoxolone Methyl Compared to Placebo
-----------------	---

End point description:

Overall treatment effect in exercise capacity, as measured by the total distance walked in 6 minutes (6MWD) mean change from baseline though Week 16. A lower 6MWD reflects greater severity thus, a positive change from baseline suggests an improvement.

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

End point timeframe:

Baseline through Week 16

End point values	Part 1:Dose Ranging Bardoxolone Methyl 2.5mg	Part 1:Dose Ranging Bardoxolone Methyl 5mg	Part 1:Dose Ranging Bardoxolone Methyl 10mg	Part 1:Dose Ranging Bardoxolone Methyl 20mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	12	9	10
Units: Meters				
arithmetic mean (standard deviation)	32.5 (± 29.14)	24 (± 30.08)	3.4 (± 31.28)	-3.2 (± 39.53)

End point values	Part 1:Dose Ranging Placebo 2.5mg	Part 1: Dose Ranging Placebo 5 mg	Part 1: Dose Ranging Placebo 10 mg	Part 1: Dose Ranging Placebo 20 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	4	3	4
Units: Meters				
arithmetic mean (standard deviation)	20.3 (± 13.08)	24.6 (± 59.4)	23.8 (± 34.54)	-21.8 (± 4.17)

End point values	Part 1: Dose Titration: Bardoxolone Methyl 10 mg	Part 1: Dose Titration: Placebo 10 mg	Change from Baseline though Week 16 for participants with PH	Change from Baseline though Week 16 for participants with PH
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	29	17	41 <sup>[1]</sup>	21 <sup>[2]</sup>
Units: Meters				
arithmetic mean (standard deviation)	13.9 (± 41.15)	19.4 (± 21.06)	7.6 (± 32.01)	10.8 (± 32.01)

Notes:

[1] - Change from Baseline though Week 16 for participants with PH in the Part 1: Dose Titration Bard 10mg

[2] - Change from Baseline though Week 16 for participants w/PH in the Part 1 Dose Titration Placebo 10mg

## Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Comparison Group Selection      Part 1: Dose-Ranging Bardoxolone Methyl 2.5 mg/Part 2: Open-Label, Part 1: Dose-Ranging Bardoxolone Methyl 5 mg/Part 2: Open-Label, Part 1: Dose-Ranging Bardoxolone Methyl 10 mg/Part 2: Open-Label, Part 1: Dose-Ranging Bardoxolone Methyl 20 mg/Part 2: Open-Label, Part 1: Dose-Ranging Placebo 2.5 mg/Part 2: Bardoxolone Methyl 2.5 mg, Part 1: Dose-Ranging Placebo 5 mg/Part 2: Bardoxolone Methyl 5 mg, Part 1: Dose-Ranging Placebo 10 mg/Part 2: Bardoxolone Methyl 10 mg, Pa	
Comparison groups	Part 1:Dose-Ranging Bardoxolone Methyl 10mg v Part 1:Dose-Ranging Bardoxolone Methyl 20mg v Part 1:Dose-Ranging Placebo 2.5mg v Part 1: Dose-Ranging Placebo 5 mg v Part 1: Dose-Ranging Placebo 10 mg v Part 1: Dose-Ranging Placebo 20 mg v Part 1: Dose Titration: Bardoxolone Methyl 10 mg v Part 1: Dose Titration: Placebo 10 mg v Part 1:Dose-Ranging Bardoxolone Methyl 5mg v Part 1:Dose Ranging Bardoxolone Methyl 2.5mg
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority <sup>[3]</sup>
P-value	= 0.8133 <sup>[4]</sup>
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-1.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.22
upper limit	12.74

Notes:

[3] - Overall treatment effect in participants with PAH. Mean overall treatment effect across all visits for change from baseline in 6MWD was estimated and compared with placebo through 16 weeks of treatment using mixed-model repeated measures (MMRM), with treatment group, visit, and the interaction between treatment and visit as fixed factors. A compound symmetry covariance matrix was assumed. Data from Wks 4, 8, 12, and 16 used in the model with the change from baseline at Wk16 as primary endpoint.

[4] - The p-value comparison is for the difference in the change in 6WMD from baseline at Week 16 for bardoxolone methyl relative to placebo in participants with pulmonary arterial hypertension (PAH)

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Part 1: Dose Titration: Bardoxolone Methyl 10 mg/Part 2: Bardoxolone Methyl 10 mg, Part 1: Dose Titration: Placebo 10 mg/Part 2: Bardoxolone Methyl 10 mg	
Comparison groups	Part 1: Dose Titration: Bardoxolone Methyl 10 mg v Part 1: Dose Titration: Placebo 10 mg
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority <sup>[5]</sup>
P-value	= 0.759 <sup>[6]</sup>
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-3.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.54
upper limit	17.2

---

Notes:

[5] - Overall treatment effect in participants with PH. Mean overall treatment effect across all visits for change from baseline in 6MWD was estimated & compared with placebo through 16 wks of treatment using mixed-model repeated measures (MMRM), with treatment group, visit, and the interaction between treatment & visit as fixed factors. Compound symmetry covariance matrix was assumed. Data from Wks 4, 8, 12, and 16 were used in the model with the change from baseline at Wk 16 as the primary endpoint

[6] - The p-value comparison is for the difference in the change in 6WMD from baseline at Week 16 for bardoxolone methyl relative to placebo in participants with pulmonary hypertension (PH)

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Part 1: 16-week double-blind, randomized, placebo-controlled treatment period (Day 1 to Week 16).

Part 2: Open-label extension period (Week 16 onwards). Part 2 is the extension period, patients were to stay until study drug became available through EAP.

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

### Dictionary used

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

Dictionary version	15
--------------------	----

### Reporting groups

Reporting group title	Part 1 of Part 1: Dose-Ranging BM 5 mg/Part 2: Open-Label
-----------------------	---

Reporting group description:

Part 1: Participants were randomized to receive bardoxolone methyl 5 mg once-daily from Day 1 to Week 16.

Reporting group title	Part 1 of Part 1: Dose-Ranging BM 2.5 mg/Part 2: Open-Label
-----------------------	---

Reporting group description:

Part 1: Participants were randomized to receive bardoxolone methyl 2.5 mg once-daily from Day 1 to Week 16.

Reporting group title	Part 1 of Part 1: Dose-Ranging BM 10 mg/Part 2: Open-Label
-----------------------	--

Reporting group description:

Part 1: Participants were randomized to receive bardoxolone methyl 10 mg once-daily from Day 1 to Week 16.

Reporting group title	Part 1 of Part 1: Dose-Ranging BM 20 mg/Part 2: Open-Label
-----------------------	--

Reporting group description:

Part 1: Participants were randomized to receive bardoxolone methyl 20 mg once-daily from Day 1 to Week 16.

Reporting group title	Part 1 of Part 1: Dose-Ranging Pbo 2.5 mg/Part 2: BM 2.5 mg
-----------------------	---

Reporting group description:

Part 1: Participants were randomized to receive bardoxolone methyl matching placebo 2.5 mg capsules once-daily from Day 1 to Week 16.

Reporting group title	Part 1 of Part 1: Dose-Ranging Pbo 5 mg/Part 2: BM 5 mg
-----------------------	---

Reporting group description:

Part 1: Participants were randomized to receive bardoxolone methyl matching placebo 5 mg capsules once-daily from Day 1 to Week 16.

Reporting group title	Part 1 of Part 1: Dose-Ranging Pbo 10 mg/Part 2: BM 10 mg
-----------------------	---

Reporting group description:

Part 1: Participants were randomized to receive bardoxolone methyl matching placebo 10 mg capsules once-daily from Day 1 to Week 16.

Reporting group title	Part 1 of Part 1: Dose Titration: BM 10 mg/Part 2: BM 10 mg
-----------------------	---

Reporting group description:

Part 1: Participants were randomized to receive bardoxolone methyl 10 mg capsules. Participants initially started with bardoxolone methyl 5 mg once-daily from Day 1 and titrated to bardoxolone methyl 10 mg once-daily starting at Week 4 up to Week 16.

Reporting group title	Part 1 of Part 1: Dose-Ranging Pbo 20 mg/Part 2: BM 20 mg
-----------------------	---

Reporting group description:

Part 1: Participants were randomized to receive bardoxolone methyl matching placebo 20 mg capsules once-daily from Day 1 to Week 16.

Reporting group title	Part 1 of Part 1: Dose Titration: Pbo 10 mg/Part 2: BM 10 mg
-----------------------	--

Reporting group description:

Part 1: Participants were randomized to receive bardoxolone methyl matching placebo 10 mg capsules once-daily from Day 1 to Week 16.

Reporting group title	Part 2 of Part 1: Dose-Ranging BM 2.5 mg/Part 2: Open-Label
-----------------------	---

Reporting group description:

Part 2: Participants who completed treatment receiving bardoxolone methyl 2.5 mg once daily in Part 1 were eligible to continue to the extension Part 2 and continued to receive the same bardoxolone methyl 2.5 mg once-daily from Week 16 onwards.

Reporting group title	Part 2 of Part 1: Dose-Ranging BM 5 mg/Part 2: Open-Label
-----------------------	---

Reporting group description:

Part 2: Participants who completed treatment receiving bardoxolone methyl 5 mg once daily in Part 1 were eligible to continue to the extension Part 2 and continued to receive the same bardoxolone methyl 5 mg once-daily from Week 16 onwards.

Reporting group title	Part 2 of Part 1: Dose-Ranging BM 10 mg/Part 2: Open-Label
-----------------------	--

Reporting group description:

Part 2: Participants who completed treatment receiving bardoxolone methyl 10 mg once daily in Part 1 were eligible to continue to the extension Part 2 and continued to receive the same bardoxolone methyl 10 mg once-daily from Week 16 onwards.

Reporting group title	Part 2 of Part 1: Dose-Ranging BM 20 mg/Part 2: Open-Label
-----------------------	--

Reporting group description:

Part 2: Participants who completed treatment receiving bardoxolone methyl 20 mg once daily in Part 1 were eligible to continue to the extension Part 2 and continued to receive the same bardoxolone methyl 20 mg once-daily from Week 16 onwards.

Reporting group title	Part 2 of Part 1: Dose-Ranging Pbo 2.5 mg/Part 2: BM 2.5 mg
-----------------------	---

Reporting group description:

Part 2: Participants who completed bardoxolone methyl matching placebo 2.5 mg capsules once-daily treatment in Part 1 were eligible to continue to the extension Part 2 and received bardoxolone methyl 2.5 mg once-daily from Week 16 and onwards.

Reporting group title	Part 2 of Part 1: Dose-Ranging Pbo 5 mg/Part 2: BM 5 mg
-----------------------	---

Reporting group description:

Part 2: Participants who completed bardoxolone methyl matching placebo 5 mg capsules once-daily treatment in Part 1 were eligible to continue to the extension Part 2 and received bardoxolone methyl 5 mg once-daily from Week 16 and onwards.

Reporting group title	Part 2 of Part 1: Dose-Ranging Pbo 10 mg/Part 2: BM 10 mg
-----------------------	---

Reporting group description:

Part 2: Participants who completed bardoxolone methyl matching placebo 10 mg capsules once-daily treatment in Part 1 were eligible to continue to the extension Part 2 and received bardoxolone methyl 10 mg once-daily from Week 16 and onwards.

Reporting group title	Part 2 of Part 1: Dose-Ranging Pbo 20 mg/Part 2: BM 20 mg
-----------------------	---

Reporting group description:

Part 2: Participants who completed bardoxolone methyl matching placebo 20 mg capsules once-daily treatment in Part 1 were eligible to continue to the extension Part 2 and received bardoxolone methyl 20 mg once-daily from Week 16 and onwards.

Reporting group title	Part 2 of Part 1: Dose Titration: BM 10 mg/Part 2: BM 10 mg
-----------------------	---

Reporting group description:

Part 2: Participants who completed treatment titrated to 10 mg bardoxolone methyl in Part 1 were eligible to continue to the extension Part 2 and received bardoxolone methyl 10 mg once-daily from Week 16 and onwards.

Reporting group title	Part 2 of Part 1: Dose Titration: Pbo 10 mg/Part 2: BM 10 mg
-----------------------	--

Reporting group description:

Part 2: Participants who completed bardoxolone methyl matching placebo 10 mg capsules once-daily treatment in Part 1 were eligible to continue to the extension Part 2 and initially received bardoxolone methyl 5 mg once-daily from Week 16 thru Week 20 and bardoxolone methyl 10 mg from Week 20 and onwards.

