Clinical trial results:
An Open-label, Multicentre, Randomised, 3-arm Study to Investigate the Comparative Efficacy and Safety of Intravenous Ferric Carboxymaltose (Ferinject® High and Low Dosage Regimens) Versus Oral Iron for the Treatment of Iron Deficiency Anaemia in Subjects with Non-dialysis-dependent Chronic Kidney Disease

Summary

EudraCT number	2009-015579-28
Trial protocol	GB BE SE FR DE DK ES IT CZ AT GR PT NL
Global end of trial date	12 February 2013

Results information

Result version number	v1 (current)
This version publication date	04 December 2016
First version publication date	04 December 2016

Trial information

Trial identification

Sponsor protocol code	FER-CKD-01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00994318
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Vifor Pharma (International) Inc.
Sponsor organisation address	Rechenstrasse 37, St. Gallen, Switzerland, CH-9001
Public contact	Medical Information, Vifor (International) Inc., medinfo@viforpharma.com
Scientific contact	Medical Information, Vifor (International) Inc., medinfo@viforpharma.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	23 May 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 February 2013
Global end of trial reached?	Yes
Global end of trial date	12 February 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the long-term efficacy of ferric carboxymaltose (FCM) (using targeted ferritin levels to determine dosing) or oral iron to delay and/or reduce erythropoiesis stimulating agent (ESA) use and/or other anaemia management options in non-dialysis-dependent chronic kidney disease (NDD-CKD) subjects with iron deficiency anaemia (IDA).

Protection of trial subjects:

A Data Safety Monitoring Board (DSMB), governed by a charter which stipulated operation procedures, met periodically to analyse aggregate and individual subject safety data, data integrity, and overall study conduct, to assess study progress and make recommendations to continue, modify, or terminate the study.

Background therapy: -

Evidence for comparator:

The standard clinically relevant oral iron dose was used in the comparator group. The oral iron dose of 100 mg iron as ferrous sulphate twice daily was considered the most appropriate for a 1-year study, chosen so that subject compliance did not suffer due to adverse events (AEs), which would likely occur at higher doses or frequency.

Actual start date of recruitment	16 December 2009
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	Germany: 104
Country: Number of subjects enrolled	Austria: 8
Country: Number of subjects enrolled	Belgium: 10
Country: Number of subjects enrolled	Denmark: 4
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Greece: 115
Country: Number of subjects enrolled	Italy: 40
Country: Number of subjects enrolled	Netherlands: 16
Country: Number of subjects enrolled	Portugal: 9
Country: Number of subjects enrolled	Spain: 18
Country: Number of subjects enrolled	Sweden: 1
Country: Number of subjects enrolled	United Kingdom: 71
Country: Number of subjects enrolled	Norway: 5

Country: Number of subjects enrolled	Czech Republic: 62
Country: Number of subjects enrolled	Poland: 44
Country: Number of subjects enrolled	Romania: 8
Country: Number of subjects enrolled	United States: 14
Country: Number of subjects enrolled	Turkey: 31
Country: Number of subjects enrolled	Australia: 62
Worldwide total number of subjects	626
EEA total number of subjects	519

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	174
From 65 to 84 years	422
85 years and over	30

Subject disposition

Recruitment

Recruitment details:

There were 938 subjects screened of which 626 were randomised, in 156 sites in 19 countries, and included in the study.

Pre-assignment

Screening details:

After an initial screening period of up to 4 weeks, eligible subjects were randomly allocated to receive 1 of 3 study drug regimens for a period of 52 weeks; FCM high-dose, FCM low-dose or oral iron in a 1:1:2 ratio.
Period 1 (pre-treatment): from informed consent to first study drug dose. For study results, only Periods 2 and 3 are described.

Period 1

Period 1 title	Period 2 (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

NOTE: Period 2 (study treatment): from first study drug dose to reaching primary endpoint (treatment failure, i.e., application of additional or alternative anaemia management or hitting the Hb trigger) or end of study.

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A: FCM high-dose

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Ferric carboxymaltose (FCM)
Investigational medicinal product code	
Other name	Ferinject, FCM
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Day 0: 1,000 mg iron as FCM (subjects ≤66 kg dosed with 500 mg on Days 0 and 7).
Week 4 to 52 (dosing every 4 weeks ±3 days with last dose at Week 48): 1,000 mg iron as FCM (subjects ≤66 kg dosed with 500 mg on day of visit and 500 mg 1 week later) when ferritin was <200 mcg/L. If ferritin range was between 200 and <400 mcg/L, a dose of 500 mg iron as FCM was administered. No dose was administered if ferritin was ≥400 mcg/L.
FCM dosing was only initiated if transferrin saturation (TSAT) was <40%. For subjects with TSAT >35% from a prior assessment (completed >10 days prior to planned FCM administration day), dosing was withheld until TSAT was confirmed as <40%.

Arm title	Arm B: FCM low-dose

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Ferric carboxymaltose (FCM)
Investigational medicinal product code	
Other name	Ferinject, FCM
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Day 0: 200 mg iron as FCM. No dose was administered if screening ferritin level (or value on day of randomisation, if available) was ≥100 mcg/L.

Week 4 to 52 (dosing every 4 weeks ±3 days with last dose at Week 48): 200 mg iron as FCM when ferritin was <100 mcg/L. No dose was administered if ferritin value was ≥100 mcg/L.
FCM dosing was only initiated if TSAT was <40%. For subjects with TSAT >35% from a prior assessment (completed >10 days prior to planned FCM administration day), dosing was withheld until TSAT was confirmed as <40%.

Arm title	Arm C: daily oral iron
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Oral iron
Investigational medicinal product code	
Other name	Plastufer® 100 mg capsules, ferrous sulphate
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Weeks 0 to 52: 200 mg iron/day (100 mg twice daily) orally. Oral iron was supplied as ferrous sulphate. Dosing was suspended if serum ferritin was ≥200 mcg/L and resumed if values fell below <100 mcg/L.

Number of subjects in period 1	Arm A: FCM high-dose	Arm B: FCM low-dose	Arm C: daily oral iron
Started	155	154	317
Completed	133	136	250
Not completed	22	18	67
Adverse event, serious fatal	6	2	12
Consent withdrawn by subject	13	8	32
Physician decision	-	1	9
Adverse event, non-fatal	-	3	10
Other	-	1	1
Lost to follow-up	2	3	2
Protocol deviation	1	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Arm A: FCM high-dose
Reporting group description: -	
Reporting group title	Arm B: FCM low-dose
Reporting group description: -	
Reporting group title	Arm C: daily oral iron
Reporting group description: -	

Reporting group values	Arm A: FCM high-dose	Arm B: FCM low-dose	Arm C: daily oral iron
Number of subjects	155	154	317
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	39	47	88
From 65-84 years	107	103	212
85 years and over	9	4	17
Age continuous Units: years			
arithmetic mean	69.5	68.2	69.2
standard deviation	± 12.6	± 13.2	± 13.4
Gender categorical Units: Subjects			
Female	93	98	199
Male	62	56	118

Reporting group values	Total		
Number of subjects	626		
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)	174		
From 65-84 years	422		
85 years and over	30		