Serious adverse events	Part 1 of Part 1: Dose-Ranging BM 5 mg/Part 2: Open-Label	Part 1 of Part 1: Dose-Ranging BM 2.5 mg/Part 2: Open-Label	Part 1 of Part 1: Dose-Ranging BM 10 mg/Part 2: Open-Label
Total subjects affected by serious adverse events			

subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Raynaud's phenomenon			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
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			
General physical health deterioration			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Haemorrhagic ovarian cyst			



subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
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			
Acute respiratory failure			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleuritic pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
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 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
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 fibrosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
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 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
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			
International normalised ratio increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
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			
Hip fracture			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax traumatic			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
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			
Acute right ventricular failure			

subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
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 acute			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
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 tamponade			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
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 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular arrhythmia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
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			
Dizziness			

subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embololic stroke			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
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 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
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 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
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			
Nephrolithiasis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
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 failure acute			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Systemic lupus erythematosus subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
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 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Campylobacter gastroenteritis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea infectious			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia urinary tract infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
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 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salpingitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
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 enterococcal			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fluid overload			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Serious adverse events</b>	Part 1 of Part 1: Dose-Ranging BM 20 mg/Part 2: Open-Label	Part 1 of Part 1: Dose-Ranging Pbo 2.5 mg/Part 2: BM 2.5 mg	Part 1 of Part 1: Dose-Ranging Pbo 5 mg/Part 2: BM 5 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 12 (16.67%)	0 / 2 (0.00%)	0 / 4 (0.00%)
number of deaths (all causes)	0	0	0

number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Raynaud's phenomenon			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
General physical health deterioration			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Haemorrhagic ovarian cyst			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal			



disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleuritic pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary arterial hypertension			
subjects affected / exposed	1 / 12 (8.33%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary fibrosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary hypertension			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			

Delirium			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
International normalised ratio increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Hip fracture			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax traumatic			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute right ventricular failure			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			

subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure acute			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac tamponade			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Right ventricular failure			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular arrhythmia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolic stroke			

subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			

subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure acute			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic lupus erythematosus			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Infections and infestations Bronchitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 12 (0.00%) 0 / 0 0 / 0	 0 / 2 (0.00%) 0 / 0 0 / 0	 0 / 4 (0.00%) 0 / 0 0 / 0
Campylobacter gastroenteritis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 12 (0.00%) 0 / 0 0 / 0	 0 / 2 (0.00%) 0 / 0 0 / 0	 0 / 4 (0.00%) 0 / 0 0 / 0
Cellulitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 12 (0.00%) 0 / 0 0 / 0	 0 / 2 (0.00%) 0 / 0 0 / 0	 0 / 4 (0.00%) 0 / 0 0 / 0
Diarrhoea infectious subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 12 (0.00%) 0 / 0 0 / 0	 0 / 2 (0.00%) 0 / 0 0 / 0	 0 / 4 (0.00%) 0 / 0 0 / 0
Escherichia urinary tract infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 12 (0.00%) 0 / 0 0 / 0	 0 / 2 (0.00%) 0 / 0 0 / 0	 0 / 4 (0.00%) 0 / 0 0 / 0
Influenza subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 12 (0.00%) 0 / 0 0 / 0	 0 / 2 (0.00%) 0 / 0 0 / 0	 0 / 4 (0.00%) 0 / 0 0 / 0
Lung infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 12 (0.00%) 0 / 0 0 / 0	 0 / 2 (0.00%) 0 / 0 0 / 0	 0 / 4 (0.00%) 0 / 0 0 / 0
Pneumonia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 1 / 12 (8.33%) 1 / 1 0 / 0	 0 / 2 (0.00%) 0 / 0 0 / 0	 0 / 4 (0.00%) 0 / 0 0 / 0
Salpingitis			

subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection enterococcal			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fluid overload			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

<b>Serious adverse events</b>	Part 1 of Part 1: Dose-Ranging Pbo 10 mg/Part 2: BM 10 mg	Part 1 of Part 1: Dose Titration: BM 10 mg/Part 2: BM 10 mg	Part 1 of Part 1: Dose-Ranging Pbo 20 mg/Part 2: BM 20 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	7 / 74 (9.46%)	1 / 4 (25.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			

subjects affected / exposed	0 / 3 (0.00%)	1 / 74 (1.35%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Raynaud's phenomenon			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
General physical health deterioration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 74 (1.35%)	0 / 4 (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
Reproductive system and breast disorders			
Haemorrhagic ovarian cyst			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			



subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 74 (1.35%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 3 (0.00%)	1 / 74 (1.35%)	0 / 4 (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
Pleuritic pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary arterial hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary fibrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Delirium			

subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
International normalised ratio increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Hip fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax traumatic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute right ventricular failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			

subjects affected / exposed	0 / 3 (0.00%)	1 / 74 (1.35%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure acute			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac tamponade			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Right ventricular failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular arrhythmia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 74 (1.35%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolic stroke			

subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			

subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure acute			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic lupus erythematosus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Infections and infestations Bronchitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 3 (0.00%) 0 / 0 0 / 0	0 / 74 (0.00%) 0 / 0 0 / 0	0 / 4 (0.00%) 0 / 0 0 / 0
Campylobacter gastroenteritis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 3 (0.00%) 0 / 0 0 / 0	0 / 74 (0.00%) 0 / 0 0 / 0	0 / 4 (0.00%) 0 / 0 0 / 0
Cellulitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 3 (0.00%) 0 / 0 0 / 0	1 / 74 (1.35%) 0 / 1 0 / 0	0 / 4 (0.00%) 0 / 0 0 / 0
Diarrhoea infectious subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 3 (0.00%) 0 / 0 0 / 0	0 / 74 (0.00%) 0 / 0 0 / 0	0 / 4 (0.00%) 0 / 0 0 / 0
Escherichia urinary tract infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 3 (0.00%) 0 / 0 0 / 0	0 / 74 (0.00%) 0 / 0 0 / 0	0 / 4 (0.00%) 0 / 0 0 / 0
Influenza subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 3 (0.00%) 0 / 0 0 / 0	0 / 74 (0.00%) 0 / 0 0 / 0	0 / 4 (0.00%) 0 / 0 0 / 0
Lung infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 3 (0.00%) 0 / 0 0 / 0	0 / 74 (0.00%) 0 / 0 0 / 0	0 / 4 (0.00%) 0 / 0 0 / 0
Pneumonia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 3 (0.00%) 0 / 0 0 / 0	0 / 74 (0.00%) 0 / 0 0 / 0	0 / 4 (0.00%) 0 / 0 0 / 0
Salpingitis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection enterococcal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fluid overload			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

<b>Serious adverse events</b>	Part 1 of Part 1: Dose Titration: Pbo 10 mg/Part 2: BM 10 mg	Part 2 of Part 1: Dose-Ranging BM 2.5 mg/Part 2: Open-Label	Part 2 of Part 1: Dose-Ranging BM 5 mg/Part 2: Open- Label
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 38 (5.26%)	2 / 5 (40.00%)	5 / 11 (45.45%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			

subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Raynaud's phenomenon			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
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			
General physical health deterioration			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Haemorrhagic ovarian cyst			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
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			
Acute respiratory failure			



subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleuritic pain			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
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 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
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 fibrosis			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary hypertension			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Delirium			

subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
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			
International normalised ratio increased			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
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			
Hip fracture			
subjects affected / exposed	0 / 38 (0.00%)	1 / 5 (20.00%)	0 / 11 (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
Pneumothorax traumatic			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
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			
Acute right ventricular failure			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			

subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure acute			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
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 tamponade			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
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 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular arrhythmia			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
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			
Dizziness			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolic stroke			

subjects affected / exposed	0 / 38 (0.00%)	1 / 5 (20.00%)	0 / 11 (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
Syncope			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
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 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			

subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
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			
Nephrolithiasis			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
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 failure acute			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 38 (0.00%)	1 / 5 (20.00%)	0 / 11 (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
Pain in extremity			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic lupus erythematosus			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Infections and infestations Bronchitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 38 (0.00%) 0 / 0 0 / 0	0 / 5 (0.00%) 0 / 0 0 / 0	0 / 11 (0.00%) 0 / 0 0 / 0
Campylobacter gastroenteritis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 38 (0.00%) 0 / 0 0 / 0	0 / 5 (0.00%) 0 / 0 0 / 0	0 / 11 (0.00%) 0 / 0 0 / 0
Cellulitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 38 (0.00%) 0 / 0 0 / 0	0 / 5 (0.00%) 0 / 0 0 / 0	0 / 11 (0.00%) 0 / 0 0 / 0
Diarrhoea infectious subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 38 (0.00%) 0 / 0 0 / 0	0 / 5 (0.00%) 0 / 0 0 / 0	0 / 11 (0.00%) 0 / 0 0 / 0
Escherichia urinary tract infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 38 (0.00%) 0 / 0 0 / 0	0 / 5 (0.00%) 0 / 0 0 / 0	0 / 11 (0.00%) 0 / 0 0 / 0
Influenza subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 38 (2.63%) 0 / 1 0 / 0	0 / 5 (0.00%) 0 / 0 0 / 0	0 / 11 (0.00%) 0 / 0 0 / 0
Lung infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 38 (2.63%) 0 / 1 0 / 0	0 / 5 (0.00%) 0 / 0 0 / 0	0 / 11 (0.00%) 0 / 0 0 / 0
Pneumonia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 38 (2.63%) 0 / 1 0 / 0	0 / 5 (0.00%) 0 / 0 0 / 0	1 / 11 (9.09%) 0 / 1 0 / 0
Salpingitis			

subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
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 enterococcal			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fluid overload			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

<b>Serious adverse events</b>	Part 2 of Part 1: Dose-Ranging BM 10 mg/Part 2: Open- Label	Part 2 of Part 1: Dose-Ranging BM 20 mg/Part 2: Open- Label	Part 2 of Part 1: Dose-Ranging Pbo 2.5 mg/Part 2: BM 2.5 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 6 (50.00%)	6 / 9 (66.67%)	0 / 1 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			

subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (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
Raynaud's phenomenon			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
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			
General physical health deterioration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Haemorrhagic ovarian cyst			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
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			
Acute respiratory failure			



subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleuritic pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
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 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (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
Pulmonary embolism			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
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 fibrosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
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	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Delirium			

subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
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			
International normalised ratio increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
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			
Hip fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax traumatic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
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			
Acute right ventricular failure			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			

subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
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 acute			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
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 tamponade			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
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 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular arrhythmia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
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			
Dizziness			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolic stroke			

subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (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
Transient ischaemic attack			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (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
Ascites			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			

subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
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			
Nephrolithiasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
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 failure acute			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic lupus erythematosus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
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 occurrences causally related to treatment / all deaths causally related to treatment / all	  0 / 6 (0.00%) 0 / 0 0 / 0	  0 / 9 (0.00%) 0 / 0 0 / 0	  0 / 1 (0.00%) 0 / 0 0 / 0
Campylobacter gastroenteritis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 6 (0.00%) 0 / 0 0 / 0	 0 / 9 (0.00%) 0 / 0 0 / 0	 0 / 1 (0.00%) 0 / 0 0 / 0
Cellulitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 1 / 6 (16.67%) 0 / 1 0 / 0	 0 / 9 (0.00%) 0 / 0 0 / 0	 0 / 1 (0.00%) 0 / 0 0 / 0
Diarrhoea infectious subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 6 (0.00%) 0 / 0 0 / 0	 0 / 9 (0.00%) 0 / 0 0 / 0	 0 / 1 (0.00%) 0 / 0 0 / 0
Escherichia urinary tract infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 6 (0.00%) 0 / 0 0 / 0	 0 / 9 (0.00%) 0 / 0 0 / 0	 0 / 1 (0.00%) 0 / 0 0 / 0
Influenza subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 1 / 6 (16.67%) 0 / 1 0 / 0	 0 / 9 (0.00%) 0 / 0 0 / 0	 0 / 1 (0.00%) 0 / 0 0 / 0
Lung infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 6 (0.00%) 0 / 0 0 / 0	 0 / 9 (0.00%) 0 / 0 0 / 0	 0 / 1 (0.00%) 0 / 0 0 / 0
Pneumonia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 6 (0.00%) 0 / 0 0 / 0	 1 / 9 (11.11%) 0 / 1 0 / 0	 0 / 1 (0.00%) 0 / 0 0 / 0
Salpingitis			

subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
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 enterococcal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (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
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fluid overload			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

<b>Serious adverse events</b>	Part 2 of Part 1: Dose-Ranging Pbo 5 mg/Part 2: BM 5 mg	Part 2 of Part 1: Dose-Ranging Pbo 10 mg/Part 2: BM 10 mg	Part 2 of Part 1: Dose-Ranging Pbo 20 mg/Part 2: BM 20 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)	2 / 3 (66.67%)	1 / 3 (33.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Raynaud's phenomenon			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
General physical health deterioration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Haemorrhagic ovarian cyst			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			



subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleuritic pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary arterial hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary fibrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Delirium			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
International normalised ratio increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Hip fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax traumatic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute right ventricular failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure acute			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac tamponade			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Right ventricular failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular arrhythmia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolic stroke			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure acute			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic lupus erythematosus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Infections and infestations Bronchitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 3 (0.00%) 0 / 0 0 / 0	1 / 3 (33.33%) 0 / 1 0 / 0	0 / 3 (0.00%) 0 / 0 0 / 0
Campylobacter gastroenteritis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 3 (0.00%) 0 / 0 0 / 0	0 / 3 (0.00%) 0 / 0 0 / 0	0 / 3 (0.00%) 0 / 0 0 / 0
Cellulitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 3 (0.00%) 0 / 0 0 / 0	0 / 3 (0.00%) 0 / 0 0 / 0	0 / 3 (0.00%) 0 / 0 0 / 0
Diarrhoea infectious subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 3 (0.00%) 0 / 0 0 / 0	0 / 3 (0.00%) 0 / 0 0 / 0	0 / 3 (0.00%) 0 / 0 0 / 0
Escherichia urinary tract infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 3 (0.00%) 0 / 0 0 / 0	0 / 3 (0.00%) 0 / 0 0 / 0	0 / 3 (0.00%) 0 / 0 0 / 0
Influenza subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 3 (0.00%) 0 / 0 0 / 0	0 / 3 (0.00%) 0 / 0 0 / 0	0 / 3 (0.00%) 0 / 0 0 / 0
Lung infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 3 (0.00%) 0 / 0 0 / 0	0 / 3 (0.00%) 0 / 0 0 / 0	0 / 3 (0.00%) 0 / 0 0 / 0
Pneumonia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 3 (0.00%) 0 / 0 0 / 0	0 / 3 (0.00%) 0 / 0 0 / 0	0 / 3 (0.00%) 0 / 0 0 / 0
Salpingitis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection enterococcal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fluid overload			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

<b>Serious adverse events</b>	Part 2 of Part 1: Dose Titration: BM 10 mg/Part 2: BM 10 mg	Part 2 of Part 1: Dose Titration: Pbo 10 mg/Part 2: BM 10 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 63 (14.29%)	9 / 33 (27.27%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			

subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Raynaud's phenomenon			
subjects affected / exposed	1 / 63 (1.59%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
General physical health deterioration			
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Haemorrhagic ovarian cyst			
subjects affected / exposed	1 / 63 (1.59%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			



subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleuritic pain			
subjects affected / exposed	1 / 63 (1.59%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary arterial hypertension			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 63 (1.59%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary fibrosis			
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary hypertension			
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Delirium			

subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
International normalised ratio increased			
subjects affected / exposed	1 / 63 (1.59%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Hip fracture			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax traumatic			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound			
subjects affected / exposed	1 / 63 (1.59%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute right ventricular failure			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			

subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure acute			
subjects affected / exposed	1 / 63 (1.59%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac tamponade			
subjects affected / exposed	1 / 63 (1.59%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Right ventricular failure			
subjects affected / exposed	1 / 63 (1.59%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular arrhythmia			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolic stroke			

subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			

subjects affected / exposed	1 / 63 (1.59%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure acute			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 63 (1.59%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic lupus erythematosus			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infections and infestations Bronchitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 63 (0.00%) 0 / 0 0 / 0	 0 / 33 (0.00%) 0 / 0 0 / 0	
Campylobacter gastroenteritis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 63 (0.00%) 0 / 0 0 / 0	 1 / 33 (3.03%) 0 / 1 0 / 0	
Cellulitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 63 (0.00%) 0 / 0 0 / 0	 0 / 33 (0.00%) 0 / 0 0 / 0	
Diarrhoea infectious subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 63 (0.00%) 0 / 0 0 / 0	 0 / 33 (0.00%) 0 / 0 0 / 0	
Escherichia urinary tract infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 1 / 63 (1.59%) 0 / 1 0 / 0	 0 / 33 (0.00%) 0 / 0 0 / 0	
Influenza subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 63 (0.00%) 0 / 0 0 / 0	 0 / 33 (0.00%) 0 / 0 0 / 0	
Lung infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 63 (0.00%) 0 / 0 0 / 0	 0 / 33 (0.00%) 0 / 0 0 / 0	
Pneumonia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 1 / 63 (1.59%) 0 / 1 0 / 0	 1 / 33 (3.03%) 0 / 1 0 / 0	
Salpingitis			

subjects affected / exposed	1 / 63 (1.59%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection enterococcal			
subjects affected / exposed	1 / 63 (1.59%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fluid overload			
subjects affected / exposed	1 / 63 (1.59%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

<b>Non-serious adverse events</b>	Part 1 of Part 1: Dose-Ranging BM 5 mg/Part 2: Open- Label	Part 1 of Part 1: Dose-Ranging BM 2.5 mg/Part 2: Open-Label	Part 1 of Part 1: Dose-Ranging BM 10 mg/Part 2: Open- Label
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 12 (91.67%)	5 / 6 (83.33%)	10 / 11 (90.91%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Basal cell carcinoma subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Colon cancer subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Squamous cell carcinoma subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Squamous cell carcinoma of skin subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Uterine leiomyoma subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Vascular disorders Flushing subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Hot flush subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Hypertension subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	1 / 11 (9.09%) 1
Hypotension subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Orthostatic hypotension subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Thrombophlebitis superficial subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
General disorders and administration site conditions			



Asthenia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Chills			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Generalised oedema			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Implant site haematoma			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Irritability			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
Oedema			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	3 / 12 (25.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	3	0	1
Pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0

Pyrexia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Vessel puncture site haematoma subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Vessel puncture site pain subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Vessel puncture site swelling subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Immune system disorders Drug hypersensitivity subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Seasonal allergy subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Social circumstances Menopause subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Reproductive system and breast disorders Benign prostatic hyperplasia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Breast mass subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Dysmenorrhoea subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Menorrhagia subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0

Menstrual disorder subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Menstruation irregular subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Ovarian cyst subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Vaginal disorder subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Vaginal haemorrhage subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			
Asthma subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 6 (16.67%) 1	0 / 11 (0.00%) 0
Bronchial hyperreactivity subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Cough subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	1 / 6 (16.67%) 1	2 / 11 (18.18%) 2
Dyspnoea subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 2	1 / 6 (16.67%) 1	3 / 11 (27.27%) 3
Dyspnoea exertional subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Dyspnoea paroxysmal nocturnal subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Epistaxis			

subjects affected / exposed	1 / 12 (8.33%)	1 / 6 (16.67%)	1 / 11 (9.09%)
occurrences (all)	1	1	1
Hypoxia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Increased upper airway secretion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Mediastinal mass			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Nasal dryness			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Nasal septum perforation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pharyngeal lesion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pulmonary arterial hypertension			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pulmonary congestion			

subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Pulmonary fibrosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pulmonary hypertension			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Rales			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Rhinalgia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Sinus congestion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Sleep apnoea syndrome			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Upper-airway cough syndrome			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Attention deficit/hyperactivity disorder			

subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hallucination			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Libido decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Blood bicarbonate decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Blood bilirubin increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			

subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Blood phosphorus decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Blood potassium decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Blood urine present			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Brain natriuretic peptide increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Cardiac murmur			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Cardiac output increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram abnormal			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Heart rate increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0

International normalised ratio increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Liver function test abnormal			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
N-terminal prohormone brain natriuretic peptide increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Oxygen saturation decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pulmonary arterial pressure increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Serum ferritin decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Venous pressure jugular increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Vital capacity abnormal			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Weight increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
White blood cell count increased			



subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Foot fracture			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hip fracture			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Joint dislocation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Joint injury			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Laceration			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Limb injury			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Muscle injury			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Radius fracture			

subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Rib fracture subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Upper limb fracture subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Wound haemorrhage subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Congenital, familial and genetic disorders Arteriovenous malformation subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Cardiac disorders Angina pectoris subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Atrial fibrillation subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Atrial flutter subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Cardiac discomfort subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Palpitations subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Pericardial effusion subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Pericarditis			

subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Postural orthostatic tachycardia syndrome			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Right ventricular failure			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Supraventricular extrasystoles			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	2 / 12 (16.67%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Nervous system disorders			
Ageusia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Burning sensation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Central nervous system lesion			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Dizziness exertional			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Headache			

subjects affected / exposed	2 / 12 (16.67%)	0 / 6 (0.00%)	3 / 11 (27.27%)
occurrences (all)	2	0	3
Memory impairment			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Multiple sclerosis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Occipital neuralgia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Sciatica			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Spinal claudication			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	1 / 12 (8.33%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
Coagulopathy			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Iron deficiency anaemia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Pancytopenia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Splenic vein thrombosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Splenomegaly			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Deafness bilateral			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Meniere's disease			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Tympanic membrane perforation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Vertigo			

subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Eye disorders			
Cataract			
subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Conjunctival hyperaemia			
subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Keratitis			
subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Ocular hyperaemia			
subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Periorbital oedema			
subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Retinal tear			
subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Scleral disorder			
subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Vision blurred			
subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Abdominal distension			
subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0	2 / 11 (18.18%) 2
Abdominal pain			

subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Abdominal pain lower			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Colonic polyp			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Dental caries			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	2 / 12 (16.67%)	0 / 6 (0.00%)	2 / 11 (18.18%)
occurrences (all)	2	0	2
Diverticulum			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Duodenitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Frequent bowel movements			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Gastritis			

subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Gingivitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hiatus hernia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Ileus			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Impaired gastric emptying			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Lip dry			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Oesophageal spasm			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Painful defaecation			



subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Retching			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Salivary gland enlargement			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Gallbladder disorder			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Gallbladder polyp			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hepatic cirrhosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hepatic cyst			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			

subjects affected / exposed	2 / 12 (16.67%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	2	0	1
Dermal cyst			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Digital ulcer			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Erythema			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Hyperkeratosis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Increased tendency to bruise			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Psoriasis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Rash			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Rash generalised			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Rash papular			

subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Rash pruritic			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Skin haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Skin irritation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Skin ulcer			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Subcutaneous nodule			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Urticaria			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Cystitis noninfective			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Dysuria			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Pollakiuria			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Renal failure acute			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0

Urinary retention subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	1 / 6 (16.67%) 1	1 / 11 (9.09%) 1
Arthritis subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Arthropathy subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Back pain subjects affected / exposed occurrences (all)	3 / 12 (25.00%) 3	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Bone pain subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Bursitis subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Chondrocalcinosis pyrophosphate subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Clubbing subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Exostosis subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Fibromyalgia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Foot deformity			

subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Intervertebral disc degeneration			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	3 / 11 (27.27%)
occurrences (all)	0	1	3
Musculoskeletal chest pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal discomfort			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	2 / 12 (16.67%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Neck pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	2 / 12 (16.67%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	2	0	1
Pain in jaw			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Plantar fasciitis			

subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Rheumatoid arthritis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Scleroderma			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Temporomandibular joint syndrome			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Breast abscess			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Candidiasis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Clostridial infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis bacterial			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis infective			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0

Ear infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Folliculitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Helicobacter gastritis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Helicobacter infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hordeolum			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Infected cyst			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Laryngitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0

Lung infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Oesophageal candidiasis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Otitis externa			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Otitis media			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pyelonephritis acute			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0



Tooth abscess			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	2 / 12 (16.67%)	2 / 6 (33.33%)	2 / 11 (18.18%)
occurrences (all)	2	2	2
Urinary tract infection			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Urinary tract infection bacterial			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	3 / 11 (27.27%)
occurrences (all)	0	1	3
Dyslipidaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Fluid overload			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Fluid retention			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Folate deficiency			

subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Glucose tolerance impaired			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Gout			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hyperalbuminaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	2 / 12 (16.67%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	2	1	0
Hypomagnesaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Iron deficiency			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Lactic acidosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Lactose intolerance			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Metabolic acidosis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Vitamin B12 deficiency			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0

<b>Non-serious adverse events</b>	Part 1 of Part 1: Dose-Ranging BM 20 mg/Part 2: Open- Label	Part 1 of Part 1: Dose-Ranging Pbo 2.5 mg/Part 2: BM 2.5 mg	Part 1 of Part 1: Dose-Ranging Pbo 5 mg/Part 2: BM 5 mg
Total subjects affected by non-serious adverse events subjects affected / exposed	12 / 12 (100.00%)	2 / 2 (100.00%)	4 / 4 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Colon cancer			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Squamous cell carcinoma			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Uterine leiomyoma			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Flushing			
subjects affected / exposed	2 / 12 (16.67%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Hot flush			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	1 / 12 (8.33%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Orthostatic hypotension			
subjects affected / exposed	1 / 12 (8.33%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0