Age continuous Units: years arithmetic mean standard deviation	- 		
Gender categorical Units: Subjects			
Female	390		
Male	236		

End points

End points reporting groups

Reporting group title	Arm A: FCM high-dose
Reporting group description: -	
Reporting group title	Arm B: FCM low-dose
Reporting group description: -	
Reporting group title	Arm C: daily oral iron
Reporting group description: -	

Primary: Time-to initiation of other anaemia management analysis, including Hb trigger based on central lab data

End point title	Time-to initiation of other anaemia management analysis, including Hb trigger based on central lab data

End point description:

Subjects (FAS population) were considered as having met the primary endpoint if at last one of the following occurred:
1- Additional or alternative anaemia management to the randomised treatment arm (including use of alternative iron product, or change to dosing schedule or total iron dose) was implemented by the treating physician to address lack of efficacy or subject treatment-related adverse events (AEs).
2 - Subject had 2 consecutive haemoglobin (Hb) values <10 g/dL (and without an Hb increase of ≥0.5 g/dL between the 2 values). This was based on central laboratory assessments. Subjects were to continue on assigned treatment per protocol.

End point type	Primary

End point timeframe:

From the first dose (either FCM high-dose, FCM low-dose or oral iron), until having met the primary endpoint after the 8-week period.

End point values	Arm A: FCM high-dose	Arm B: FCM low-dose	Arm C: daily oral iron	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	153	152	308	
Units: day				
arithmetic mean (standard error)	295.7 (± 7.65)	283.8 (± 9.47)	286.7 (± 7.71)	

Statistical analyses

Statistical analysis title	Subjects requiring ESA
Comparison groups	Arm A: FCM high-dose v Arm C: daily oral iron
Number of subjects included in analysis	461
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0.57
Method	Logrank
Parameter estimate	Log odds ratio
Point estimate	0.85

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.48
upper limit	1.49

Notes:

[1] - There were 3 primary comparisons planned, using a hierarchical step-down procedure on the log-rank test to preserve the overall alpha level of 0.05. Analyses were performed in the following order:
1. FCM high-dose compared with oral iron
2. FCM high-dose compared with FCM low-dose
3. FCM low-dose compared with oral iron

Statistical analysis title	Subjects requiring ESA
Comparison groups	Arm A: FCM high-dose v Arm B: FCM low-dose
Number of subjects included in analysis	305
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.15
Method	Logrank
Parameter estimate	Log odds ratio
Point estimate	0.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.34
upper limit	1.18

Statistical analysis title	Subjects requiring ESA
Comparison groups	Arm C: daily oral iron v Arm B: FCM low-dose
Number of subjects included in analysis	460
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.27
Method	Logrank
Parameter estimate	Log odds ratio
Point estimate	1.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	2.27

Secondary: Time to first occurrence of Hb increase ≥1 g/dL prior to any other anaemia management

End point title	Time to first occurrence of Hb increase ≥1 g/dL prior to any other anaemia management

End point description:

End point type	Secondary

End point timeframe:

From the first dose (either FCM high-dose, FCM low-dose or oral iron), until having met the primary endpoint after the 8-week period.

End point values	Arm A: FCM high-dose	Arm B: FCM low-dose	Arm C: daily oral iron	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	153	152	308	
Units: days				
arithmetic mean (standard error)	192.6 (± 12.84)	268.2 (± 11.88)	272 (± 8.74)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to discontinuation of study drug due to intolerance

End point title	Time to discontinuation of study drug due to intolerance

End point description:

Discontinuation of study drug due to intolerance was defined as subject experiencing a related AE for which the "action to study drug" was permanent discontinuation of study drug.
Frequency counts and percentages were constructed for the number of subjects who had discontinued from the study drug due to intolerance.
Time to first occurrence of discontinuation of study drug due to intolerance was defined as the earliest start date of AE meeting the above definition. If the start date was partial or missing, imputation rules were used.

End point type	Secondary

End point timeframe:

From the first dose (either FCM high-dose, FCM low-dose or oral iron), until having met the primary endpoint after the 8-week period.

End point values	Arm A: FCM high-dose	Arm B: FCM low-dose	Arm C: daily oral iron	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	153	152	308	
Units: days				
arithmetic mean (full range (min-max))	242 (56 to 419)	225.1 (44 to 437)	329.4 (1 to 419)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events (AEs) reporting occurred from screening until Week 56.

Adverse event reporting additional description:

For reporting AEs, Periods 2 and 3 were considered.
Period 3: study treatment failure (from reaching primary endpoint to end of follow-up).
The results are described for safety set (SS).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.1

Reporting groups

Reporting group title	Period 2: Arm A
Reporting group description: -	
Reporting group title	Period 2: Arm B
Reporting group description: -	
Reporting group title	Period 2: Arm C
Reporting group description: -	
Reporting group title	Period 3: Arm A
Reporting group description: -	
Reporting group title	Period 3: Arm B
Reporting group description: -	
Reporting group title	Period 3: Arm C
Reporting group description: -	
Reporting group title	Period 3: Additional or Alternative Anaemia Management Only

Reporting group description:

This reporting group includes all AEs that occurred from day of treatment failure until end of study.

These medications included all non-study drug therapies to treat anemia, including other intravenous or oral iron preparations, ESAs, or blood transfusions.

Serious adverse events	Period 2: Arm A	Period 2: Arm B	Period 2: Arm C
Total subjects affected by serious adverse events			
subjects affected / exposed	39 / 154 (25.32%)	36 / 150 (24.00%)	59 / 312 (18.91%)
number of deaths (all causes)	5	1	6
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer			
subjects affected / exposed	1 / 154 (0.65%)	1 / 150 (0.67%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
B-cell lymphoma			

subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 312 (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
Basal cell carcinoma			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Burkitt's lymphoma			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 312 (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
Cholesteatoma			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 312 (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
Laryngeal cancer recurrent			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Lung carcinoma cell type unspecified recurrent			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 312 (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
Lung neoplasm			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 312 (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
Multiple myeloma			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Myelodysplastic syndrome			

subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 312 (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
Neuroendocrine carcinoma of the skin			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 312 (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 cell lung cancer stage unspecified			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 312 (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
Thyroid cancer			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 312 (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
Endometrial cancer			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to peritoneum			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
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-small cell lung cancer			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian neoplasm			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
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			

Hypertension			
subjects affected / exposed	1 / 154 (0.65%)	1 / 150 (0.67%)	3 / 312 (0.96%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic stenosis			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 312 (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
Circulatory collapse			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 312 (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
Hypertensive crisis			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 312 (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
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 312 (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
Deep vein thrombosis			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Carotid artery stent insertion			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
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			
Chest pain			
subjects affected / exposed	1 / 154 (0.65%)	1 / 150 (0.67%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device failure			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hernia obstructive			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 154 (0.00%)	2 / 150 (1.33%)	2 / 312 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea exertional			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
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 oedema			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Acute pulmonary oedema			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
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			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
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 distresss			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
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			
Haemoglobin decreased			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 312 (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
International normalised ratio increased			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
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			
Tibia fracture			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical vertebral fracture			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 312 (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
Concussion			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 312 (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
Femur fracture			

subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laceration			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 312 (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
Ligament rupture			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple injuries			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Overdose			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 312 (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
Pelvic fracture			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perirenal haematoma			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 312 (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
Renal haematoma			

subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 312 (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
Rib fracture			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal fracture			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 312 (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
Upper limb fracture			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clavicle fracture			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxicity to various agents			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transfusion reaction			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriovenous fistula site haemorrhage			

subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
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 myocardial infarction			
subjects affected / exposed	2 / 154 (1.30%)	0 / 150 (0.00%)	4 / 312 (1.28%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 5
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	3 / 312 (0.96%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	2 / 154 (1.30%)	1 / 150 (0.67%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute coronary syndrome			
subjects affected / exposed	2 / 154 (1.30%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	1 / 154 (0.65%)	1 / 150 (0.67%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Cardiac arrest			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Coronary artery disease			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			

subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arrhythmia			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 312 (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
Atrial fibrillation			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block complete			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
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 / 154 (0.00%)	1 / 150 (0.67%)	0 / 312 (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
Extrasystoles			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive heart disease			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Left ventricular dysfunction			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 312 (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
Myocardial ischaemia			

subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 312 (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
Sinus arrhythmia			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 312 (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
Atrioventricular block second degree			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
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 chronic			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiogenic shock			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mitral valve disease			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
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 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			

subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	3 / 312 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral ischaemia			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 312 (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
Cerebrovascular accident			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Hypoglycaemic coma			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotonia			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Loss of consciousness			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 312 (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
Orthostatic intolerance			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 312 (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
Vertebrobasilar insufficiency			

subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular insufficiency			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Guillain-Barre syndrome			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
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	1 / 154 (0.65%)	2 / 150 (1.33%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrogenic anaemia			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			

subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 312 (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
Haemorrhagic anaemia			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
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			
Diarrhoea			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 312 (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
Duodenal ulcer			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 312 (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
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenitis			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 312 (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
Dyspepsia			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 312 (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
Enterocolitis			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 312 (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
Gastric ulcer			

subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematemesis			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 312 (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
Pancreatic disorder			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 312 (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
Pancreatitis			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 312 (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
Umbilical hernia, obstructive			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 312 (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
Colonic polyp			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			

subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Melaena			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Diabetic ulcer			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 312 (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
Drug eruption			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pemphigoid			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 312 (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
Rash			

subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure chronic			
subjects affected / exposed	1 / 154 (0.65%)	1 / 150 (0.67%)	6 / 312 (1.92%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	2 / 312 (0.64%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Azotaemia			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrotic syndrome			
subjects affected / exposed	1 / 154 (0.65%)	1 / 150 (0.67%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure acute			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	2 / 312 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis glandularis			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			

subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 312 (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
Renal artery stenosis			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 312 (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
Urinary retention			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Hyperparathyroidism primary			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
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	2 / 154 (1.30%)	1 / 150 (0.67%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar spinal stenosis			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal pain			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 312 (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
Osteoarthritis			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Rheumatoid arthritis			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoporotic fracture			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	4 / 312 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	2 / 312 (0.64%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	1 / 154 (0.65%)	1 / 150 (0.67%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Abscess			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bacteraemia			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 312 (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
Bronchopneumonia			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 312 (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
Endophthalmitis			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infected skin ulcer			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 312 (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
Infection			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 312 (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
Staphylococcal sepsis			

subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 312 (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 abscess			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection staphylococcal			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atypical pneumonia			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lobar pneumonia			

subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
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 staphylococcal			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
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			
Hyperglycaemia			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	1 / 154 (0.65%)	1 / 150 (0.67%)	5 / 312 (1.60%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			
subjects affected / exposed	0 / 154 (0.00%)	3 / 150 (2.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic foot			
subjects affected / exposed	1 / 154 (0.65%)	1 / 150 (0.67%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 312 (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
Diabetic ketoacidosis			

subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 312 (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
Fluid overload			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fluid retention			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 312 (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
Hyperkalaemia			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gout			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Period 3: Arm A	Period 3: Arm B	Period 3: Arm C
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 16 (50.00%)	7 / 22 (31.82%)	38 / 86 (44.19%)
number of deaths (all causes)	0	0	8
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1

B-cell lymphoma			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal cell carcinoma			
subjects affected / exposed	0 / 16 (0.00%)	1 / 22 (4.55%)	0 / 86 (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
Burkitt's lymphoma			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholesteatoma			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal cancer recurrent			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
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 carcinoma cell type unspecified recurrent			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
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 neoplasm			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple myeloma			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelodysplastic syndrome			

subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuroendocrine carcinoma of the skin			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
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 cell lung cancer stage unspecified			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thyroid cancer			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometrial cancer			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to peritoneum			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Non-small cell lung cancer			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Ovarian neoplasm			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			

Hypertension			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic stenosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Circulatory collapse			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive crisis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	2 / 86 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Carotid artery stent insertion			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
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			
Chest pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device failure			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hernia obstructive			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
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 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Sudden death			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
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			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pneumonia aspiration			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea exertional			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
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 oedema			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute pulmonary oedema			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	2 / 86 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pneumothorax			
subjects affected / exposed	1 / 16 (6.25%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory distresss			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
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			
Haemoglobin decreased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
International normalised ratio increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
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 creatinine increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 22 (4.55%)	0 / 86 (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
Injury, poisoning and procedural complications			
Tibia fracture			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical vertebral fracture			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			
subjects affected / exposed	1 / 16 (6.25%)	0 / 22 (0.00%)	0 / 86 (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
Femur fracture			

subjects affected / exposed	0 / 16 (0.00%)	1 / 22 (4.55%)	0 / 86 (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
Humerus fracture			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laceration			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ligament rupture			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple injuries			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic fracture			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perirenal haematoma			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
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 haematoma			

subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal fracture			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper limb fracture			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clavicle fracture			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxicity to various agents			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transfusion reaction			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			
subjects affected / exposed	0 / 16 (0.00%)	1 / 22 (4.55%)	0 / 86 (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
Arteriovenous fistula site haemorrhage			

subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
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 disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	2 / 86 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	1 / 16 (6.25%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute coronary syndrome			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
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 arrest			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	2 / 86 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Coronary artery disease			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			

subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	2 / 86 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arrhythmia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
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 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block complete			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
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 / 16 (0.00%)	0 / 22 (0.00%)	2 / 86 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Extrasystoles			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive heart disease			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Left ventricular dysfunction			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			

subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus arrhythmia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block second degree			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
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 chronic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiogenic shock			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mitral valve disease			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			

subjects affected / exposed	1 / 16 (6.25%)	0 / 22 (0.00%)	0 / 86 (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
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral ischaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemic coma			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotonia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Loss of consciousness			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orthostatic intolerance			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vertebrobasilar insufficiency			

subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular insufficiency			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 16 (0.00%)	1 / 22 (4.55%)	0 / 86 (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
Epilepsy			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Guillain-Barre syndrome			
subjects affected / exposed	1 / 16 (6.25%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrogenic anaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			

subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic anaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
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			
Diarrhoea			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	2 / 86 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspepsia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
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 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
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 / 16 (0.00%)	0 / 22 (0.00%)	2 / 86 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematemesis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic disorder			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Umbilical hernia, obstructive			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colonic polyp			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids			
subjects affected / exposed	0 / 16 (0.00%)	1 / 22 (4.55%)	0 / 86 (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
Inguinal hernia			

subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Melaena			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 16 (0.00%)	1 / 22 (4.55%)	0 / 86 (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
Skin and subcutaneous tissue disorders			
Diabetic ulcer			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug eruption			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pemphigoid			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash			

subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure chronic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 22 (0.00%)	3 / 86 (3.49%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Azotaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrotic syndrome			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
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 / 16 (0.00%)	0 / 22 (0.00%)	2 / 86 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis glandularis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			

subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal artery stenosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
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 retention			
subjects affected / exposed	1 / 16 (6.25%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Hyperparathyroidism primary			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
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 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar spinal stenosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
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 pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
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 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Rheumatoid arthritis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoporotic fracture			
subjects affected / exposed	1 / 16 (6.25%)	0 / 22 (0.00%)	0 / 86 (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
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	5 / 86 (5.81%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Urinary tract infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bacteraemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
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 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endophthalmitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infected skin ulcer			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal sepsis			

subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
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 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
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 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
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 abscess			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
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 infection staphylococcal			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atypical pneumonia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lobar pneumonia			

subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia staphylococcal			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 22 (4.55%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic foot			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic ketoacidosis			

subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
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 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
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 retention			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	2 / 86 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gout			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Period 3: Additional or Alternative Anaemia Management Only		
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 61 (21.31%)		
number of deaths (all causes)	5		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer			

subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
B-cell lymphoma				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Basal cell carcinoma				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Burkitt's lymphoma				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholesteatoma				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Laryngeal cancer recurrent				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung carcinoma cell type unspecified recurrent				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung neoplasm				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Multiple myeloma				

subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myelodysplastic syndrome				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neuroendocrine carcinoma of the skin				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Small cell lung cancer stage unspecified				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thyroid cancer				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Endometrial cancer				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metastases to peritoneum				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Non-small cell lung cancer				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ovarian neoplasm				

subjects affected / exposed	0 / 61 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Aortic stenosis			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Circulatory collapse			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haemorrhage			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypertensive crisis			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Deep vein thrombosis			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			

Carotid artery stent insertion				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Chest pain				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Device failure				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fatigue				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hernia obstructive				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Non-cardiac chest pain				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Death				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sudden death				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia aspiration			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute respiratory failure			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dyspnoea exertional			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary oedema			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Acute pulmonary oedema			

subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumothorax				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory distresss				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
Haemoglobin decreased				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
International normalised ratio increased				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood creatinine increased				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Tibia fracture				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cervical vertebral fracture				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Concussion				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Femur fracture				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Humerus fracture				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Laceration				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ligament rupture				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Multiple injuries				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Overdose				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pelvic fracture				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Perirenal haematoma				

subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal haematoma				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rib fracture				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spinal fracture				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper limb fracture				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Clavicle fracture				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Toxicity to various agents				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Transfusion reaction				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Femoral neck fracture				

subjects affected / exposed	1 / 61 (1.64%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Arteriovenous fistula site haemorrhage				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Acute myocardial infarction				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac failure congestive				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Acute coronary syndrome				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac arrest				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coronary artery disease				

subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Angina unstable				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Arrhythmia				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrioventricular block complete				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac failure acute				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Extrasystoles				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertensive heart disease				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Left ventricular dysfunction				

subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial ischaemia				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sinus arrhythmia				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrioventricular block second degree				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure chronic				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiogenic shock				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Mitral valve disease				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pericardial effusion				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pericarditis				

subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Angina pectoris				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Syncope				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral ischaemia				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Hypoglycaemic coma				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypotonia				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Loss of consciousness				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Orthostatic intolerance				

subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vertebrobasilar insufficiency				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral infarction				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular insufficiency				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dizziness				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Epilepsy				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Guillain-Barre syndrome				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anaemia				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nephrogenic anaemia				

subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancytopenia				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhagic anaemia				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Diarrhoea				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Duodenal ulcer				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Duodenal ulcer haemorrhage				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Duodenitis				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dyspepsia				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Enterocolitis				

subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastric ulcer				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal haemorrhage				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haematemesis				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatic disorder				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Umbilical hernia, obstructive				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colonic polyp				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhoids				

subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Inguinal hernia				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Melaena				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rectal haemorrhage				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholecystitis				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholecystitis acute				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Diabetic ulcer				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Drug eruption				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pemphigoid				

subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rash				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Renal failure chronic				
subjects affected / exposed	3 / 61 (4.92%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Renal failure				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Azotaemia				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nephrotic syndrome				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal failure acute				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal impairment				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cystitis glandularis				

subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haematuria				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal artery stenosis				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary retention				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Endocrine disorders				
Hyperparathyroidism primary				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Back pain				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lumbar spinal stenosis				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal pain				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Osteoarthritis				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rheumatoid arthritis				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Osteoporotic fracture				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Pneumonia				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infective exacerbation of chronic obstructive airways disease				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Abscess				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bacteraemia				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchopneumonia				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cystitis				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Endophthalmitis				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infected skin ulcer				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infection				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection				

subjects affected / exposed	2 / 61 (3.28%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 1			
Staphylococcal sepsis				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urosepsis				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Viral upper respiratory tract infection				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wound abscess				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wound infection staphylococcal				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atypical pneumonia				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				

subjects affected / exposed	1 / 61 (1.64%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lobar pneumonia				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Osteomyelitis				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia staphylococcal				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Hyperglycaemia				
subjects affected / exposed	1 / 61 (1.64%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypoglycaemia				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diabetes mellitus				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diabetic foot				
subjects affected / exposed	0 / 61 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dehydration				

subjects affected / exposed	0 / 61 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diabetic ketoacidosis			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fluid overload			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fluid retention			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperkalaemia			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gout			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	Period 2: Arm A	Period 2: Arm B	Period 2: Arm C
Total subjects affected by non-serious adverse events			
subjects affected / exposed	122 / 154 (79.22%)	125 / 150 (83.33%)	248 / 312 (79.49%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	3 / 154 (1.95%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences (all)	3	0	0
Endocrine neoplasm			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	20 / 154 (12.99%)	14 / 150 (9.33%)	29 / 312 (9.29%)
occurrences (all)	22	17	31
Hypotension			
subjects affected / exposed	8 / 154 (5.19%)	4 / 150 (2.67%)	5 / 312 (1.60%)
occurrences (all)	11	5	5
Haemorrhage			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	21 / 154 (13.64%)	21 / 150 (14.00%)	29 / 312 (9.29%)
occurrences (all)	26	22	36
Fatigue			
subjects affected / exposed	1 / 154 (0.65%)	6 / 150 (4.00%)	14 / 312 (4.49%)
occurrences (all)	1	6	15
Asthenia			
subjects affected / exposed	3 / 154 (1.95%)	2 / 150 (1.33%)	6 / 312 (1.92%)
occurrences (all)	3	2	6
Chest pain			
subjects affected / exposed	4 / 154 (2.60%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences (all)	4	0	1
Oedema			
subjects affected / exposed	3 / 154 (1.95%)	2 / 150 (1.33%)	4 / 312 (1.28%)
occurrences (all)	4	4	4