Thrombophlebitis superficial subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
General disorders and administration site conditions			
Asthenia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Chest discomfort subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Chills subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Fatigue subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 2	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Generalised oedema subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Implant site haematoma subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Irritability subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Malaise subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Non-cardiac chest pain subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 2 (0.00%) 0	1 / 4 (25.00%) 1
Oedema subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Oedema peripheral			

subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Pain subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 2	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Pyrexia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Vessel puncture site haematoma subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Vessel puncture site pain subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Vessel puncture site swelling subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Immune system disorders Drug hypersensitivity subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Seasonal allergy subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Social circumstances Menopause subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Reproductive system and breast disorders Benign prostatic hyperplasia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Breast mass subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Dysmenorrhoea			

subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Menorrhagia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Menstrual disorder			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Menstruation irregular			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Ovarian cyst			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vaginal disorder			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Bronchial hyperreactivity			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	1 / 12 (8.33%)	0 / 2 (0.00%)	1 / 4 (25.00%)
occurrences (all)	1	0	1
Dyspnoea			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dyspnoea exertional			

subjects affected / exposed	1 / 12 (8.33%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Dyspnoea paroxysmal nocturnal			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Hypoxia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Increased upper airway secretion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Mediastinal mass			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nasal dryness			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Nasal septum perforation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 2 (0.00%)	2 / 4 (50.00%)
occurrences (all)	1	0	2
Pharyngeal lesion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Productive cough			

subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pulmonary arterial hypertension			
subjects affected / exposed	1 / 12 (8.33%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Pulmonary congestion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pulmonary fibrosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pulmonary hypertension			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rales			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rhinalgia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	1 / 12 (8.33%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Sinus congestion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Sleep apnoea syndrome			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Upper-airway cough syndrome			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			



Anxiety			
subjects affected / exposed	1 / 12 (8.33%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Attention deficit/hyperactivity disorder			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	1 / 12 (8.33%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Hallucination			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Libido decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Blood bicarbonate decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			

subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood phosphorus decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood potassium decreased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Blood urine present			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Brain natriuretic peptide increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cardiac murmur			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cardiac output increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram abnormal			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Heart rate increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0

Hepatic enzyme increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
International normalised ratio increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Liver function test abnormal			
subjects affected / exposed	1 / 12 (8.33%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
N-terminal prohormone brain natriuretic peptide increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Oxygen saturation decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pulmonary arterial pressure increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Serum ferritin decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Venous pressure jugular increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vital capacity abnormal			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	2 / 12 (16.67%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Weight increased			

subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
White blood cell count increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 12 (0.00%)	1 / 2 (50.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Foot fracture			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hip fracture			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Joint dislocation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Joint injury			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Laceration			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Limb injury			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Muscle injury			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Procedural pain			

subjects affected / exposed	1 / 12 (8.33%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Radius fracture			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rib fracture			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Upper limb fracture			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Wound haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Congenital, familial and genetic disorders			
Arteriovenous malformation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Atrial fibrillation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Atrial flutter			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cardiac discomfort			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	2 / 12 (16.67%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Pericardial effusion			

subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pericarditis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Postural orthostatic tachycardia syndrome			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Right ventricular failure			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Supraventricular extrasystoles			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Ageusia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Burning sensation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Central nervous system lesion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	2 / 12 (16.67%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Dizziness exertional			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			

subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	5 / 12 (41.67%)	1 / 2 (50.00%)	1 / 4 (25.00%)
occurrences (all)	5	1	1
Memory impairment			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Multiple sclerosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Occipital neuralgia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	2 / 12 (16.67%)	1 / 2 (50.00%)	0 / 4 (0.00%)
occurrences (all)	2	1	0
Spinal claudication			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	1 / 12 (8.33%)	0 / 2 (0.00%)	2 / 4 (50.00%)
occurrences (all)	1	0	2
Tremor			

subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Coagulopathy			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Iron deficiency anaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pancytopenia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Splenic vein thrombosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Splenomegaly			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Deafness bilateral			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Meniere's disease			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Tympanic membrane perforation			



subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Cataract			
subjects affected / exposed	1 / 12 (8.33%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Conjunctival hyperaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Keratitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Ocular hyperaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Periorbital oedema			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Retinal tear			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Scleral disorder			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	1 / 12 (8.33%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			

subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Colonic polyp			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	1 / 12 (8.33%)	0 / 2 (0.00%)	1 / 4 (25.00%)
occurrences (all)	1	0	1
Dental caries			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	2 / 12 (16.67%)	0 / 2 (0.00%)	1 / 4 (25.00%)
occurrences (all)	2	0	1
Diverticulum			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Duodenitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Frequent bowel movements			

subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastritis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 12 (16.67%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Gingivitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hiatus hernia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Ileus			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Impaired gastric emptying			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Lip dry			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	4 / 12 (33.33%)	0 / 2 (0.00%)	1 / 4 (25.00%)
occurrences (all)	4	0	1
Oesophageal spasm			

subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Painful defaecation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Retching			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Salivary gland enlargement			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	1 / 12 (8.33%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gallbladder disorder			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gallbladder polyp			
subjects affected / exposed	1 / 12 (8.33%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Hepatic cirrhosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hepatic cyst			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dermal cyst			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Digital ulcer			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	1 / 12 (8.33%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Erythema			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hyperkeratosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Increased tendency to bruise			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Psoriasis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rash generalised			

subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rash papular			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rash pruritic			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin irritation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin ulcer			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Subcutaneous nodule			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Cystitis noninfective			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	1 / 12 (8.33%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Pollakiuria			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Renal failure acute subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Urinary retention subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 2 (0.00%) 0	1 / 4 (25.00%) 1
Arthritis subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Arthropathy subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Back pain subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 2	1 / 2 (50.00%) 1	1 / 4 (25.00%) 1
Bone pain subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Bursitis subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Chondrocalcinosis pyrophosphate subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Clubbing subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Exostosis subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Fibromyalgia			

subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Foot deformity			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Intervertebral disc degeneration			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Intervertebral disc protrusion			
subjects affected / exposed	1 / 12 (8.33%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Joint swelling			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Muscle spasms			
subjects affected / exposed	3 / 12 (25.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	3	0	0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal discomfort			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Neck pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 2 (50.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	3 / 12 (25.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	3	0	0
Pain in jaw			



subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Plantar fasciitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rheumatoid arthritis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Scleroderma			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Temporomandibular joint syndrome			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Breast abscess			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Candidiasis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Clostridial infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis bacterial			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Conjunctivitis infective			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Folliculitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Helicobacter gastritis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Helicobacter infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	1 / 12 (8.33%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Hordeolum			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Infected cyst			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Laryngitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Lower respiratory tract infection subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Lung infection subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 2 (0.00%) 0	1 / 4 (25.00%) 1
Oesophageal candidiasis subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Oral herpes subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Otitis externa subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Otitis media subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Pharyngitis subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Pneumonia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Pyelonephritis acute subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Respiratory tract infection subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Rhinitis subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0

Sinusitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Tooth abscess			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 12 (8.33%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	3 / 12 (25.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	3	0	0
Urinary tract infection bacterial			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	5 / 12 (41.67%)	1 / 2 (50.00%)	0 / 4 (0.00%)
occurrences (all)	5	1	0
Dyslipidaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Fluid overload			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Fluid retention			

subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Folate deficiency			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Glucose tolerance impaired			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gout			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hyperalbuminaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypomagnesaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Iron deficiency			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Lactic acidosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Lactose intolerance			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Metabolic acidosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vitamin B12 deficiency			

subjects affected / exposed	0 / 12 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

<b>Non-serious adverse events</b>	Part 1 of Part 1: Dose-Ranging Pbo 10 mg/Part 2: BM 10 mg	Part 1 of Part 1: Dose Titration: BM 10 mg/Part 2: BM 10 mg	Part 1 of Part 1: Dose-Ranging Pbo 20 mg/Part 2: BM 20 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	63 / 74 (85.14%)	4 / 4 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 3 (0.00%)	1 / 74 (1.35%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Colon cancer			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Squamous cell carcinoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Uterine leiomyoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hot flush			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	2 / 74 (2.70%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Hypotension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Orthostatic hypotension subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 74 (0.00%) 0	0 / 4 (0.00%) 0
Thrombophlebitis superficial subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 74 (0.00%) 0	0 / 4 (0.00%) 0
General disorders and administration site conditions			
Asthenia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 74 (0.00%) 0	1 / 4 (25.00%) 1
Chest discomfort subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 74 (0.00%) 0	0 / 4 (0.00%) 0
Chills subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 74 (0.00%) 0	0 / 4 (0.00%) 0
Fatigue subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	7 / 74 (9.46%) 7	0 / 4 (0.00%) 0
Generalised oedema subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 74 (0.00%) 0	0 / 4 (0.00%) 0
Implant site haematoma subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 74 (0.00%) 0	0 / 4 (0.00%) 0
Irritability subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 74 (0.00%) 0	0 / 4 (0.00%) 0
Malaise subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 74 (0.00%) 0	0 / 4 (0.00%) 0
Non-cardiac chest pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	3 / 74 (4.05%) 3	0 / 4 (0.00%) 0
Oedema			

subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	1 / 3 (33.33%)	3 / 74 (4.05%)	0 / 4 (0.00%)
occurrences (all)	1	3	0
Pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 74 (1.35%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 74 (2.70%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Vessel puncture site haematoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 3 (0.00%)	1 / 74 (1.35%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Seasonal allergy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Social circumstances			
Menopause			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Breast mass			



subjects affected / exposed	0 / 3 (0.00%)	1 / 74 (1.35%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Dysmenorrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Menorrhagia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Menstrual disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Menstruation irregular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Ovarian cyst			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vaginal disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	1 / 74 (1.35%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Bronchial hyperreactivity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 3 (0.00%)	4 / 74 (5.41%)	0 / 4 (0.00%)
occurrences (all)	0	4	0
Dyspnoea			

subjects affected / exposed	0 / 3 (0.00%)	8 / 74 (10.81%)	0 / 4 (0.00%)
occurrences (all)	0	8	0
Dyspnoea exertional			
subjects affected / exposed	0 / 3 (0.00%)	2 / 74 (2.70%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Dyspnoea paroxysmal nocturnal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 3 (0.00%)	2 / 74 (2.70%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Hypoxia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Increased upper airway secretion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Mediastinal mass			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nasal dryness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nasal septum perforation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 3 (0.00%)	3 / 74 (4.05%)	0 / 4 (0.00%)
occurrences (all)	0	3	0
Pharyngeal lesion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			

subjects affected / exposed	0 / 3 (0.00%)	1 / 74 (1.35%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Productive cough			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pulmonary arterial hypertension			
subjects affected / exposed	0 / 3 (0.00%)	1 / 74 (1.35%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Pulmonary congestion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pulmonary fibrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pulmonary hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rales			
subjects affected / exposed	0 / 3 (0.00%)	2 / 74 (2.70%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Rhinalgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Sinus congestion			
subjects affected / exposed	0 / 3 (0.00%)	2 / 74 (2.70%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Sleep apnoea syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Upper-airway cough syndrome			
subjects affected / exposed	0 / 3 (0.00%)	1 / 74 (1.35%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Wheezing			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 74 (0.00%) 0	0 / 4 (0.00%) 0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 3 (0.00%)	2 / 74 (2.70%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Attention deficit/hyperactivity disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 3 (0.00%)	1 / 74 (1.35%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Hallucination			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 74 (1.35%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Libido decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	5 / 74 (6.76%)	0 / 4 (0.00%)
occurrences (all)	0	5	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	4 / 74 (5.41%)	0 / 4 (0.00%)
occurrences (all)	0	4	0
Blood bicarbonate decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			

subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood phosphorus decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood potassium decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood urine present			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Brain natriuretic peptide increased			
subjects affected / exposed	0 / 3 (0.00%)	3 / 74 (4.05%)	0 / 4 (0.00%)
occurrences (all)	0	3	0
Cardiac murmur			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cardiac output increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram abnormal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			

subjects affected / exposed	0 / 3 (0.00%)	3 / 74 (4.05%)	0 / 4 (0.00%)
occurrences (all)	0	3	0
Heart rate increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
International normalised ratio increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Liver function test abnormal			
subjects affected / exposed	0 / 3 (0.00%)	2 / 74 (2.70%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
N-terminal prohormone brain natriuretic peptide increased			
subjects affected / exposed	0 / 3 (0.00%)	2 / 74 (2.70%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Oxygen saturation decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pulmonary arterial pressure increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Serum ferritin decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 74 (1.35%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Venous pressure jugular increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vital capacity abnormal			

subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	1 / 3 (33.33%)	3 / 74 (4.05%)	0 / 4 (0.00%)
occurrences (all)	1	3	0
Weight increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	2 / 4 (50.00%)
occurrences (all)	0	0	2
White blood cell count increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 3 (33.33%)	3 / 74 (4.05%)	0 / 4 (0.00%)
occurrences (all)	1	3	0
Foot fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hip fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Joint dislocation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Joint injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Laceration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Limb injury			

subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Muscle injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Radius fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rib fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Upper limb fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Wound haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Congenital, familial and genetic disorders			
Arteriovenous malformation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Atrial fibrillation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 74 (1.35%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Atrial flutter			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cardiac discomfort			



subjects affected / exposed	0 / 3 (0.00%)	1 / 74 (1.35%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Palpitations			
subjects affected / exposed	0 / 3 (0.00%)	2 / 74 (2.70%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Pericardial effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pericarditis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Postural orthostatic tachycardia syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Right ventricular failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Supraventricular extrasystoles			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 74 (2.70%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Nervous system disorders			
Ageusia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Burning sensation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Central nervous system lesion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dizziness			