Influenza like illness			
subjects affected / exposed	0 / 154 (0.00%)	2 / 150 (1.33%)	2 / 312 (0.64%)
occurrences (all)	0	2	3
Medical device complication			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	7 / 154 (4.55%)	11 / 150 (7.33%)	11 / 312 (3.53%)
occurrences (all)	8	11	11
Cough			
subjects affected / exposed	4 / 154 (2.60%)	6 / 150 (4.00%)	9 / 312 (2.88%)
occurrences (all)	5	6	9
Rales			
subjects affected / exposed	2 / 154 (1.30%)	3 / 150 (2.00%)	5 / 312 (1.60%)
occurrences (all)	2	3	5
Psychiatric disorders			
Sleep disorder			
subjects affected / exposed	1 / 154 (0.65%)	1 / 150 (0.67%)	2 / 312 (0.64%)
occurrences (all)	1	1	2
Investigations			
Blood pressure increased			
subjects affected / exposed	3 / 154 (1.95%)	0 / 150 (0.00%)	5 / 312 (1.60%)
occurrences (all)	4	0	7
Blood glucose increased			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	4 / 312 (1.28%)
occurrences (all)	1	0	4
Blood parathyroid hormone increased			
subjects affected / exposed	1 / 154 (0.65%)	1 / 150 (0.67%)	1 / 312 (0.32%)
occurrences (all)	2	1	1
Blood urea increased			

subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 312 (0.00%)
occurrences (all)	0	1	0
Cardiac murmur			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	1 / 312 (0.32%)
occurrences (all)	0	1	1
Glomerular filtration rate decreased			
subjects affected / exposed	1 / 154 (0.65%)	1 / 150 (0.67%)	2 / 312 (0.64%)
occurrences (all)	1	1	2
Heart rate increased			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	1 / 154 (0.65%)	1 / 150 (0.67%)	1 / 312 (0.32%)
occurrences (all)	1	1	1
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	4 / 154 (2.60%)	6 / 150 (4.00%)	6 / 312 (1.92%)
occurrences (all)	4	7	6
Fall			
subjects affected / exposed	3 / 154 (1.95%)	1 / 150 (0.67%)	3 / 312 (0.96%)
occurrences (all)	3	1	3
Excoriation			
subjects affected / exposed	0 / 154 (0.00%)	2 / 150 (1.33%)	2 / 312 (0.64%)
occurrences (all)	0	2	2
Joint dislocation			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences (all)	0	0	0
Muscle strain			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences (all)	2	0	1
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	3 / 154 (1.95%)	5 / 150 (3.33%)	2 / 312 (0.64%)
occurrences (all)	3	6	2
Atrial fibrillation			

subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	3 / 312 (0.96%)
occurrences (all)	1	0	3
Cardiac failure			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	4 / 312 (1.28%)
occurrences (all)	0	0	4
Tachyarrhythmia			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	9 / 154 (5.84%)	8 / 150 (5.33%)	7 / 312 (2.24%)
occurrences (all)	10	9	8
Headache			
subjects affected / exposed	6 / 154 (3.90%)	10 / 150 (6.67%)	7 / 312 (2.24%)
occurrences (all)	7	12	8
Convulsion			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences (all)	0	0	1
Guillain-Barre syndrome			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	6 / 154 (3.90%)	6 / 150 (4.00%)	9 / 312 (2.88%)
occurrences (all)	6	6	9
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	4 / 154 (2.60%)	5 / 150 (3.33%)	4 / 312 (1.28%)
occurrences (all)	4	5	5
Eye disorders			
Eyelid oedema			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences (all)	0	0	0
Scleral haemorrhage			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	15 / 154 (9.74%)	10 / 150 (6.67%)	45 / 312 (14.42%)
occurrences (all)	19	12	49
Constipation			
subjects affected / exposed	2 / 154 (1.30%)	5 / 150 (3.33%)	37 / 312 (11.86%)
occurrences (all)	2	5	41
Nausea			
subjects affected / exposed	9 / 154 (5.84%)	7 / 150 (4.67%)	15 / 312 (4.81%)
occurrences (all)	11	7	16
Dyspepsia			
subjects affected / exposed	2 / 154 (1.30%)	2 / 150 (1.33%)	17 / 312 (5.45%)
occurrences (all)	2	2	17
Vomiting			
subjects affected / exposed	6 / 154 (3.90%)	4 / 150 (2.67%)	13 / 312 (4.17%)
occurrences (all)	6	4	18
Gastritis			
subjects affected / exposed	2 / 154 (1.30%)	1 / 150 (0.67%)	4 / 312 (1.28%)
occurrences (all)	2	1	4
Gastritis haemorrhagic			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 154 (0.65%)	1 / 150 (0.67%)	2 / 312 (0.64%)
occurrences (all)	1	1	2
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	5 / 154 (3.25%)	4 / 150 (2.67%)	9 / 312 (2.88%)
occurrences (all)	6	4	9
Skin ulcer			
subjects affected / exposed	2 / 154 (1.30%)	1 / 150 (0.67%)	4 / 312 (1.28%)
occurrences (all)	4	1	4
Dry skin			
subjects affected / exposed	1 / 154 (0.65%)	1 / 150 (0.67%)	0 / 312 (0.00%)
occurrences (all)	1	1	0
Eczema			

subjects affected / exposed	2 / 154 (1.30%)	1 / 150 (0.67%)	0 / 312 (0.00%)
occurrences (all)	3	1	0
Scar			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 154 (0.65%)	3 / 150 (2.00%)	5 / 312 (1.60%)
occurrences (all)	1	3	5
Renal impairment			
subjects affected / exposed	3 / 154 (1.95%)	2 / 150 (1.33%)	4 / 312 (1.28%)
occurrences (all)	3	2	4
Renal failure chronic			
subjects affected / exposed	3 / 154 (1.95%)	1 / 150 (0.67%)	3 / 312 (0.96%)
occurrences (all)	3	1	3
Endocrine disorders			
Hyperparathyroidism secondary			
subjects affected / exposed	1 / 154 (0.65%)	1 / 150 (0.67%)	4 / 312 (1.28%)
occurrences (all)	1	1	4
Hyperparathyroidism			
subjects affected / exposed	0 / 154 (0.00%)	2 / 150 (1.33%)	0 / 312 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	15 / 154 (9.74%)	11 / 150 (7.33%)	11 / 312 (3.53%)
occurrences (all)	15	12	12
Arthralgia			
subjects affected / exposed	10 / 154 (6.49%)	7 / 150 (4.67%)	15 / 312 (4.81%)
occurrences (all)	14	7	17
Pain in extremity			
subjects affected / exposed	2 / 154 (1.30%)	8 / 150 (5.33%)	15 / 312 (4.81%)
occurrences (all)	2	8	17
Muscle spasms			
subjects affected / exposed	1 / 154 (0.65%)	7 / 150 (4.67%)	3 / 312 (0.96%)
occurrences (all)	1	7	3
Musculoskeletal pain			