subjects affected / exposed	0 / 3 (0.00%)	4 / 74 (5.41%)	1 / 4 (25.00%)
occurrences (all)	0	4	1
Dizziness exertional			
subjects affected / exposed	0 / 3 (0.00%)	1 / 74 (1.35%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Dysgeusia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 74 (2.70%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Headache			
subjects affected / exposed	1 / 3 (33.33%)	8 / 74 (10.81%)	1 / 4 (25.00%)
occurrences (all)	1	8	1
Memory impairment			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Multiple sclerosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Occipital neuralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	0 / 3 (0.00%)	1 / 74 (1.35%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Sciatica			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Spinal claudication			

subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Syncope			
subjects affected / exposed	0 / 3 (0.00%)	1 / 74 (1.35%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Tremor			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 74 (1.35%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Coagulopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Iron deficiency anaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pancytopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Splenic vein thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Splenomegaly			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 74 (1.35%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Deafness bilateral			

subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Meniere's disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Tympanic membrane perforation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 3 (0.00%)	1 / 74 (1.35%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Conjunctival hyperaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Keratitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Ocular hyperaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Periorbital oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Retinal tear			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Scleral disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	1 / 3 (33.33%)	1 / 74 (1.35%)	1 / 4 (25.00%)
occurrences (all)	1	1	1
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	4 / 74 (5.41%)	0 / 4 (0.00%)
occurrences (all)	0	4	0
Abdominal pain lower			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Colonic polyp			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 3 (0.00%)	3 / 74 (4.05%)	0 / 4 (0.00%)
occurrences (all)	0	3	0
Dental caries			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	10 / 74 (13.51%)	0 / 4 (0.00%)
occurrences (all)	0	10	0
Diverticulum			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 3 (0.00%)	2 / 74 (2.70%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Duodenitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			

subjects affected / exposed	0 / 3 (0.00%)	1 / 74 (1.35%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Flatulence			
subjects affected / exposed	0 / 3 (0.00%)	1 / 74 (1.35%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Frequent bowel movements			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 3 (0.00%)	5 / 74 (6.76%)	0 / 4 (0.00%)
occurrences (all)	0	5	0
Gingivitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hiatus hernia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Ileus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Impaired gastric emptying			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Lip dry			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Lower gastrointestinal haemorrhage			

subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	10 / 74 (13.51%)	0 / 4 (0.00%)
occurrences (all)	0	10	0
Oesophageal spasm			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Painful defaecation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Retching			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Salivary gland enlargement			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 3 (0.00%)	1 / 74 (1.35%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	2 / 74 (2.70%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gallbladder disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gallbladder polyp			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Hepatic cirrhosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hepatic cyst			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 74 (1.35%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Dermal cyst			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Digital ulcer			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hyperkeratosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Increased tendency to bruise			
subjects affected / exposed	0 / 3 (0.00%)	2 / 74 (2.70%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Pruritus			
subjects affected / exposed	0 / 3 (0.00%)	2 / 74 (2.70%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Psoriasis			



subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rash generalised			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rash papular			
subjects affected / exposed	0 / 3 (0.00%)	1 / 74 (1.35%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Rash pruritic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin irritation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin ulcer			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Subcutaneous nodule			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Cystitis noninfective			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Dysuria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 74 (1.35%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Pollakiuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Renal failure acute			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Urinary retention			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	3 / 74 (4.05%)	0 / 4 (0.00%)
occurrences (all)	0	3	0
Arthritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Arthropathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	4 / 74 (5.41%)	0 / 4 (0.00%)
occurrences (all)	0	4	0
Bone pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Bursitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Chondrocalcinosis pyrophosphate			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Clubbing			

subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Exostosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Fibromyalgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Foot deformity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Intervertebral disc degeneration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Intervertebral disc protrusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	1 / 3 (33.33%)	11 / 74 (14.86%)	0 / 4 (0.00%)
occurrences (all)	1	11	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 74 (1.35%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Neck pain			

subjects affected / exposed	0 / 3 (0.00%)	1 / 74 (1.35%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Pain in extremity			
subjects affected / exposed	1 / 3 (33.33%)	2 / 74 (2.70%)	0 / 4 (0.00%)
occurrences (all)	1	2	0
Pain in jaw			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Plantar fasciitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rheumatoid arthritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Scleroderma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Temporomandibular joint syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Breast abscess			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 3 (0.00%)	2 / 74 (2.70%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Candidiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 74 (1.35%)	0 / 4 (0.00%)
occurrences (all)	0	1	0

Clostridial infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis bacterial			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis infective			
subjects affected / exposed	0 / 3 (0.00%)	1 / 74 (1.35%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Ear infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Folliculitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 3 (0.00%)	2 / 74 (2.70%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Gastrointestinal infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Helicobacter gastritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Helicobacter infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 3 (0.00%)	2 / 74 (2.70%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Hordeolum			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Infected cyst			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Influenza			
subjects affected / exposed	0 / 3 (0.00%)	1 / 74 (1.35%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Laryngitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Lung infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	2 / 3 (66.67%)	7 / 74 (9.46%)	0 / 4 (0.00%)
occurrences (all)	2	7	0
Oesophageal candidiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Otitis externa			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Otitis media			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pyelonephritis acute			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Respiratory tract infection subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 74 (0.00%) 0	0 / 4 (0.00%) 0
Rhinitis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 74 (1.35%) 1	0 / 4 (0.00%) 0
Sinusitis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	4 / 74 (5.41%) 4	0 / 4 (0.00%) 0
Tooth abscess subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	2 / 74 (2.70%) 2	1 / 4 (25.00%) 1
Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	10 / 74 (13.51%) 10	0 / 4 (0.00%) 0
Urinary tract infection subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	5 / 74 (6.76%) 5	1 / 4 (25.00%) 1
Urinary tract infection bacterial subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 74 (0.00%) 0	0 / 4 (0.00%) 0
Viral infection subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 74 (0.00%) 0	0 / 4 (0.00%) 0
Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 74 (0.00%) 0	0 / 4 (0.00%) 0
Vulvovaginal mycotic infection subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 74 (0.00%) 0	0 / 4 (0.00%) 0
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	7 / 74 (9.46%) 7	0 / 4 (0.00%) 0
Dyslipidaemia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Fluid overload			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Fluid retention			
subjects affected / exposed	0 / 3 (0.00%)	1 / 74 (1.35%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Folate deficiency			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Glucose tolerance impaired			
subjects affected / exposed	0 / 3 (0.00%)	1 / 74 (1.35%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Gout			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hyperalbuminaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypomagnesaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Iron deficiency			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Lactic acidosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Lactose intolerance			



subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Metabolic acidosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vitamin B12 deficiency			
subjects affected / exposed	0 / 3 (0.00%)	0 / 74 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

<b>Non-serious adverse events</b>	Part 1 of Part 1: Dose Titration: Pbo 10 mg/Part 2: BM 10 mg	Part 2 of Part 1: Dose-Ranging BM 2.5 mg/Part 2: Open-Label	Part 2 of Part 1: Dose-Ranging BM 5 mg/Part 2: Open- Label
Total subjects affected by non-serious adverse events			
subjects affected / exposed	33 / 38 (86.84%)	5 / 5 (100.00%)	11 / 11 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Colon cancer			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Squamous cell carcinoma			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Uterine leiomyoma			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hot flush			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0

Hypertension			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	2 / 38 (5.26%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Orthostatic hypotension			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Thrombophlebitis superficial			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Chest discomfort			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	4 / 38 (10.53%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	4	0	0
Generalised oedema			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Implant site haematoma			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Irritability			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Malaise			

subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Oedema			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	5 / 38 (13.16%)	2 / 5 (40.00%)	3 / 11 (27.27%)
occurrences (all)	5	2	3
Pain			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	2 / 38 (5.26%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Vessel puncture site haematoma			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Vessel puncture site pain			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site swelling			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Seasonal allergy			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Social circumstances			
Menopause			

subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Reproductive system and breast disorders			
Benign prostatic hyperplasia subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	1 / 5 (20.00%) 1	0 / 11 (0.00%) 0
Breast mass subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Dysmenorrhoea subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Menorrhagia subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Menstrual disorder subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Menstruation irregular subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Ovarian cyst subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Vaginal disorder subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	1 / 5 (20.00%) 1	0 / 11 (0.00%) 0
Vaginal haemorrhage subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	1 / 11 (9.09%) 1
Respiratory, thoracic and mediastinal disorders			
Asthma subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	1 / 5 (20.00%) 1	0 / 11 (0.00%) 0
Bronchial hyperreactivity			

subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	4 / 38 (10.53%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	4	0	1
Dyspnoea			
subjects affected / exposed	1 / 38 (2.63%)	1 / 5 (20.00%)	2 / 11 (18.18%)
occurrences (all)	1	1	2
Dyspnoea exertional			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Dyspnoea paroxysmal nocturnal			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	2 / 38 (5.26%)	1 / 5 (20.00%)	0 / 11 (0.00%)
occurrences (all)	2	1	0
Hypoxia			
subjects affected / exposed	0 / 38 (0.00%)	1 / 5 (20.00%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Increased upper airway secretion			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Mediastinal mass			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Nasal dryness			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Nasal septum perforation			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Oropharyngeal pain			

subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Pharyngeal lesion			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Productive cough			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pulmonary arterial hypertension			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Pulmonary congestion			
subjects affected / exposed	0 / 38 (0.00%)	1 / 5 (20.00%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Pulmonary fibrosis			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Pulmonary hypertension			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Rales			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Rhinalgia			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Sinus congestion			
subjects affected / exposed	3 / 38 (7.89%)	1 / 5 (20.00%)	0 / 11 (0.00%)
occurrences (all)	3	1	0
Sleep apnoea syndrome			

subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Upper-airway cough syndrome subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Wheezing subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Psychiatric disorders			
Anxiety subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Attention deficit/hyperactivity disorder subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Confusional state subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Depression subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Hallucination subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Insomnia subjects affected / exposed occurrences (all)	1 / 38 (2.63%) 1	1 / 5 (20.00%) 1	1 / 11 (9.09%) 1
Libido decreased subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Investigations			
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Aspartate aminotransferase increased			

subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Blood bicarbonate decreased			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Blood phosphorus decreased			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Blood potassium decreased			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Blood urine present			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Brain natriuretic peptide increased			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Cardiac murmur			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Cardiac output increased			
subjects affected / exposed	0 / 38 (0.00%)	1 / 5 (20.00%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0



Electrocardiogram abnormal subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Heart rate increased subjects affected / exposed occurrences (all)	1 / 38 (2.63%) 1	0 / 5 (0.00%) 0	1 / 11 (9.09%) 1
Hepatic enzyme increased subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	1 / 5 (20.00%) 1	0 / 11 (0.00%) 0
International normalised ratio increased subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Liver function test abnormal subjects affected / exposed occurrences (all)	1 / 38 (2.63%) 1	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
N-terminal prohormone brain natriuretic peptide increased subjects affected / exposed occurrences (all)	2 / 38 (5.26%) 2	1 / 5 (20.00%) 1	2 / 11 (18.18%) 2
Oxygen saturation decreased subjects affected / exposed occurrences (all)	1 / 38 (2.63%) 1	0 / 5 (0.00%) 0	1 / 11 (9.09%) 1
Platelet count decreased subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	1 / 11 (9.09%) 1
Pulmonary arterial pressure increased subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Serum ferritin decreased subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Venous pressure jugular increased			

subjects affected / exposed	0 / 38 (0.00%)	1 / 5 (20.00%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Vital capacity abnormal			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Weight increased			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
White blood cell count increased			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Foot fracture			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hip fracture			
subjects affected / exposed	0 / 38 (0.00%)	1 / 5 (20.00%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Joint dislocation			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Joint injury			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Laceration			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			

subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Limb injury			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Muscle injury			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Procedural pain			
subjects affected / exposed	0 / 38 (0.00%)	1 / 5 (20.00%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Radius fracture			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Rib fracture			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Upper limb fracture			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Wound haemorrhage			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Congenital, familial and genetic disorders			
Arteriovenous malformation			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Atrial fibrillation			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Atrial flutter			

subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Cardiac discomfort			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 38 (0.00%)	1 / 5 (20.00%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
Pericardial effusion			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pericarditis			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Postural orthostatic tachycardia syndrome			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Right ventricular failure			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Supraventricular extrasystoles			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Tachycardia			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Ageusia			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Burning sensation			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Central nervous system lesion			

subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	3 / 38 (7.89%)	1 / 5 (20.00%)	1 / 11 (9.09%)
occurrences (all)	3	1	1
Dizziness exertional			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Dysgeusia			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	7 / 38 (18.42%)	3 / 5 (60.00%)	0 / 11 (0.00%)
occurrences (all)	7	3	0
Memory impairment			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Migraine			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Multiple sclerosis			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Occipital neuralgia			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Somnolence			

subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Spinal claudication			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	2 / 38 (5.26%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Tremor			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 38 (0.00%)	1 / 5 (20.00%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
Coagulopathy			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Iron deficiency anaemia			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pancytopenia			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Splenic vein thrombosis			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Splenomegaly			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Deafness			

subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Deafness bilateral			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Meniere's disease			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Tympanic membrane perforation			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Cataract			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Conjunctival hyperaemia			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Keratitis			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Ocular hyperaemia			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Periorbital oedema			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Retinal tear			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Scleral disorder			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0