subjects affected / exposed	0 / 154 (0.00%)	5 / 150 (3.33%)	4 / 312 (1.28%)
occurrences (all)	0	5	4
Myalgia			
subjects affected / exposed	2 / 154 (1.30%)	1 / 150 (0.67%)	3 / 312 (0.96%)
occurrences (all)	2	2	3
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	17 / 154 (11.04%)	10 / 150 (6.67%)	15 / 312 (4.81%)
occurrences (all)	21	12	16
Nasopharyngitis			
subjects affected / exposed	13 / 154 (8.44%)	10 / 150 (6.67%)	16 / 312 (5.13%)
occurrences (all)	18	10	20
Influenza			
subjects affected / exposed	4 / 154 (2.60%)	8 / 150 (5.33%)	7 / 312 (2.24%)
occurrences (all)	5	9	7
Upper respiratory tract infection			
subjects affected / exposed	6 / 154 (3.90%)	4 / 150 (2.67%)	9 / 312 (2.88%)
occurrences (all)	8	4	10
Bronchitis			
subjects affected / exposed	4 / 154 (2.60%)	1 / 150 (0.67%)	11 / 312 (3.53%)
occurrences (all)	4	1	11
Lower respiratory tract infection			
subjects affected / exposed	5 / 154 (3.25%)	4 / 150 (2.67%)	5 / 312 (1.60%)
occurrences (all)	5	4	7
Gastroenteritis			
subjects affected / exposed	1 / 154 (0.65%)	4 / 150 (2.67%)	5 / 312 (1.60%)
occurrences (all)	1	4	6
Wound infection			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	3 / 154 (1.95%)	2 / 150 (1.33%)	4 / 312 (1.28%)
occurrences (all)	3	2	7
Vulvitis			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 312 (0.00%)
occurrences (all)	0	0	0

Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	5 / 154 (3.25%)	7 / 150 (4.67%)	6 / 312 (1.92%)
occurrences (all)	6	8	6
Hypoglycaemia			
subjects affected / exposed	7 / 154 (4.55%)	4 / 150 (2.67%)	7 / 312 (2.24%)
occurrences (all)	14	4	8
Hyperuricaemia			
subjects affected / exposed	2 / 154 (1.30%)	5 / 150 (3.33%)	6 / 312 (1.92%)
occurrences (all)	3	5	8
Hyperglycaemia			
subjects affected / exposed	7 / 154 (4.55%)	0 / 150 (0.00%)	5 / 312 (1.60%)
occurrences (all)	9	0	6
Decreased appetite			
subjects affected / exposed	1 / 154 (0.65%)	1 / 150 (0.67%)	4 / 312 (1.28%)
occurrences (all)	1	1	4
Diabetes mellitus			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	1 / 312 (0.32%)
occurrences (all)	0	0	1
Hyperphosphataemia			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	3 / 312 (0.96%)
occurrences (all)	0	0	3

Non-serious adverse events	Period 3: Arm A	Period 3: Arm B	Period 3: Arm C
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 16 (100.00%)	16 / 22 (72.73%)	65 / 86 (75.58%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 16 (0.00%)	1 / 22 (4.55%)	0 / 86 (0.00%)
occurrences (all)	0	1	0
Endocrine neoplasm			
subjects affected / exposed	1 / 16 (6.25%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 16 (12.50%)	2 / 22 (9.09%)	7 / 86 (8.14%)
occurrences (all)	2	2	8

Hypotension			
subjects affected / exposed	0 / 16 (0.00%)	1 / 22 (4.55%)	0 / 86 (0.00%)
occurrences (all)	0	2	0
Haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)	1 / 22 (4.55%)	0 / 86 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	2 / 16 (12.50%)	1 / 22 (4.55%)	5 / 86 (5.81%)
occurrences (all)	2	1	6
Fatigue			
subjects affected / exposed	1 / 16 (6.25%)	0 / 22 (0.00%)	4 / 86 (4.65%)
occurrences (all)	1	0	4
Asthenia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 22 (4.55%)	2 / 86 (2.33%)
occurrences (all)	0	1	2
Chest pain			
subjects affected / exposed	1 / 16 (6.25%)	0 / 22 (0.00%)	3 / 86 (3.49%)
occurrences (all)	1	0	3
Oedema			
subjects affected / exposed	1 / 16 (6.25%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences (all)	1	0	1
Influenza like illness			
subjects affected / exposed	0 / 16 (0.00%)	1 / 22 (4.55%)	0 / 86 (0.00%)
occurrences (all)	0	1	0
Medical device complication			
subjects affected / exposed	1 / 16 (6.25%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	1 / 16 (6.25%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			

subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	2 / 86 (2.33%)
occurrences (all)	0	0	2
Cough			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences (all)	0	0	1
Rales			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	3 / 86 (3.49%)
occurrences (all)	0	0	4
Psychiatric disorders			
Sleep disorder			
subjects affected / exposed	1 / 16 (6.25%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences (all)	1	0	1
Investigations			
Blood pressure increased			
subjects affected / exposed	1 / 16 (6.25%)	1 / 22 (4.55%)	0 / 86 (0.00%)
occurrences (all)	1	1	0
Blood glucose increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 22 (4.55%)	0 / 86 (0.00%)
occurrences (all)	0	1	0
Blood parathyroid hormone increased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences (all)	1	0	0
Blood urea increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 22 (4.55%)	0 / 86 (0.00%)
occurrences (all)	0	1	0
Cardiac murmur			
subjects affected / exposed	1 / 16 (6.25%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences (all)	1	0	0
Glomerular filtration rate decreased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 22 (4.55%)	0 / 86 (0.00%)
occurrences (all)	0	1	0
Heart rate increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 22 (4.55%)	0 / 86 (0.00%)
occurrences (all)	0	1	0
Weight decreased			

subjects affected / exposed	1 / 16 (6.25%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	1 / 16 (6.25%)	2 / 22 (9.09%)	1 / 86 (1.16%)
occurrences (all)	1	2	1
Excoriation			
subjects affected / exposed	0 / 16 (0.00%)	1 / 22 (4.55%)	0 / 86 (0.00%)
occurrences (all)	0	1	0
Joint dislocation			
subjects affected / exposed	1 / 16 (6.25%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences (all)	1	0	0
Muscle strain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 22 (4.55%)	0 / 86 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	2 / 86 (2.33%)
occurrences (all)	0	0	5
Atrial fibrillation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences (all)	0	0	1
Cardiac failure			
subjects affected / exposed	2 / 16 (12.50%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences (all)	2	0	1
Tachyarrhythmia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 22 (4.55%)	0 / 86 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences (all)	0	0	1
Headache			

subjects affected / exposed	1 / 16 (6.25%)	0 / 22 (0.00%)	3 / 86 (3.49%)
occurrences (all)	1	0	5
Convulsion			
subjects affected / exposed	1 / 16 (6.25%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences (all)	1	0	0
Guillain-Barre syndrome			
subjects affected / exposed	1 / 16 (6.25%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 22 (4.55%)	2 / 86 (2.33%)
occurrences (all)	0	1	2
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Eyelid oedema			
subjects affected / exposed	0 / 16 (0.00%)	1 / 22 (4.55%)	0 / 86 (0.00%)
occurrences (all)	0	1	0
Scleral haemorrhage			
subjects affected / exposed	1 / 16 (6.25%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 16 (0.00%)	2 / 22 (9.09%)	7 / 86 (8.14%)
occurrences (all)	0	2	7
Constipation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	4 / 86 (4.65%)
occurrences (all)	0	0	4
Nausea			
subjects affected / exposed	1 / 16 (6.25%)	0 / 22 (0.00%)	5 / 86 (5.81%)
occurrences (all)	1	0	5
Dyspepsia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences (all)	0	0	0
Vomiting			

subjects affected / exposed	1 / 16 (6.25%)	0 / 22 (0.00%)	2 / 86 (2.33%)
occurrences (all)	1	0	3
Gastritis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences (all)	1	0	0
Gastritis haemorrhagic			
subjects affected / exposed	0 / 16 (0.00%)	1 / 22 (4.55%)	0 / 86 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 16 (6.25%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	2 / 86 (2.33%)
occurrences (all)	0	0	2
Skin ulcer			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	4 / 86 (4.65%)
occurrences (all)	0	0	5
Dry skin			
subjects affected / exposed	1 / 16 (6.25%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences (all)	1	0	0
Eczema			
subjects affected / exposed	0 / 16 (0.00%)	1 / 22 (4.55%)	0 / 86 (0.00%)
occurrences (all)	0	1	0
Scar			
subjects affected / exposed	0 / 16 (0.00%)	1 / 22 (4.55%)	0 / 86 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 16 (0.00%)	1 / 22 (4.55%)	2 / 86 (2.33%)
occurrences (all)	0	1	2
Renal impairment			
subjects affected / exposed	2 / 16 (12.50%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences (all)	2	0	1
Renal failure chronic			

subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	3 / 86 (3.49%)
occurrences (all)	0	0	3
Endocrine disorders			
Hyperparathyroidism secondary			
subjects affected / exposed	1 / 16 (6.25%)	1 / 22 (4.55%)	0 / 86 (0.00%)
occurrences (all)	1	1	0
Hyperparathyroidism			
subjects affected / exposed	1 / 16 (6.25%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences (all)	1	0	1
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 16 (6.25%)	1 / 22 (4.55%)	2 / 86 (2.33%)
occurrences (all)	1	1	2
Arthralgia			
subjects affected / exposed	0 / 16 (0.00%)	2 / 22 (9.09%)	5 / 86 (5.81%)
occurrences (all)	0	5	6
Pain in extremity			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	2 / 86 (2.33%)
occurrences (all)	0	0	2
Musculoskeletal pain			
subjects affected / exposed	1 / 16 (6.25%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences (all)	1	0	1
Myalgia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 22 (4.55%)	2 / 86 (2.33%)
occurrences (all)	0	1	2
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 16 (0.00%)	2 / 22 (9.09%)	2 / 86 (2.33%)
occurrences (all)	0	2	2
Nasopharyngitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	2 / 86 (2.33%)
occurrences (all)	0	0	2
Influenza			

subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	2 / 86 (2.33%)
occurrences (all)	0	0	2
Bronchitis			
subjects affected / exposed	3 / 16 (18.75%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences (all)	3	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	3 / 86 (3.49%)
occurrences (all)	0	0	4
Gastroenteritis			
subjects affected / exposed	0 / 16 (0.00%)	2 / 22 (9.09%)	3 / 86 (3.49%)
occurrences (all)	0	2	4
Wound infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 22 (0.00%)	2 / 86 (2.33%)
occurrences (all)	1	0	2
Cellulitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 22 (4.55%)	1 / 86 (1.16%)
occurrences (all)	0	1	1
Vulvitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	2 / 16 (12.50%)	0 / 22 (0.00%)	2 / 86 (2.33%)
occurrences (all)	3	0	2
Hypoglycaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	0 / 86 (0.00%)
occurrences (all)	0	0	0
Hyperuricaemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences (all)	1	0	1
Hyperglycaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	1 / 86 (1.16%)
occurrences (all)	0	0	1

Decreased appetite			
subjects affected / exposed	0 / 16 (0.00%)	0 / 22 (0.00%)	3 / 86 (3.49%)
occurrences (all)	0	0	3
Diabetes mellitus			
subjects affected / exposed	0 / 16 (0.00%)	1 / 22 (4.55%)	1 / 86 (1.16%)
occurrences (all)	0	1	1
Hyperphosphataemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 22 (4.55%)	0 / 86 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Period 3: Additional or Alternative Anaemia Management Only		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 61 (44.26%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Endocrine neoplasm			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Hypotension			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Haemorrhage			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	4 / 61 (6.56%)		
occurrences (all)	4		
Fatigue			

subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Asthenia			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	2		
Chest pain			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Oedema			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Influenza like illness			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Medical device complication			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
Cough			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Rales			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Sleep disorder			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Investigations			

Blood pressure increased			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Blood glucose increased			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Blood parathyroid hormone increased			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Blood urea increased			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Cardiac murmur			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Glomerular filtration rate decreased			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Heart rate increased			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Weight decreased			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Fall			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Excoriation			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Joint dislocation			

subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Muscle strain			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Atrial fibrillation			
subjects affected / exposed	2 / 61 (3.28%)		
occurrences (all)	2		
Cardiac failure			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Tachyarrhythmia			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
Convulsion			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Guillain-Barre syndrome			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
Ear and labyrinth disorders			

Vertigo			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Eye disorders			
Eyelid oedema			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Scleral haemorrhage			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Dyspepsia			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Gastritis			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
Gastritis haemorrhagic			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			

Pruritus			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Skin ulcer			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Dry skin			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Eczema			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Scar			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	2 / 61 (3.28%)		
occurrences (all)	2		
Renal impairment			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
Renal failure chronic			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Endocrine disorders			
Hyperparathyroidism secondary			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
Hyperparathyroidism			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		