Vision blurred subjects affected / exposed occurrences (all)	1 / 38 (2.63%) 1	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Gastrointestinal disorders			
Abdominal discomfort subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Abdominal distension subjects affected / exposed occurrences (all)	1 / 38 (2.63%) 1	0 / 5 (0.00%) 0	1 / 11 (9.09%) 1
Abdominal pain subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	3 / 11 (27.27%) 3
Abdominal pain lower subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	1 / 11 (9.09%) 1
Colonic polyp subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	1 / 11 (9.09%) 1
Constipation subjects affected / exposed occurrences (all)	3 / 38 (7.89%) 3	1 / 5 (20.00%) 1	3 / 11 (27.27%) 3
Dental caries subjects affected / exposed occurrences (all)	1 / 38 (2.63%) 1	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Diarrhoea subjects affected / exposed occurrences (all)	3 / 38 (7.89%) 3	2 / 5 (40.00%) 2	2 / 11 (18.18%) 2
Diverticulum subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	1 / 11 (9.09%) 1
Dry mouth subjects affected / exposed occurrences (all)	1 / 38 (2.63%) 1	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Duodenitis			



subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Dyspepsia			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Flatulence			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Frequent bowel movements			
subjects affected / exposed	0 / 38 (0.00%)	1 / 5 (20.00%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Gastritis			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Haematochezia			
subjects affected / exposed	2 / 38 (5.26%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Haemorrhoids			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Hiatus hernia			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Ileus			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Impaired gastric emptying			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Lip dry			

subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	6 / 38 (15.79%)	3 / 5 (60.00%)	4 / 11 (36.36%)
occurrences (all)	6	3	4
Oesophageal spasm			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Painful defaecation			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Retching			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Salivary gland enlargement			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Toothache			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	1 / 38 (2.63%)	2 / 5 (40.00%)	0 / 11 (0.00%)
occurrences (all)	1	2	0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Gallbladder disorder			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0

Gallbladder polyp subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Hepatic cirrhosis subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Hepatic cyst subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Skin and subcutaneous tissue disorders			
Alopecia subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	1 / 5 (20.00%) 1	0 / 11 (0.00%) 0
Dermal cyst subjects affected / exposed occurrences (all)	1 / 38 (2.63%) 1	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Digital ulcer subjects affected / exposed occurrences (all)	1 / 38 (2.63%) 1	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Dry skin subjects affected / exposed occurrences (all)	1 / 38 (2.63%) 1	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Erythema subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	1 / 5 (20.00%) 1	1 / 11 (9.09%) 1
Hyperhidrosis subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Hyperkeratosis subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Increased tendency to bruise subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Pruritus			

subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Psoriasis			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Rash generalised			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Rash papular			
subjects affected / exposed	2 / 38 (5.26%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Rash pruritic			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Skin haemorrhage			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Skin irritation			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Skin lesion			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Skin ulcer			
subjects affected / exposed	0 / 38 (0.00%)	1 / 5 (20.00%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Subcutaneous nodule			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			

Cystitis noninfective subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Dysuria subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Pollakiuria subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Renal failure acute subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Urinary retention subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	1 / 38 (2.63%) 1	2 / 5 (40.00%) 2	0 / 11 (0.00%) 0
Arthritis subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	1 / 11 (9.09%) 1
Arthropathy subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Back pain subjects affected / exposed occurrences (all)	4 / 38 (10.53%) 4	0 / 5 (0.00%) 0	1 / 11 (9.09%) 1
Bone pain subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Bursitis subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	0 / 5 (0.00%) 0	0 / 11 (0.00%) 0
Chondrocalcinosis pyrophosphate			

subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Clubbing			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Exostosis			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Fibromyalgia			
subjects affected / exposed	0 / 38 (0.00%)	1 / 5 (20.00%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Foot deformity			
subjects affected / exposed	0 / 38 (0.00%)	1 / 5 (20.00%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Intervertebral disc degeneration			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 38 (0.00%)	1 / 5 (20.00%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			
subjects affected / exposed	2 / 38 (5.26%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	2	0	1
Musculoskeletal chest pain			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal discomfort			
subjects affected / exposed	0 / 38 (0.00%)	1 / 5 (20.00%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal pain			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Myalgia			

subjects affected / exposed	1 / 38 (2.63%)	2 / 5 (40.00%)	0 / 11 (0.00%)
occurrences (all)	1	2	0
Neck pain			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pain in jaw			
subjects affected / exposed	0 / 38 (0.00%)	2 / 5 (40.00%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
Plantar fasciitis			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Rheumatoid arthritis			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Scleroderma			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Temporomandibular joint syndrome			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Breast abscess			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	1 / 38 (2.63%)	2 / 5 (40.00%)	1 / 11 (9.09%)
occurrences (all)	1	2	1
Candidiasis			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0

Cellulitis			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Clostridial infection			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis bacterial			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis infective			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Folliculitis			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	1 / 38 (2.63%)	1 / 5 (20.00%)	2 / 11 (18.18%)
occurrences (all)	1	1	2
Gastrointestinal infection			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Helicobacter gastritis			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Helicobacter infection			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Herpes zoster			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hordeolum			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0



Infected cyst			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 38 (0.00%)	1 / 5 (20.00%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Laryngitis			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Lung infection			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	3 / 38 (7.89%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0
Oesophageal candidiasis			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Otitis externa			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Otitis media			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	2 / 11 (18.18%)
occurrences (all)	1	0	2

Pyelonephritis acute			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Rhinitis			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Sinusitis			
subjects affected / exposed	0 / 38 (0.00%)	1 / 5 (20.00%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
Tooth abscess			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Upper respiratory tract infection			
subjects affected / exposed	7 / 38 (18.42%)	2 / 5 (40.00%)	4 / 11 (36.36%)
occurrences (all)	7	2	4
Urinary tract infection			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection bacterial			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Viral infection			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	1 / 38 (2.63%)	1 / 5 (20.00%)	1 / 11 (9.09%)
occurrences (all)	1	1	1
Dyslipidaemia			
subjects affected / exposed	0 / 38 (0.00%)	1 / 5 (20.00%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Fluid overload			
subjects affected / exposed	2 / 38 (5.26%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Fluid retention			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Folate deficiency			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Glucose tolerance impaired			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Gout			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Hyperalbuminaemia			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Hypokalaemia			
subjects affected / exposed	0 / 38 (0.00%)	2 / 5 (40.00%)	2 / 11 (18.18%)
occurrences (all)	0	2	2
Hypomagnesaemia			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Iron deficiency			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Lactic acidosis			

subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Lactose intolerance			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Metabolic acidosis			
subjects affected / exposed	0 / 38 (0.00%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Vitamin B12 deficiency			
subjects affected / exposed	1 / 38 (2.63%)	0 / 5 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1

<b>Non-serious adverse events</b>	Part 2 of Part 1: Dose-Ranging BM 10 mg/Part 2: Open- Label	Part 2 of Part 1: Dose-Ranging BM 20 mg/Part 2: Open- Label	Part 2 of Part 1: Dose-Ranging Pbo 2.5 mg/Part 2: BM 2.5 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	8 / 9 (88.89%)	1 / 1 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Colon cancer			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Squamous cell carcinoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Uterine leiomyoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0

Hot flush			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Hypotension			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Orthostatic hypotension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Thrombophlebitis superficial			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Chills			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	3 / 6 (50.00%)	1 / 9 (11.11%)	1 / 1 (100.00%)
occurrences (all)	3	1	1
Generalised oedema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Implant site haematoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Irritability			

subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Oedema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Vessel puncture site haematoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site swelling			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Seasonal allergy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0

Social circumstances			
Menopause			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Breast mass			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Dysmenorrhoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Menorrhagia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Menstrual disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Menstruation irregular			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Ovarian cyst			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Vaginal disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0

Bronchial hyperreactivity			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Cough			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	1 / 6 (16.67%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Dyspnoea exertional			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Dyspnoea paroxysmal nocturnal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	4 / 6 (66.67%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	4	1	0
Hypoxia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Increased upper airway secretion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Mediastinal mass			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Nasal congestion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Nasal dryness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Nasal septum perforation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0



Oropharyngeal pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Pharyngeal lesion			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Pleural effusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pulmonary arterial hypertension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pulmonary congestion			
subjects affected / exposed	1 / 6 (16.67%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Pulmonary fibrosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pulmonary hypertension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Rales			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Rhinalgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Sinus congestion			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0

Sleep apnoea syndrome subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 9 (0.00%) 0	0 / 1 (0.00%) 0
Upper-airway cough syndrome subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 1 (0.00%) 0
Wheezing subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 1 (0.00%) 0
Psychiatric disorders			
Anxiety subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 1 (0.00%) 0
Attention deficit/hyperactivity disorder subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	1 / 1 (100.00%) 1
Confusional state subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	0 / 1 (0.00%) 0
Depression subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 1 (0.00%) 0
Hallucination subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 1 (0.00%) 0
Insomnia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 9 (0.00%) 0	0 / 1 (0.00%) 0
Libido decreased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	0 / 1 (0.00%) 0
Investigations			
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 9 (0.00%) 0	1 / 1 (100.00%) 1
Aspartate aminotransferase increased			

subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	1 / 1 (100.00%)
occurrences (all)	1	0	1
Blood bicarbonate decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blood phosphorus decreased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Blood potassium decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blood urine present			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Brain natriuretic peptide increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Cardiac murmur			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Cardiac output increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0

Electrocardiogram abnormal subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 1 (0.00%) 0
Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 1 (0.00%) 0
Heart rate increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 1 (0.00%) 0
Hepatic enzyme increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 1 (0.00%) 0
International normalised ratio increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	0 / 1 (0.00%) 0
Liver function test abnormal subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 1 (0.00%) 0
N-terminal prohormone brain natriuretic peptide increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 1 (0.00%) 0
Oxygen saturation decreased subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 9 (0.00%) 0	0 / 1 (0.00%) 0
Platelet count decreased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 1 (0.00%) 0
Pulmonary arterial pressure increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	0 / 1 (0.00%) 0
Serum ferritin decreased subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 9 (0.00%) 0	0 / 1 (0.00%) 0
Venous pressure jugular increased			

subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Vital capacity abnormal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Weight increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
White blood cell count increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Foot fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hip fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Joint dislocation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Joint injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Laceration			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Ligament sprain			

subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Limb injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Muscle injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Radius fracture			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Rib fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Upper limb fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Wound haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Congenital, familial and genetic disorders			
Arteriovenous malformation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Atrial fibrillation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Atrial flutter			

subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Cardiac discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Pericardial effusion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Pericarditis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Postural orthostatic tachycardia syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Right ventricular failure			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Supraventricular extrasystoles			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Ageusia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Burning sensation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Central nervous system lesion			

subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	1 / 6 (16.67%)	1 / 9 (11.11%)	1 / 1 (100.00%)
occurrences (all)	1	1	1
Dizziness exertional			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	2 / 6 (33.33%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	2	1	0
Memory impairment			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Multiple sclerosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Occipital neuralgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Presyncope			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Somnolence			



subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Spinal claudication			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Coagulopathy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Iron deficiency anaemia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Pancytopenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Splenic vein thrombosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Splenomegaly			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Deafness			

subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Deafness bilateral			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Meniere's disease			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Tympanic membrane perforation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Cataract			
subjects affected / exposed	1 / 6 (16.67%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Conjunctival hyperaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Keratitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Ocular hyperaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Periorbital oedema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Retinal tear			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Scleral disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0

Vision blurred subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	0 / 1 (0.00%) 0
Gastrointestinal disorders			
Abdominal discomfort subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 9 (0.00%) 0	0 / 1 (0.00%) 0
Abdominal distension subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 1 (0.00%) 0
Abdominal pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	0 / 1 (0.00%) 0
Abdominal pain lower subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 1 (0.00%) 0
Colonic polyp subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 1 (0.00%) 0
Constipation subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	2 / 9 (22.22%) 2	0 / 1 (0.00%) 0
Dental caries subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 1 (0.00%) 0
Diarrhoea subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	1 / 1 (100.00%) 1
Diverticulum subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 1 (0.00%) 0
Dry mouth subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 1 (0.00%) 0
Duodenitis			

subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Frequent bowel movements			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Gastritis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Gingivitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hiatus hernia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Ileus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Impaired gastric emptying			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Lip dry			

subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Oesophageal spasm			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Painful defaecation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Retching			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Salivary gland enlargement			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	2 / 9 (22.22%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Gallbladder disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0

Gallbladder polyp			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hepatic cirrhosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hepatic cyst			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Dermal cyst			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Digital ulcer			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hyperkeratosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Increased tendency to bruise			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pruritus			

subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Psoriasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Rash generalised			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Rash papular			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Rash pruritic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Skin haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Skin irritation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Skin ulcer			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Subcutaneous nodule			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			