Arthralgia subjects affected / exposed occurrences (all)	1 / 61 (1.64%) 1			
Pain in extremity subjects affected / exposed occurrences (all)	0 / 61 (0.00%) 0			
Muscle spasms subjects affected / exposed occurrences (all)	2 / 61 (3.28%) 2			
Musculoskeletal pain subjects affected / exposed occurrences (all)	0 / 61 (0.00%) 0			
Myalgia subjects affected / exposed occurrences (all)	0 / 61 (0.00%) 0			
Infections and infestations Urinary tract infection subjects affected / exposed occurrences (all)	0 / 61 (0.00%) 0			
Nasopharyngitis subjects affected / exposed occurrences (all)	2 / 61 (3.28%) 2			
Influenza subjects affected / exposed occurrences (all)	1 / 61 (1.64%) 1			
Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 61 (0.00%) 0			
Bronchitis subjects affected / exposed occurrences (all)	1 / 61 (1.64%) 1			
Lower respiratory tract infection subjects affected / exposed occurrences (all)	0 / 61 (0.00%) 0			
Gastroenteritis				

subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Wound infection			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Cellulitis			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Vulvitis			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Hypoglycaemia			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Hyperuricaemia			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Hyperglycaemia			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Decreased appetite			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Diabetes mellitus			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Hyperphosphataemia			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 July 2010	Amendment 1: Included the following major changes:•ESA or additional or alternative anaemia management use not permitted in subjects with Hb ≥10 g/dL.•More specific details to state no change of iron product from the treatment assigned by randomisation (when Hb >10 g/dL) was permitted except if "subject was not able to comply or tolerate the randomised treatment arm.".•Statement to advise that "After the 8-week period, subjects with 2 consecutive Hb values <10 g/dL (and without an Hb increase of ≥0.5 g/dL rise in last 4 weeks) were considered to have met the primary endpoint but should continue on assigned treatment per protocol".•Within the oral arm, "Dosing may be suspended if serum ferritin ≥200 mcg/L and should be resumed if values fall below <100 mcg/L".•Inclusion criterion 3: Updated to include clarification on 'previous eGFR loss'.•Inclusion criterion 4: Amended to permit a screening Hb average between 9 and 11 g/dL. The wording was also clarified.•Inclusion criterion 6: Amended to define ESA naïve subjects.•Inclusion criterion 7: Amended to ensure that the pregnancy test was completed 4 weeks prior to randomisation rather than screening.•Exclusion criterion 5: Amended to define the term 'active malignancy'.•Exclusion criterion 11: Amended to permit subjects on low doses of oral iron (or oral iron from multivitamin supplements) permitted for inclusion.•Exclusion criterion 12: Amended to define limited immunosuppressive therapies, i.e., those "that may lead to anaemia, such as cyclophosphamide, azathioprine, mycophenolate mofetil, etc. Steroid therapy was permitted". This clarified questions from several participating sites.•Exclusion criterion 13: Updated to state explicitly that renal dialysis refers to subjects "Currently requiring renal dialysis".•Exclusion criterion 17: More explicit in definition of poorly controlled hypertension – from >160/100 mmHg to >60 mmHg systolic pressure or >100 mmHg diastolic pressure.•Dosing time updated for FCM arms.
16 December 2010	Amendment 2: Included the following major changes:•Inclusion criterion 4: Amended from "Screening Hb between 9 and 11 g/dL based on an average of at least 2 Hb readings taken in the 4 weeks prior to randomisation with a minimum of 2 days and a maximum of 4 weeks between values (with no single value ≥12 g/dL). At least 1 value had to be <10.5 g/dL" to "Hb between 9 and 11 g/dL within 4 weeks of randomisation. A value taken as part of routine medical care could be used".•Inclusion criterion 5: Amended from "Screening ferritin <100 mcg/L" to "Serum ferritin <100 mcg/L or <200 mcg/L with TSAT <20% within 4 weeks of randomisation. Measurements taken as part of routine medical care may be used". The Arm B treatment section was also amended from "Day 0: 200 mg iron as FCM" to "Day 0: 200 mg iron as FCM. No dose administered if ferritin value is ≥100 mcg/L".•Inclusion criterion 7: Amended from "Females of childbearing potential must have a negative pregnancy test at within 4 weeks of randomisation" to "Females of childbearing potential must have a negative pregnancy test prior to randomisation".•Exclusion criterion 11: Amended from "Oral iron therapy at doses >100 mg/day in previous 4 weeks prior to randomisation. Upon randomisation the oral iron therapy must be discontinued. Ongoing use of multivitamins containing iron are permitted" to "Oral iron therapy at doses >100 mg/day in previous 1 week prior to randomisation and/or subjects who have been continuously treated with >100 mg/day of oral iron for the last 3 months. Upon randomisation the oral iron therapy must be discontinued. Ongoing use of multivitamins containing iron was permitted". Exclusion criterion 3 (no changes in this amendment) excludes subjects that are intolerant to oral iron due to GI distress.•Schedule of Events: the following text added to footnote number 5 "Values collected as part of routine medical practice and prior to consent may be used to confirm eligibility".•Minor clarifying wording.

01 September 2011	Amendment 3: Included the following major changes:•Inclusion criterion 3: To provide more explicit instructions for obtaining the right number of eGFR measurements, their values and time intervals for obtaining them of eGFR measurements required for subjects' eligibility in the study.•Inclusion criterion 4: Language clarification for accepting of a(ny) single Hb value between 9 to 11 g/dL obtained as part of routine medical practice or study specific screening/randomisation visit procedures obtained within 4 weeks prior to the date of randomisation.•Inclusion criterion 5: Clarification for accepting a(ny) single serum ferritin value of <100 mcg/mL or <200 mcg/mL with TSAT of <20% that was obtained either as part of routine medical practice or study specific screening/randomisation visit procedures but within 4 weeks prior to the date of randomisation.•Inclusion criterion 7: Administrative change to clarify how pregnancy tests are accepted as medically valid in medical practice.•Exclusion criterion 8: Further guidance and clarification for using results from various serology tests.•Exclusion criterion 10: To clarify that IV iron administration or blood transfusions were prohibited at any time from 30 days prior to screening until randomisation.•Exclusion criterion 11: To further clarify language of oral iron therapy discontinuation in relation to randomisation time.•Procedures section: To clarify acceptance of central laboratory values when more convenient than local laboratory values.•Sample size section: Changed from "approximately 1,016 subjects." to "…a maximum of 1,016 subjects."•Statistical methods section: To calculate and confirm the study sample size based on the main comparison (FCM high-dose versus oral iron) within the primary endpoint and to clarify the recruitment end date if there was a reduced sample size.•Schema: Text addition of "last investigational product kit handed out at Week 48" at the end of Ferinject sentence.•Minor clarifying wording.
14 August 2012	Amendment 4: Included the following major changes:•Study design: Current protocol wording stipulated "2 consecutive Hb values <10 g/dL (and without an Hb increase of ≥0.5 g/dL rise in the last 4 weeks).•Laboratory procedures: Laboratory assessments could be performed before the study visit so the laboratory results were available at the time of visit.•Risks and precautions: Section 8 of the protocol was amended in accordance with the updated version of the Company Core Data Sheet from 12 December 2011, the revised Summary of Product Characteristics, approved by the Medicines and Healthcare products Regulatory Agency on 29 September 2011, and the changes implemented in the latest version of the product's Investigator's Brochure (Version 14.0, dated 14 March 2012).•There were other minor editorial changes to improve consistency and correct minor typographical errors in the overall protocol.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
31 December 2011	Because of slow recruitment, the Sponsor decided to stop recruitment in December 2011 after sufficient subjects had been recruited to make the primary comparison between FCM high-dose and oral iron.	-

Notes:

Limitations and caveats

None reported