Cystitis noninfective subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 1 (0.00%) 0
Dysuria subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 1 (0.00%) 0
Pollakiuria subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 1 (0.00%) 0
Renal failure acute subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 1 (0.00%) 0
Urinary retention subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	0 / 1 (0.00%) 0
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	0 / 1 (0.00%) 0
Arthritis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 1 (0.00%) 0
Arthropathy subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 1 (0.00%) 0
Back pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 1 (0.00%) 0
Bone pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 1 (0.00%) 0
Bursitis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 1 (0.00%) 0
Chondrocalcinosis pyrophosphate			



subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Clubbing			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Exostosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Fibromyalgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Foot deformity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Intervertebral disc degeneration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Myalgia			

subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pain in jaw			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Plantar fasciitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Rheumatoid arthritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Scleroderma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Temporomandibular joint syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Breast abscess			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 6 (0.00%)	2 / 9 (22.22%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Candidiasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0

Cellulitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Clostridial infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis bacterial			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis infective			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	2 / 6 (33.33%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Folliculitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Helicobacter gastritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Helicobacter infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Hordeolum			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0

Infected cyst			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Laryngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Lung infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Oesophageal candidiasis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Oral herpes			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Otitis externa			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Otitis media			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 9 (22.22%)	0 / 1 (0.00%)
occurrences (all)	0	2	0

Pyelonephritis acute			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	1 / 6 (16.67%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Tooth abscess			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	1 / 6 (16.67%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Urinary tract infection bacterial			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Dyslipidaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Fluid overload			
subjects affected / exposed	0 / 6 (0.00%)	2 / 9 (22.22%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Fluid retention			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Folate deficiency			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Glucose tolerance impaired			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Gout			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hyperalbuminaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 9 (22.22%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Hypomagnesaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Iron deficiency			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Lactic acidosis			

subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Lactose intolerance			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Metabolic acidosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Vitamin B12 deficiency			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0

<b>Non-serious adverse events</b>	Part 2 of Part 1: Dose-Ranging Pbo 5 mg/Part 2: BM 5 mg	Part 2 of Part 1: Dose-Ranging Pbo 10 mg/Part 2: BM 10 mg	Part 2 of Part 1: Dose-Ranging Pbo 20 mg/Part 2: BM 20 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)	3 / 3 (100.00%)	3 / 3 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Colon cancer			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Squamous cell carcinoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Uterine leiomyoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Hot flush			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Orthostatic hypotension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Thrombophlebitis superficial			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Generalised oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Implant site haematoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Irritability			



subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site haematoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Seasonal allergy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Social circumstances			
Menopause			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Breast mass			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysmenorrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Menorrhagia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Menstrual disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Menstruation irregular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ovarian cyst			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vaginal disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Bronchial hyperreactivity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dyspnoea exertional			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dyspnoea paroxysmal nocturnal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypoxia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Increased upper airway secretion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mediastinal mass			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasal dryness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Nasal septum perforation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Oropharyngeal pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pharyngeal lesion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pulmonary arterial hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pulmonary congestion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pulmonary fibrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pulmonary hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rales			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rhinalgia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sinus congestion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Sleep apnoea syndrome subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0
Upper-airway cough syndrome subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Wheezing subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Psychiatric disorders			
Anxiety subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Attention deficit/hyperactivity disorder subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Confusional state subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Depression subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Hallucination subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Insomnia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Libido decreased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Investigations			
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0
Aspartate aminotransferase increased			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood bicarbonate decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood phosphorus decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood potassium decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood urine present			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Brain natriuretic peptide increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cardiac murmur			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cardiac output increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Electrocardiogram abnormal subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0
Heart rate increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Hepatic enzyme increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
International normalised ratio increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0
Liver function test abnormal subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
N-terminal prohormone brain natriuretic peptide increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Oxygen saturation decreased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Platelet count decreased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Pulmonary arterial pressure increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Serum ferritin decreased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Venous pressure jugular increased			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vital capacity abnormal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Weight increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
White blood cell count increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Foot fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hip fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Joint dislocation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Joint injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Laceration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			



subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Limb injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Muscle injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Radius fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rib fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Upper limb fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Wound haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Congenital, familial and genetic disorders			
Arteriovenous malformation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Atrial fibrillation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Atrial flutter			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cardiac discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Pericardial effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pericarditis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Postural orthostatic tachycardia syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Right ventricular failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Supraventricular extrasystoles			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Ageusia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Burning sensation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Central nervous system lesion			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dizziness exertional			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 3 (0.00%)	2 / 3 (66.67%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Memory impairment			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Multiple sclerosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Occipital neuralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Sciatica			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Somnolence			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Spinal claudication			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Coagulopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Iron deficiency anaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Pancytopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Splenic vein thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Splenomegaly			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Deafness			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Deafness bilateral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Meniere's disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tympanic membrane perforation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Conjunctival hyperaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Keratitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ocular hyperaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Periorbital oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Retinal tear			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Scleral disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Vision blurred subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Gastrointestinal disorders			
Abdominal discomfort subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Abdominal distension subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Abdominal pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Abdominal pain lower subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Colonic polyp subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Constipation subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0
Dental caries subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Diarrhoea subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0
Diverticulum subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Dry mouth subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Duodenitis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Flatulence			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Frequent bowel movements			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hiatus hernia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ileus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Impaired gastric emptying			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lip dry			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Oesophageal spasm			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Painful defaecation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Retching			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Salivary gland enlargement			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gallbladder disorder			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0



Gallbladder polyp			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hepatic cirrhosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hepatic cyst			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dermal cyst			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Digital ulcer			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperkeratosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Increased tendency to bruise			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pruritus			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Psoriasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash generalised			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Rash papular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash pruritic			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Skin haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin irritation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin ulcer			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Subcutaneous nodule			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			

Cystitis noninfective subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Dysuria subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Pollakiuria subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Renal failure acute subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Urinary retention subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	2 / 3 (66.67%) 2	0 / 3 (0.00%) 0
Arthritis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Arthropathy subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0
Back pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Bone pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Bursitis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Chondrocalcinosis pyrophosphate			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Clubbing			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Exostosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fibromyalgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Foot deformity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Intervertebral disc degeneration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 3 (0.00%)	2 / 3 (66.67%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Myalgia			

subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Neck pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Pain in jaw			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Plantar fasciitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rheumatoid arthritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Scleroderma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Temporomandibular joint syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Breast abscess			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Candidiasis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

Cellulitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Clostridial infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis bacterial			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis infective			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Ear infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Folliculitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Gastrointestinal infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Helicobacter gastritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Helicobacter infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hordeolum			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Infected cyst			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Laryngitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Lower respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lung infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Oesophageal candidiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Otitis externa			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Otitis media			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Pyelonephritis acute			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tooth abscess			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	0	0	2
Urinary tract infection bacterial			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			



subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Dyslipidaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fluid overload			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fluid retention			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Folate deficiency			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Glucose tolerance impaired			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gout			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperalbuminaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypomagnesaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Iron deficiency			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lactic acidosis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lactose intolerance			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Metabolic acidosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vitamin B12 deficiency			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

<b>Non-serious adverse events</b>	Part 2 of Part 1: Dose Titration: BM 10 mg/Part 2: BM 10 mg	Part 2 of Part 1: Dose Titration: Pbo 10 mg/Part 2: BM 10 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	47 / 63 (74.60%)	30 / 33 (90.91%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Colon cancer			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Squamous cell carcinoma			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Uterine leiomyoma			
subjects affected / exposed	1 / 63 (1.59%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	

Hot flush			
subjects affected / exposed	0 / 63 (0.00%)	2 / 33 (6.06%)	
occurrences (all)	0	2	
Hypertension			
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Hypotension			
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Orthostatic hypotension			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Thrombophlebitis superficial			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Chest discomfort			
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Chills			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Fatigue			
subjects affected / exposed	4 / 63 (6.35%)	4 / 33 (12.12%)	
occurrences (all)	4	4	
Generalised oedema			
subjects affected / exposed	1 / 63 (1.59%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Implant site haematoma			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Irritability			

subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Malaise			
subjects affected / exposed	1 / 63 (1.59%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Non-cardiac chest pain			
subjects affected / exposed	4 / 63 (6.35%)	0 / 33 (0.00%)	
occurrences (all)	4	0	
Oedema			
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Oedema peripheral			
subjects affected / exposed	4 / 63 (6.35%)	3 / 33 (9.09%)	
occurrences (all)	4	3	
Pain			
subjects affected / exposed	0 / 63 (0.00%)	2 / 33 (6.06%)	
occurrences (all)	0	2	
Pyrexia			
subjects affected / exposed	0 / 63 (0.00%)	2 / 33 (6.06%)	
occurrences (all)	0	2	
Vessel puncture site haematoma			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Vessel puncture site pain			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Vessel puncture site swelling			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Seasonal allergy			
subjects affected / exposed	1 / 63 (1.59%)	0 / 33 (0.00%)	
occurrences (all)	1	0	

Social circumstances			
Menopause			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Breast mass			
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Dysmenorrhoea			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Menorrhagia			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Menstrual disorder			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Menstruation irregular			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Ovarian cyst			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Vaginal disorder			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Vaginal haemorrhage			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	

Bronchial hyperreactivity		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Cough		
subjects affected / exposed	5 / 63 (7.94%)	4 / 33 (12.12%)
occurrences (all)	5	4
Dyspnoea		
subjects affected / exposed	5 / 63 (7.94%)	4 / 33 (12.12%)
occurrences (all)	5	4
Dyspnoea exertional		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Dyspnoea paroxysmal nocturnal		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Epistaxis		
subjects affected / exposed	1 / 63 (1.59%)	1 / 33 (3.03%)
occurrences (all)	1	1
Hypoxia		
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Increased upper airway secretion		
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Mediastinal mass		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Nasal congestion		
subjects affected / exposed	0 / 63 (0.00%)	3 / 33 (9.09%)
occurrences (all)	0	3
Nasal dryness		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Nasal septum perforation		
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1

Oropharyngeal pain		
subjects affected / exposed	1 / 63 (1.59%)	2 / 33 (6.06%)
occurrences (all)	1	2
Pharyngeal lesion		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Pleural effusion		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Productive cough		
subjects affected / exposed	3 / 63 (4.76%)	1 / 33 (3.03%)
occurrences (all)	3	1
Pulmonary arterial hypertension		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Pulmonary congestion		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Pulmonary fibrosis		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Pulmonary hypertension		
subjects affected / exposed	1 / 63 (1.59%)	1 / 33 (3.03%)
occurrences (all)	1	1
Rales		
subjects affected / exposed	1 / 63 (1.59%)	1 / 33 (3.03%)
occurrences (all)	1	1
Rhinalgia		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Rhinorrhoea		
subjects affected / exposed	1 / 63 (1.59%)	0 / 33 (0.00%)
occurrences (all)	1	0
Sinus congestion		
subjects affected / exposed	1 / 63 (1.59%)	0 / 33 (0.00%)
occurrences (all)	1	0

Sleep apnoea syndrome subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	1 / 33 (3.03%) 1	
Upper-airway cough syndrome subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	1 / 33 (3.03%) 1	
Wheezing subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	1 / 33 (3.03%) 1	
Psychiatric disorders			
Anxiety subjects affected / exposed occurrences (all)	1 / 63 (1.59%) 1	1 / 33 (3.03%) 1	
Attention deficit/hyperactivity disorder subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	0 / 33 (0.00%) 0	
Confusional state subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	0 / 33 (0.00%) 0	
Depression subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	1 / 33 (3.03%) 1	
Hallucination subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	1 / 33 (3.03%) 1	
Insomnia subjects affected / exposed occurrences (all)	1 / 63 (1.59%) 1	0 / 33 (0.00%) 0	
Libido decreased subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	0 / 33 (0.00%) 0	
Investigations			
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	1 / 63 (1.59%) 1	2 / 33 (6.06%) 2	
Aspartate aminotransferase increased			



subjects affected / exposed	1 / 63 (1.59%)	1 / 33 (3.03%)
occurrences (all)	1	1
Blood bicarbonate decreased		
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Blood bilirubin increased		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Blood creatine phosphokinase increased		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Blood creatinine increased		
subjects affected / exposed	2 / 63 (3.17%)	0 / 33 (0.00%)
occurrences (all)	2	0
Blood phosphorus decreased		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Blood potassium decreased		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Blood urine present		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Brain natriuretic peptide increased		
subjects affected / exposed	3 / 63 (4.76%)	3 / 33 (9.09%)
occurrences (all)	3	3
Cardiac murmur		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Cardiac output increased		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Electrocardiogram QT prolonged		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0

Electrocardiogram abnormal subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	1 / 33 (3.03%) 1	
Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	0 / 33 (0.00%) 0	
Heart rate increased subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	0 / 33 (0.00%) 0	
Hepatic enzyme increased subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	1 / 33 (3.03%) 1	
International normalised ratio increased subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	0 / 33 (0.00%) 0	
Liver function test abnormal subjects affected / exposed occurrences (all)	1 / 63 (1.59%) 1	2 / 33 (6.06%) 2	
N-terminal prohormone brain natriuretic peptide increased subjects affected / exposed occurrences (all)	4 / 63 (6.35%) 4	2 / 33 (6.06%) 2	
Oxygen saturation decreased subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	0 / 33 (0.00%) 0	
Platelet count decreased subjects affected / exposed occurrences (all)	1 / 63 (1.59%) 1	0 / 33 (0.00%) 0	
Pulmonary arterial pressure increased subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	0 / 33 (0.00%) 0	
Serum ferritin decreased subjects affected / exposed occurrences (all)	1 / 63 (1.59%) 1	0 / 33 (0.00%) 0	
Venous pressure jugular increased			

subjects affected / exposed	2 / 63 (3.17%)	0 / 33 (0.00%)	
occurrences (all)	2	0	
Vital capacity abnormal			
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Weight decreased			
subjects affected / exposed	1 / 63 (1.59%)	2 / 33 (6.06%)	
occurrences (all)	1	2	
Weight increased			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
White blood cell count increased			
subjects affected / exposed	3 / 63 (4.76%)	0 / 33 (0.00%)	
occurrences (all)	3	0	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 63 (1.59%)	1 / 33 (3.03%)	
occurrences (all)	1	1	
Foot fracture			
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Hip fracture			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Joint dislocation			
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Joint injury			
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Laceration			
subjects affected / exposed	3 / 63 (4.76%)	0 / 33 (0.00%)	
occurrences (all)	3	0	
Ligament sprain			

subjects affected / exposed	2 / 63 (3.17%)	0 / 33 (0.00%)	
occurrences (all)	2	0	
Limb injury			
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Muscle injury			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Procedural pain			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Radius fracture			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Rib fracture			
subjects affected / exposed	1 / 63 (1.59%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Upper limb fracture			
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Wound haemorrhage			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Congenital, familial and genetic disorders			
Arteriovenous malformation			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Atrial fibrillation			
subjects affected / exposed	1 / 63 (1.59%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Atrial flutter			

subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Cardiac discomfort			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Palpitations			
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Pericardial effusion			
subjects affected / exposed	2 / 63 (3.17%)	0 / 33 (0.00%)	
occurrences (all)	2	0	
Pericarditis			
subjects affected / exposed	1 / 63 (1.59%)	1 / 33 (3.03%)	
occurrences (all)	1	1	
Postural orthostatic tachycardia syndrome			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Right ventricular failure			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Supraventricular extrasystoles			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Tachycardia			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Ageusia			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Burning sensation			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Central nervous system lesion			

subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Dizziness		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Dizziness exertional		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Dysgeusia		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Headache		
subjects affected / exposed	2 / 63 (3.17%)	3 / 33 (9.09%)
occurrences (all)	2	3
Memory impairment		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Migraine		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Multiple sclerosis		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Occipital neuralgia		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Paraesthesia		
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Presyncope		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Sciatica		
subjects affected / exposed	1 / 63 (1.59%)	0 / 33 (0.00%)
occurrences (all)	1	0
Somnolence		

subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Spinal claudication			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Syncope			
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Tremor			
subjects affected / exposed	1 / 63 (1.59%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 63 (4.76%)	0 / 33 (0.00%)	
occurrences (all)	3	0	
Coagulopathy			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Iron deficiency anaemia			
subjects affected / exposed	1 / 63 (1.59%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Pancytopenia			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Splenic vein thrombosis			
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Splenomegaly			
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Thrombocytopenia			
subjects affected / exposed	1 / 63 (1.59%)	1 / 33 (3.03%)	
occurrences (all)	1	1	
Ear and labyrinth disorders			
Deafness			

subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Deafness bilateral			
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Meniere's disease			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Tympanic membrane perforation			
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Vertigo			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
Cataract			
subjects affected / exposed	1 / 63 (1.59%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Conjunctival hyperaemia			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Keratitis			
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Ocular hyperaemia			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Periorbital oedema			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Retinal tear			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Scleral disorder			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	



Vision blurred subjects affected / exposed occurrences (all)	1 / 63 (1.59%) 1	1 / 33 (3.03%) 1	
Gastrointestinal disorders			
Abdominal discomfort subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	1 / 33 (3.03%) 1	
Abdominal distension subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	1 / 33 (3.03%) 1	
Abdominal pain subjects affected / exposed occurrences (all)	3 / 63 (4.76%) 3	2 / 33 (6.06%) 2	
Abdominal pain lower subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	0 / 33 (0.00%) 0	
Colonic polyp subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	1 / 33 (3.03%) 1	
Constipation subjects affected / exposed occurrences (all)	4 / 63 (6.35%) 4	1 / 33 (3.03%) 1	
Dental caries subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	0 / 33 (0.00%) 0	
Diarrhoea subjects affected / exposed occurrences (all)	1 / 63 (1.59%) 1	7 / 33 (21.21%) 7	
Diverticulum subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	0 / 33 (0.00%) 0	
Dry mouth subjects affected / exposed occurrences (all)	1 / 63 (1.59%) 1	0 / 33 (0.00%) 0	
Duodenitis			

subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Dyspepsia		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Flatulence		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Frequent bowel movements		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Gastritis		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Gastrooesophageal reflux disease		
subjects affected / exposed	1 / 63 (1.59%)	2 / 33 (6.06%)
occurrences (all)	1	2
Gingivitis		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Haematochezia		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Haemorrhoids		
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Hiatus hernia		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Ileus		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Impaired gastric emptying		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Lip dry		

subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Nausea			
subjects affected / exposed	2 / 63 (3.17%)	3 / 33 (9.09%)	
occurrences (all)	2	3	
Oesophageal spasm			
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Painful defaecation			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Rectal haemorrhage			
subjects affected / exposed	0 / 63 (0.00%)	2 / 33 (6.06%)	
occurrences (all)	0	2	
Retching			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Salivary gland enlargement			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Toothache			
subjects affected / exposed	1 / 63 (1.59%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	1 / 63 (1.59%)	1 / 33 (3.03%)	
occurrences (all)	1	1	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Gallbladder disorder			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	

Gallbladder polyp			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Hepatic cirrhosis			
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Hepatic cyst			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Dermal cyst			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Digital ulcer			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Dry skin			
subjects affected / exposed	1 / 63 (1.59%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Erythema			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Hyperhidrosis			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Hyperkeratosis			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Increased tendency to bruise			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Pruritus			

subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Psoriasis			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Rash			
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Rash generalised			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Rash papular			
subjects affected / exposed	1 / 63 (1.59%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Rash pruritic			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Skin haemorrhage			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Skin irritation			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Skin lesion			
subjects affected / exposed	1 / 63 (1.59%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Skin ulcer			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Subcutaneous nodule			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Urticaria			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Renal and urinary disorders			

Cystitis noninfective subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	0 / 33 (0.00%) 0	
Dysuria subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	0 / 33 (0.00%) 0	
Pollakiuria subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	0 / 33 (0.00%) 0	
Renal failure acute subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	1 / 33 (3.03%) 1	
Urinary retention subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	0 / 33 (0.00%) 0	
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	4 / 63 (6.35%) 4	0 / 33 (0.00%) 0	
Arthritis subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	1 / 33 (3.03%) 1	
Arthropathy subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	0 / 33 (0.00%) 0	
Back pain subjects affected / exposed occurrences (all)	1 / 63 (1.59%) 1	1 / 33 (3.03%) 1	
Bone pain subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	1 / 33 (3.03%) 1	
Bursitis subjects affected / exposed occurrences (all)	0 / 63 (0.00%) 0	1 / 33 (3.03%) 1	
Chondrocalcinosis pyrophosphate			

subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Clubbing		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Exostosis		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Fibromyalgia		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Foot deformity		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Intervertebral disc degeneration		
subjects affected / exposed	1 / 63 (1.59%)	0 / 33 (0.00%)
occurrences (all)	1	0
Intervertebral disc protrusion		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Joint swelling		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Muscle spasms		
subjects affected / exposed	5 / 63 (7.94%)	5 / 33 (15.15%)
occurrences (all)	5	5
Musculoskeletal chest pain		
subjects affected / exposed	1 / 63 (1.59%)	0 / 33 (0.00%)
occurrences (all)	1	0
Musculoskeletal discomfort		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Musculoskeletal pain		
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Myalgia		

subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Neck pain			
subjects affected / exposed	1 / 63 (1.59%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Pain in extremity			
subjects affected / exposed	3 / 63 (4.76%)	1 / 33 (3.03%)	
occurrences (all)	3	1	
Pain in jaw			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Plantar fasciitis			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Rheumatoid arthritis			
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Scleroderma			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Temporomandibular joint syndrome			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Breast abscess			
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Bronchitis			
subjects affected / exposed	1 / 63 (1.59%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Candidiasis			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	



Cellulitis		
subjects affected / exposed	2 / 63 (3.17%)	0 / 33 (0.00%)
occurrences (all)	2	0
Clostridial infection		
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Conjunctivitis bacterial		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Conjunctivitis infective		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Ear infection		
subjects affected / exposed	0 / 63 (0.00%)	2 / 33 (6.06%)
occurrences (all)	0	2
Folliculitis		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Gastroenteritis		
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Gastrointestinal infection		
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Helicobacter gastritis		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Helicobacter infection		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Herpes zoster		
subjects affected / exposed	1 / 63 (1.59%)	1 / 33 (3.03%)
occurrences (all)	1	1
Hordeolum		
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1

Infected cyst		
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Influenza		
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Laryngitis		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Lower respiratory tract infection		
subjects affected / exposed	0 / 63 (0.00%)	2 / 33 (6.06%)
occurrences (all)	0	2
Lung infection		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Nasopharyngitis		
subjects affected / exposed	1 / 63 (1.59%)	2 / 33 (6.06%)
occurrences (all)	1	2
Oesophageal candidiasis		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Oral herpes		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Otitis externa		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Otitis media		
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Pharyngitis		
subjects affected / exposed	2 / 63 (3.17%)	1 / 33 (3.03%)
occurrences (all)	2	1
Pneumonia		
subjects affected / exposed	1 / 63 (1.59%)	1 / 33 (3.03%)
occurrences (all)	1	1

Pyelonephritis acute			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Respiratory tract infection			
subjects affected / exposed	1 / 63 (1.59%)	2 / 33 (6.06%)	
occurrences (all)	1	2	
Rhinitis			
subjects affected / exposed	1 / 63 (1.59%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Sinusitis			
subjects affected / exposed	4 / 63 (6.35%)	2 / 33 (6.06%)	
occurrences (all)	4	2	
Tooth abscess			
subjects affected / exposed	1 / 63 (1.59%)	1 / 33 (3.03%)	
occurrences (all)	1	1	
Upper respiratory tract infection			
subjects affected / exposed	12 / 63 (19.05%)	9 / 33 (27.27%)	
occurrences (all)	12	9	
Urinary tract infection			
subjects affected / exposed	4 / 63 (6.35%)	2 / 33 (6.06%)	
occurrences (all)	4	2	
Urinary tract infection bacterial			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Viral infection			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Vulvovaginal mycotic infection			
subjects affected / exposed	1 / 63 (1.59%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	3 / 63 (4.76%)	6 / 33 (18.18%)
occurrences (all)	3	6
Dyslipidaemia		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Fluid overload		
subjects affected / exposed	3 / 63 (4.76%)	0 / 33 (0.00%)
occurrences (all)	3	0
Fluid retention		
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Folate deficiency		
subjects affected / exposed	1 / 63 (1.59%)	1 / 33 (3.03%)
occurrences (all)	1	1
Glucose tolerance impaired		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Gout		
subjects affected / exposed	1 / 63 (1.59%)	0 / 33 (0.00%)
occurrences (all)	1	0
Hyperalbuminaemia		
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0
Hypercholesterolaemia		
subjects affected / exposed	0 / 63 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Hypokalaemia		
subjects affected / exposed	1 / 63 (1.59%)	1 / 33 (3.03%)
occurrences (all)	1	1
Hypomagnesaemia		
subjects affected / exposed	1 / 63 (1.59%)	0 / 33 (0.00%)
occurrences (all)	1	0
Iron deficiency		
subjects affected / exposed	0 / 63 (0.00%)	2 / 33 (6.06%)
occurrences (all)	0	2
Lactic acidosis		

subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Lactose intolerance			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Metabolic acidosis			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	
Vitamin B12 deficiency			
subjects affected / exposed	0 / 63 (0.00%)	0 / 33 (0.00%)	
occurrences (all)	0	0	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 October 2013	Protocol Version 1.0 (No patients were enrolled under protocol version 1.0)
05 December 2013	Protocol Version 2.0
20 August 2014	Protocol Version 3.0
24 November 2014	Protocol Version 4.0
31 August 2015	Protocol Version 5.0
01 June 2016	Protocol Version 6.0
26 January 2017	Protocol Version 7.0

Notes:

---

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported