



Clinical trial results:

A Randomized, Double-Masked, Placebo-Controlled, Multicenter, Phase 2 Study to Evaluate the Safety and Renal Efficacy of LY2382770 in Patients With Diabetic Kidney Disease Due to Type 1 or Type 2 Diabetes.

Summary

EudraCT number	2010-020404-29
Trial protocol	HU CZ
Global end of trial date	22 July 2014

Results information

Result version number	v1 (current)
This version publication date	14 October 2017
First version publication date	14 October 2017

Trial information

Trial identification

Sponsor protocol code	H9V-MC-GFRF
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01113801
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 10168

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, IN, United States, 46285
Public contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 877CTLilly,
Scientific contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 8772854559,

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	22 July 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 July 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to determine if LY2382770 is safe and effective at protecting kidney function in participants with kidney disease due to diabetes.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy:

Stable dose of angiotensin-converting enzyme (ACE) inhibitor or angiotensin II receptor blocker (ARB).

Evidence for comparator: -

Actual start date of recruitment	12 July 2010
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	France: 32
Country: Number of subjects enrolled	United States: 145
Country: Number of subjects enrolled	Czech Republic: 45
Country: Number of subjects enrolled	Hungary: 57
Country: Number of subjects enrolled	Puerto Rico: 15
Country: Number of subjects enrolled	Australia: 40
Country: Number of subjects enrolled	Israel: 82
Worldwide total number of subjects	416
EEA total number of subjects	134

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)	245
From 65 to 84 years	168
85 years and over	3

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

No Text Entered

Period 1

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

Arms

Are arms mutually exclusive?	Yes
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Arm title	Placebo
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Arm description:

Placebo given subcutaneous (SC) injection monthly for 12 months

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo given subcutaneous (SC) injection monthly for 12 months.

Arm title	2 mg LY2382770
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Arm description:

2 milligrams (mg) LY2382770 given (SC) injection monthly for 12 months

Arm type	Experimental
Investigational medicinal product name	LY2382770
Investigational medicinal product code	
Other name	TGF- β 1 monoclonal antibody
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

2 milligrams (mg) LY2382770 given (SC) injection monthly for 12 months

Arm title	10 mg LY2382770
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Arm description:

10 mg LY2382770 given SC injection monthly for 12 months

Arm type	Experimental
Investigational medicinal product name	LY2382770
Investigational medicinal product code	
Other name	TGF- β 1 monoclonal antibody
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

10 mg LY2382770 given SC injection monthly for 12 months.

Arm title	50 mg LY2382770
Arm description: 50 mg LY2382770 given SC injection monthly for 12 months. The number of participants stated is based on those who were randomized and received at least one 50 mg dose of study drug? The number of participants randomized is 106.	
Arm type	Experimental
Investigational medicinal product name	LY2382770
Investigational medicinal product code	
Other name	TGF-β1 monoclonal antibody
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details: 50 mg LY2382770 given SC injection monthly for 12 months.	

Number of subjects in period 1	Placebo	2 mg LY2382770	10 mg LY2382770
Started	103	105	103
Received at least one dose of drug	103	105	103
Completed	62	65	66
Not completed	41	40	37
Consent withdrawn by subject	9	7	7
Physician decision	2	2	3
Clinical Endpoint (ESRD)	7	4	2
Adverse event, non-fatal	4	-	2
Sponsor Decision	15	21	20
Death	4	5	3
Protocol deviation	-	1	-

Number of subjects in period 1	50 mg LY2382770
Started	105
Received at least one dose of drug	105
Completed	65
Not completed	40
Consent withdrawn by subject	8
Physician decision	2
Clinical Endpoint (ESRD)	5
Adverse event, non-fatal	6
Sponsor Decision	15
Death	4
Protocol deviation	-

Baseline characteristics

Reporting groups

Reporting group title	Overall Study
Reporting group description:	
Baseline Analysis Population Description: All participants who received at least 1 dose of study drug.	

Reporting group values	Overall Study	Total	
Number of subjects	416	416	
Age categorical			
Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		0	
Newborns (0-27 days)		0	
Infants and toddlers (28 days-23 months)		0	
Children (2-11 years)		0	
Adolescents (12-17 years)		0	
Adults (18-64 years)		0	
From 65-84 years		0	
85 years and over		0	
Age Continuous			
All participants who received at least 1 dose of study drug.			
Units: years			
arithmetic mean	62.2		
standard deviation	± 10.16	-	
Gender, Male/Female			
Units:			
Male	320	320	
Female	96	96	
Region of Enrollment			
Units: Subjects			
France	32	32	
United States	145	145	
Czech Republic	45	45	
Hungary	57	57	
Puerto Rico	15	15	
Australia	40	40	
Israel	82	82	
Ethnicity			
Units: Subjects			
Hispanic or Latino	45	45	
Not Hispanic or Latino	211	211	
Unknown or Not Reported	160	160	
Race			
Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	8	8	

Native Hawaiian or Other Pacific Islander	2	2	
Black or African American	39	39	
White	347	347	
More than one race	3	3	
Unknown or Not Reported	17	17	
Serum Creatinine Units: milligram/deciliter (mg/dl) arithmetic mean standard deviation	2.14 ± 0.6141	-	
Urine Protein/Creatinine Ratio Units: gram/gram arithmetic mean standard deviation	3.262 ± 2.5148	-	
Estimated Glomerular Filtration Rate (eGFR) Units: milliliter/minute/1.73 meter squared arithmetic mean standard deviation	35.464 ± 11.8539	-	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Placebo given subcutaneous (SC) injection monthly for 12 months	
Reporting group title	2 mg LY2382770
Reporting group description: 2 milligrams (mg) LY2382770 given (SC) injection monthly for 12 months	
Reporting group title	10 mg LY2382770
Reporting group description: 10 mg LY2382770 given SC injection monthly for 12 months	
Reporting group title	50 mg LY2382770
Reporting group description: 50 mg LY2382770 given SC injection monthly for 12 months. The number of participants stated is based on those who were randomized and received at least one 50 mg dose of study drug? The number of participants randomized is 106.	
Subject analysis set title	Overall Study
Subject analysis set type	Full analysis
Subject analysis set description: All participants who received at least 1 dose of study drug.	

Primary: Change in Log Transformed (ln) Serum Creatinine from baseline to 12 month endpoint

End point title	Change in Log Transformed (ln) Serum Creatinine from baseline to 12 month endpoint
End point description: Log-transformed serum creatinine change from baseline. Analysis of covariance (ANCOVA) model was used with treatment, visit, and treatment-by-visit interaction as fixed effects, subject as random effect, baseline Serum Creatinine log transformed (ln) and first morning urine protein to creatinine ratio (PCR) log transformed (ln) as covariates. Analysis Population Description: All randomized participants who received at least 1 dose of drug and had evaluable baseline and post baseline serum creatinine values.	
End point type	Primary
End point timeframe: Baseline, 12 months	

End point values	Placebo	2 mg LY2382770	10 mg LY2382770	50 mg LY2382770
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	85	90	91	82
Units: ln milligrams per deciliter [ln(mg/dL)]				
least squares mean (standard error)	0.13 (± 0.019)	0.18 (± 0.019)	0.17 (± 0.019)	0.17 (± 0.02)

Statistical analyses

Statistical analysis title	Primary : Serum Creatinine (log transformed)
Comparison groups	Placebo v 2 mg LY2382770 v 10 mg LY2382770 v 50 mg LY2382770
Number of subjects included in analysis	348
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.89
Method	Maximum trend multivariate ttest,1-sided

Secondary: Change in Log Transformed (ln) Urine Protein/Creatinine Ratio from baseline to 12 month endpoint

End point title	Change in Log Transformed (ln) Urine Protein/Creatinine Ratio from baseline to 12 month endpoint
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End point description:

Log transformed urine protein to creatinine ratio change from baseline.

Analysis of covariance (ANCOVA) model was used with treatment, visit, and treatment-by-visit interaction as fixed effects, subject as random effect, baseline Serum Creatinine log transformed (ln) and first morning urine protein to creatinine ratio (PCR) log transformed (ln) as covariates.

Analysis Population Description: All randomized participants who received at least 1 dose of drug and had evaluable urine protein and creatinine ratio values.

End point type	Secondary
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End point timeframe:

Baseline, 12 months

End point values	Placebo	2 mg LY2382770	10 mg LY2382770	50 mg LY2382770
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	82	87	85	81
Units: ln grams/grams [ln(g/g)]				
least squares mean (standard error)	0.06 (± 0.076)	0.05 (± 0.072)	0.05 (± 0.073)	-0.01 (± 0.075)

Statistical analyses

No statistical analyses for this end point

Secondary: Population Pharmacokinetics (PK) - Model-Estimated Area Under the Concentration –Time Curve (AUC) Over a Dosing Interval

End point title	Population Pharmacokinetics (PK) - Model-Estimated Area Under the Concentration –Time Curve (AUC) Over a Dosing Interval
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End point description:

Analysis Population Description : All randomized participants who received at least 1 dose of drug and had evaluable PK data.

End point type	Secondary
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End point timeframe:

Baseline through 12 months (samples collected pre and/or postdose at monthly intervals)

End point values	Placebo	2 mg LY2382770	10 mg LY2382770	50 mg LY2382770
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[1]	105	101	104
Units: microgram*hour per milliliter($\mu\text{g}\cdot\text{hr/mL}$)				
geometric mean (geometric coefficient of variation)	()	54.4 (\pm 49)	197 (\pm 45)	957 (\pm 44)

Notes:

[1] - There were no participants analyzed in the placebo arm.

Statistical analyses

No statistical analyses for this end point

Secondary: Log Transformed (ln) Serum creatinine slope of change from baseline through 12 months

End point title	Log Transformed (ln) Serum creatinine slope of change from baseline through 12 months
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End point description:

Log transformed serum creatinine slope of change from baseline through 12 months.

Analysis of covariance (ANCOVA) model was used with treatment as fixed effects and baseline Serum Creatinine log transformed (ln) and first morning urine protein to creatinine ratio (PCR) log transformed (ln) as covariates.

Analysis Population Description: All randomized participants who received at least 1 dose of drug.

End point type	Secondary
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End point timeframe:

Baseline through 12 months

End point values	Placebo	2 mg LY2382770	10 mg LY2382770	50 mg LY2382770
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	103	105	103	105
Units: ln milligrams per deciliter(mg/dL)/month				
least squares mean (standard error)	0.01605 (\pm 0.002685)	0.01408 (\pm 0.002731)	0.01716 (\pm 0.002658)	0.01337 (\pm 0.002712)

Statistical analyses

No statistical analyses for this end point

Secondary: Estimated Glomerular Filtration Rate (eGFR) Slope of Change from Baseline Through 12 Months

End point title	Estimated Glomerular Filtration Rate (eGFR) Slope of Change
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End point description:

eGFR slope of change from baseline through 12 months.

Analysis of covariance (ANCOVA) model was used with treatment as fixed effects, baseline Serum Creatinine log transformed (ln) and first morning urine protein to creatinine ratio (PCR) log transformed (ln) as covariates.

Analysis Population Description: All randomized participants who received at least 1 dose of drug.

End point type Secondary

End point timeframe:

Baseline through 12 months

End point values	Placebo	2 mg LY2382770	10 mg LY2382770	50 mg LY2382770
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	103	105	103	105
Units: mL/min/1.73 m ² /month				
least squares mean (standard error)	-0.3727 (± 0.08599)	-0.3664 (± 0.08742)	-0.5554 (± 0.08512)	-0.398 (± 0.08683)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Entire Study

All randomized participants who received at least 1 dose of drug. All serious adverse events following randomization are reported.

Adverse event reporting additional description:

H9V-MC-GFRF

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.0
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Reporting groups

Reporting group title	LY2382770 2 mg
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Reporting group description: -

Reporting group title	LY2382770 10 mg
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Reporting group description: -

Reporting group title	LY2382770 50 mg
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Reporting group description: -

Reporting group title	Placebo
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Reporting group description: -

Serious adverse events	LY2382770 2 mg	LY2382770 10 mg	LY2382770 50 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	44 / 105 (41.90%)	37 / 103 (35.92%)	41 / 105 (39.05%)
number of deaths (all causes)	5	3	4
number of deaths resulting from adverse events	0	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
adenocarcinoma pancreas			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
melanocytic naevus			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	0 / 105 (0.00%)
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			

alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	0 / 105 (0.00%)
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 cell carcinoma			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	0 / 105 (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
sweat gland tumour			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	0 / 105 (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
Vascular disorders			
arteriosclerosis			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	0 / 105 (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
hypertension			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	1 / 103 (0.97%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypertensive crisis			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypotension			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	0 / 105 (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 hypotension alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	0 / 105 (0.00%)
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 ischaemia alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
vena cava thrombosis alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
chest pain alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	0 / 105 (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
chills alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
device failure alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	0 / 105 (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
generalised oedema			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
multi-organ failure			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	0 / 105 (0.00%)
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			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
oedema peripheral			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	2 / 103 (1.94%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pyrexia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	0 / 105 (0.00%)
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			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	0 / 105 (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

Respiratory, thoracic and mediastinal disorders			
acute pulmonary oedema			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	0 / 105 (0.00%)
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			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	1 / 103 (0.97%)	0 / 105 (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
asthma			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
chronic obstructive pulmonary disease			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	2 / 105 (1.90%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
dyspnoea			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	2 / 105 (1.90%)	0 / 103 (0.00%)	0 / 105 (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
dyspnoea exertional			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
lung disorder			
alternative dictionary used:			

MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	1 / 103 (0.97%)	0 / 105 (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
pneumonia aspiration			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pulmonary congestion			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pulmonary hypertension			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	2 / 103 (1.94%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pulmonary oedema			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	1 / 105 (0.95%)
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			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	0 / 105 (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
Psychiatric disorders			
anxiety			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
ankle fracture			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	0 / 105 (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
arteriovenous fistula occlusion			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	1 / 103 (0.97%)	0 / 105 (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
fall			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	1 / 103 (0.97%)	0 / 105 (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
foot fracture			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	1 / 105 (0.95%)
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			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	1 / 103 (0.97%)	0 / 105 (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
postoperative thoracic procedure complication			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	1 / 105 (0.95%)
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 compression fracture alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	1 / 103 (0.97%)	0 / 105 (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
upper limb fracture alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	0 / 105 (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 postoperative alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	0 / 105 (0.00%)
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 coronary syndrome alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	1 / 103 (0.97%)	2 / 105 (1.90%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
acute myocardial infarction alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	4 / 105 (3.81%)	1 / 103 (0.97%)	3 / 105 (2.86%)
occurrences causally related to treatment / all	0 / 5	0 / 1	0 / 5
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
angina pectoris alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	2 / 105 (1.90%)	0 / 103 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
angina unstable			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	2 / 105 (1.90%)	2 / 103 (1.94%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	1 / 3	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
atrial fibrillation			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
bradycardia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cardiac arrest			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	1 / 105 (0.95%)
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			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	3 / 103 (2.91%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 1	1 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
cardiac failure congestive			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	4 / 103 (3.88%)	6 / 105 (5.71%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 8
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1

cardiomegaly			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
coronary artery disease			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	1 / 103 (0.97%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
mitral valve disease			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
myocardial infarction			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	2 / 105 (1.90%)	2 / 103 (1.94%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 2	0 / 2	1 / 1
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
myocardial ischaemia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pericardial effusion			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
tachycardia			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	0 / 105 (0.00%)	1 / 103 (0.97%)	0 / 105 (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
Nervous system disorders			
carotid artery stenosis			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	0 / 105 (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
central nervous system lesion			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cerebellar ischaemia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	0 / 105 (0.00%)
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			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	0 / 105 (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
cerebrovascular accident			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	3 / 105 (2.86%)	1 / 103 (0.97%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
diabetic hyperosmolar coma			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
diabetic mononeuropathy alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	0 / 105 (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
dysarthria alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	0 / 105 (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
epilepsy alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	1 / 103 (0.97%)	0 / 105 (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
hemiparesis alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	0 / 105 (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
hydrocephalus alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	1 / 103 (0.97%)	0 / 105 (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
hypoglycaemic coma alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	1 / 103 (0.97%)	0 / 105 (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

hypoglycaemic seizure alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	1 / 103 (0.97%)	0 / 105 (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
ischaemic cerebral infarction alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	1 / 103 (0.97%)	0 / 105 (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
ischaemic stroke alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	2 / 103 (1.94%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
transient ischaemic attack alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	0 / 105 (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 alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
anaemia alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	1 / 103 (0.97%)	2 / 105 (1.90%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
vertigo positional alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	0 / 105 (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
Eye disorders			
cataract			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
corneal oedema			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	0 / 105 (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
macular hole			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	1 / 103 (0.97%)	0 / 105 (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
posterior capsule rupture			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	0 / 105 (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
retinal artery occlusion			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	0 / 105 (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
retinal detachment			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	0 / 105 (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
vitreous haemorrhage			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	1 / 103 (0.97%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
abdominal pain			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	1 / 103 (0.97%)	0 / 105 (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
colitis ischaemic			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	1 / 103 (0.97%)	0 / 105 (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
colitis ulcerative			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
diarrhoea			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	2 / 103 (1.94%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
gastritis			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	0 / 105 (0.00%)
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 alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	1 / 103 (0.97%)	0 / 105 (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
gastrointestinal inflammation alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	0 / 105 (0.00%)
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 ulcer haemorrhage alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	0 / 105 (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
haematemesis alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
haemorrhoidal haemorrhage alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	0 / 105 (0.00%)
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, obstructive alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	0 / 105 (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

intestinal obstruction alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 105 (0.00%) 0 / 0 0 / 0	 0 / 103 (0.00%) 0 / 0 0 / 0	 0 / 105 (0.00%) 0 / 0 0 / 0
intestinal polyp alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 1 / 105 (0.95%) 1 / 1 0 / 0	 0 / 103 (0.00%) 0 / 0 0 / 0	 0 / 105 (0.00%) 0 / 0 0 / 0
large intestine polyp alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 105 (0.00%) 0 / 0 0 / 0	 1 / 103 (0.97%) 0 / 1 0 / 0	 0 / 105 (0.00%) 0 / 0 0 / 0
mallory-weiss syndrome alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 105 (0.00%) 0 / 0 0 / 0	 0 / 103 (0.00%) 0 / 0 0 / 0	 0 / 105 (0.00%) 0 / 0 0 / 0
nausea alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 1 / 105 (0.95%) 0 / 1 0 / 0	 0 / 103 (0.00%) 0 / 0 0 / 0	 0 / 105 (0.00%) 0 / 0 0 / 0
vomiting alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 2 / 105 (1.90%) 0 / 2 0 / 0	 0 / 103 (0.00%) 0 / 0 0 / 0	 0 / 105 (0.00%) 0 / 0 0 / 0
Hepatobiliary disorders cholecystitis acute alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
liver disorder			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	0 / 105 (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
Skin and subcutaneous tissue disorders			
angioedema			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	0 / 105 (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
skin ulcer			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	1 / 105 (0.95%)
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 and urinary disorders			
azotaemia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	0 / 105 (0.00%)
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 nephropathy			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	1 / 103 (0.97%)	0 / 105 (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
dysuria			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	0 / 105 (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
nephrolithiasis			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
nephropathy			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	0 / 105 (0.00%)
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			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	2 / 105 (1.90%)	1 / 103 (0.97%)	2 / 105 (1.90%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
renal failure acute			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	5 / 105 (4.76%)	3 / 103 (2.91%)	8 / 105 (7.62%)
occurrences causally related to treatment / all	0 / 5	0 / 3	1 / 10
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
renal failure chronic			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	4 / 105 (3.81%)	2 / 103 (1.94%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 4	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
renal impairment			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	0 / 105 (0.00%)
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			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	0 / 105 (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
myopathy			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	0 / 105 (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
neuropathic arthropathy			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	0 / 105 (0.00%)
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			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	0 / 105 (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
vertebral foraminal stenosis			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	0 / 105 (0.00%)
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			
bacteraemia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
breast abscess			

alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	0 / 105 (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
bronchiolitis			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	0 / 105 (0.00%)
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			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	0 / 105 (0.00%)
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			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	2 / 105 (1.90%)	2 / 103 (1.94%)	2 / 105 (1.90%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
clostridium difficile colitis			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
dermatitis infected			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	1 / 105 (0.95%)
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 related infection			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
enterobacter bacteraemia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
furuncle			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
gangrene			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	1 / 103 (0.97%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
gastroenteritis			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	1 / 103 (0.97%)	0 / 105 (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
gastroenteritis viral			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	2 / 105 (1.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
infective exacerbation of bronchiectasis			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
intervertebral discitis			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	1 / 103 (0.97%)	0 / 105 (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
klebsiella sepsis			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	1 / 103 (0.97%)	0 / 105 (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
orchitis			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed ^[1]	1 / 84 (1.19%)	0 / 74 (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
osteomyelitis			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
otitis externa			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	0 / 105 (0.00%)
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			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	2 / 105 (1.90%)	0 / 103 (0.00%)	4 / 105 (3.81%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

pneumonia bacterial alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	1 / 105 (0.95%)
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 alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	0 / 105 (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
pseudomembranous colitis alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	1 / 103 (0.97%)	0 / 105 (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
sepsis alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
staphylococcal abscess alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	1 / 103 (0.97%)	0 / 105 (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 bacteraemia alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
streptococcal urinary tract infection alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
subcutaneous abscess alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	0 / 105 (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
superinfection bacterial alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
tonsillitis alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	0 / 105 (0.00%)
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 alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
urinary tract infection alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	2 / 105 (1.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders dehydration alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
diabetes mellitus inadequate control alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	0 / 105 (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
diabetic ketoacidosis alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	0 / 105 (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 alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 105 (0.95%)	1 / 103 (0.97%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 3	0 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hyperglycaemia alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	2 / 105 (1.90%)	0 / 103 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hyperglycaemic hyperosmolar nonketotic syndrome alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	1 / 105 (0.95%)
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 alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	2 / 105 (1.90%)	1 / 103 (0.97%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypoglycaemia alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	2 / 105 (1.90%)	1 / 103 (0.97%)	2 / 105 (1.90%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
hypokalaemia alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	0 / 103 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
type 1 diabetes mellitus alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 105 (0.00%)	1 / 103 (0.97%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	39 / 103 (37.86%)		
number of deaths (all causes)	4		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps) adenocarcinoma pancreas alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 103 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
melanocytic naevus alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	1 / 103 (0.97%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
non-small cell lung cancer alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 103 (0.97%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
renal cell carcinoma alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 103 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
sweat gland tumour alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 103 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
arteriosclerosis alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 103 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
hypertension alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	2 / 103 (1.94%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
hypertensive crisis alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	1 / 103 (0.97%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
hypotension			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 103 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
orthostatic hypotension			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 103 (0.97%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
peripheral ischaemia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 103 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
vena cava thrombosis			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 103 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
chest pain			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 103 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
chills			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	1 / 103 (0.97%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
device failure				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	0 / 103 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
generalised oedema				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	0 / 103 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
multi-organ failure				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	1 / 103 (0.97%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
non-cardiac chest pain				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	1 / 103 (0.97%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
oedema peripheral				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	1 / 103 (0.97%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
pyrexia				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	1 / 103 (0.97%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			

sudden death alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 103 (0.00%) 0 / 0 0 / 0			
Respiratory, thoracic and mediastinal disorders acute pulmonary oedema alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 103 (0.97%) 0 / 1 0 / 0			
acute respiratory failure alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	2 / 103 (1.94%) 0 / 2 0 / 0			
asthma alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 103 (0.00%) 0 / 0 0 / 0			
chronic obstructive pulmonary disease alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 103 (0.00%) 0 / 0 0 / 0			
dyspnoea alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	2 / 103 (1.94%) 1 / 2 0 / 0			
dyspnoea exertional alternative dictionary used:				

MedDRA 17.0				
subjects affected / exposed	0 / 103 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
lung disorder				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	0 / 103 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
pneumonia aspiration				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	1 / 103 (0.97%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
pulmonary congestion				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	0 / 103 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
pulmonary hypertension				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	0 / 103 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
pulmonary oedema				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	1 / 103 (0.97%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
respiratory failure				
alternative dictionary used: MedDRA 17.0				

subjects affected / exposed	0 / 103 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
anxiety			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 103 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
ankle fracture			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 103 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
arteriovenous fistula occlusion			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 103 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
fall			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 103 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
foot fracture			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 103 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
humerus fracture			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	0 / 103 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
postoperative thoracic procedure complication			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 103 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
spinal compression fracture			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 103 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
upper limb fracture			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 103 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
urinary retention postoperative			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 103 (0.97%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
acute coronary syndrome			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 103 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
acute myocardial infarction			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	3 / 103 (2.91%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
angina pectoris				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	0 / 103 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
angina unstable				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	0 / 103 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
atrial fibrillation				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	4 / 103 (3.88%)			
occurrences causally related to treatment / all	1 / 4			
deaths causally related to treatment / all	0 / 0			
bradycardia				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	0 / 103 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
cardiac arrest				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	0 / 103 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
cardiac failure				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	5 / 103 (4.85%)			
occurrences causally related to treatment / all	1 / 5			
deaths causally related to treatment / all	0 / 1			

cardiac failure congestive alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	2 / 103 (1.94%) 0 / 2 0 / 0			
cardiomegaly alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 103 (0.00%) 0 / 0 0 / 0			
coronary artery disease alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 103 (0.00%) 0 / 0 0 / 0			
mitral valve disease alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 103 (0.00%) 0 / 0 0 / 0			
myocardial infarction alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 103 (0.97%) 0 / 1 0 / 1			
myocardial ischaemia alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 103 (0.00%) 0 / 0 0 / 0			
pericardial effusion alternative dictionary used: MedDRA 17.0				

subjects affected / exposed	1 / 103 (0.97%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
tachycardia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 103 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
carotid artery stenosis			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 103 (0.97%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
central nervous system lesion			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 103 (0.97%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
cerebellar ischaemia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 103 (0.97%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
cerebral ischaemia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 103 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
cerebrovascular accident			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	0 / 103 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
diabetic hyperosmolar coma alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	0 / 103 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
diabetic mononeuropathy alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	0 / 103 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
dysarthria alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	0 / 103 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
epilepsy alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	0 / 103 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
hemiparesis alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	0 / 103 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
hydrocephalus alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	0 / 103 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

hypoglycaemic coma alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 103 (0.00%) 0 / 0 0 / 0			
hypoglycaemic seizure alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 103 (0.00%) 0 / 0 0 / 0			
ischaemic cerebral infarction alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 103 (0.00%) 0 / 0 0 / 0			
ischaemic stroke alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	2 / 103 (1.94%) 0 / 2 0 / 0			
transient ischaemic attack alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	2 / 103 (1.94%) 1 / 2 0 / 0			
vertebrobasilar insufficiency alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 103 (0.00%) 0 / 0 0 / 0			
Blood and lymphatic system disorders anaemia alternative dictionary used: MedDRA 17.0				

subjects affected / exposed	2 / 103 (1.94%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
vertigo positional			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 103 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
cataract			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 103 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
corneal oedema			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 103 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
macular hole			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 103 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
posterior capsule rupture			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 103 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
retinal artery occlusion			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	0 / 103 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
retinal detachment			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 103 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
vitreous haemorrhage			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 103 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
abdominal pain			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 103 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
colitis ischaemic			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 103 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
colitis ulcerative			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 103 (0.97%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
diarrhoea			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	0 / 103 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
gastritis				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	1 / 103 (0.97%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
gastrointestinal haemorrhage				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	1 / 103 (0.97%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
gastrointestinal inflammation				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	1 / 103 (0.97%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
gastrointestinal ulcer haemorrhage				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	0 / 103 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
haematemesis				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	1 / 103 (0.97%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
haemorrhoidal haemorrhage				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	1 / 103 (0.97%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

inguinal hernia, obstructive alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 103 (0.00%) 0 / 0 0 / 0			
intestinal obstruction alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 103 (0.97%) 0 / 1 0 / 0			
intestinal polyp alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 103 (0.00%) 0 / 0 0 / 0			
large intestine polyp alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 103 (0.00%) 0 / 0 0 / 0			
mallory-weiss syndrome alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 103 (0.97%) 0 / 1 0 / 0			
nausea alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 103 (0.00%) 0 / 0 0 / 0			
vomiting alternative dictionary used: MedDRA 17.0				

subjects affected / exposed	0 / 103 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
cholecystitis acute			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 103 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
liver disorder			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 103 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
angioedema			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 103 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
skin ulcer			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 103 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
azotaemia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 103 (0.97%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
diabetic nephropathy			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	0 / 103 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
dysuria				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	0 / 103 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
nephrolithiasis				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	1 / 103 (0.97%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
nephropathy				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	1 / 103 (0.97%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
renal failure				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	1 / 103 (0.97%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
renal failure acute				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	2 / 103 (1.94%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
renal failure chronic				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	5 / 103 (4.85%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 1			

renal impairment alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 103 (0.97%) 0 / 1 0 / 0		
Musculoskeletal and connective tissue disorders back pain alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 103 (0.00%) 0 / 0 0 / 0		
myopathy alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 103 (0.00%) 0 / 0 0 / 0		
neuropathic arthropathy alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 103 (0.97%) 0 / 1 0 / 0		
osteoarthritis alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 103 (0.97%) 0 / 1 0 / 0		
vertebral foraminal stenosis alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 103 (0.97%) 0 / 1 0 / 0		
Infections and infestations bacteraemia			

alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	1 / 103 (0.97%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
breast abscess				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	0 / 103 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
bronchiolitis				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	1 / 103 (0.97%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
bronchopneumonia				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	1 / 103 (0.97%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
cellulitis				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	2 / 103 (1.94%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
clostridium difficile colitis				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	1 / 103 (0.97%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
dermatitis infected				
alternative dictionary used: MedDRA 17.0				

subjects affected / exposed	0 / 103 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
device related infection				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	0 / 103 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
enterobacter bacteraemia				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	0 / 103 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
furuncle				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	0 / 103 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
gangrene				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	0 / 103 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
gastroenteritis				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	0 / 103 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
gastroenteritis viral				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	0 / 103 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

infective exacerbation of bronchiectasis				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	1 / 103 (0.97%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
intervertebral discitis				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	0 / 103 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
klebsiella sepsis				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	0 / 103 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
orchitis				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed ^[1]	0 / 76 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
osteomyelitis				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	1 / 103 (0.97%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
otitis externa				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	1 / 103 (0.97%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
pneumonia				
alternative dictionary used: MedDRA 17.0				

subjects affected / exposed	1 / 103 (0.97%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
pneumonia bacterial				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	0 / 103 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
pneumonia staphylococcal				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	0 / 103 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
pseudomembranous colitis				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	0 / 103 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
sepsis				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	1 / 103 (0.97%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
staphylococcal abscess				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	0 / 103 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
staphylococcal bacteraemia				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	0 / 103 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

streptococcal urinary tract infection alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 103 (0.00%) 0 / 0 0 / 0			
subcutaneous abscess alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 103 (0.00%) 0 / 0 0 / 0			
superinfection bacterial alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 103 (0.00%) 0 / 0 0 / 0			
tonsillitis alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 103 (0.97%) 0 / 1 0 / 0			
upper respiratory tract infection alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 103 (0.00%) 0 / 0 0 / 0			
urinary tract infection alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 103 (0.00%) 0 / 0 0 / 0			
Metabolism and nutrition disorders dehydration alternative dictionary used: MedDRA 17.0				

subjects affected / exposed	0 / 103 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
diabetes mellitus inadequate control				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	0 / 103 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
diabetic ketoacidosis				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	3 / 103 (2.91%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
fluid overload				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	1 / 103 (0.97%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
hyperglycaemia				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	1 / 103 (0.97%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
hyperglycaemic hyperosmolar nonketotic syndrome				
alternative dictionary used: MedDRA 17.0				
subjects affected / exposed	0 / 103 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
hyperkalaemia				
alternative dictionary used: MedDRA 17.0				

subjects affected / exposed	2 / 103 (1.94%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
hypoglycaemia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 103 (0.97%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
hypokalaemia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 103 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
type 1 diabetes mellitus			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 103 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	LY2382770 2 mg	LY2382770 10 mg	LY2382770 50 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	67 / 105 (63.81%)	62 / 103 (60.19%)	62 / 105 (59.05%)
Vascular disorders			
hypertension			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	6 / 105 (5.71%)	9 / 103 (8.74%)	5 / 105 (4.76%)
occurrences (all)	6	9	5
Nervous system disorders			
dizziness			
alternative dictionary used: MedDRA 17.0			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>8 / 105 (7.62%)</p> <p>9</p>	<p>4 / 103 (3.88%)</p> <p>4</p>	<p>9 / 105 (8.57%)</p> <p>12</p>
<p>headache</p> <p>alternative dictionary used: MedDRA 17.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>7 / 105 (6.67%)</p> <p>7</p>	<p>8 / 103 (7.77%)</p> <p>9</p>	<p>2 / 105 (1.90%)</p> <p>2</p>
<p>Blood and lymphatic system disorders</p> <p>anaemia</p> <p>alternative dictionary used: MedDRA 17.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>6 / 105 (5.71%)</p> <p>6</p>	<p>4 / 103 (3.88%)</p> <p>4</p>	<p>5 / 105 (4.76%)</p> <p>5</p>
<p>General disorders and administration site conditions</p> <p>fatigue</p> <p>alternative dictionary used: MedDRA 17.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>3 / 105 (2.86%)</p> <p>3</p> <p>local swelling</p> <p>alternative dictionary used: MedDRA 17.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>2 / 105 (1.90%)</p> <p>3</p> <p>oedema peripheral</p> <p>alternative dictionary used: MedDRA 17.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>20 / 105 (19.05%)</p> <p>22</p>	<p>6 / 103 (5.83%)</p> <p>6</p> <p>1 / 103 (0.97%)</p> <p>2</p> <p>11 / 103 (10.68%)</p> <p>11</p>	<p>5 / 105 (4.76%)</p> <p>5</p> <p>1 / 105 (0.95%)</p> <p>2</p> <p>5 / 105 (4.76%)</p> <p>5</p>
<p>Gastrointestinal disorders</p> <p>constipation</p> <p>alternative dictionary used: MedDRA 17.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>8 / 105 (7.62%)</p> <p>10</p> <p>diarrhoea</p> <p>alternative dictionary used: MedDRA 17.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>10 / 105 (9.52%)</p> <p>15</p> <p>nausea</p> <p>alternative dictionary used: MedDRA 17.0</p>	<p>8 / 103 (7.77%)</p> <p>8</p> <p>11 / 103 (10.68%)</p> <p>14</p>	<p>5 / 105 (4.76%)</p> <p>7</p> <p>6 / 105 (5.71%)</p> <p>6</p>

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>8</p>	<p>7 / 105 (6.67%)</p> <p>8</p>	<p>5 / 103 (4.85%)</p> <p>5</p>	<p>7 / 105 (6.67%)</p> <p>8</p>
<p>vomiting</p> <p>alternative dictionary used: MedDRA 17.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>3</p>	<p>3 / 105 (2.86%)</p> <p>3</p>	<p>5 / 103 (4.85%)</p> <p>6</p>	<p>8 / 105 (7.62%)</p> <p>10</p>
<p>Reproductive system and breast disorders</p> <p>uterine polyp</p> <p>alternative dictionary used: MedDRA 17.0</p> <p>subjects affected / exposed^[2]</p> <p>occurrences (all)</p> <p>0</p>	<p>0 / 21 (0.00%)</p> <p>0</p>	<p>0 / 29 (0.00%)</p> <p>0</p>	<p>1 / 19 (5.26%)</p> <p>1</p>
<p>vaginal discharge</p> <p>alternative dictionary used: MedDRA 17.0</p> <p>subjects affected / exposed^[3]</p> <p>occurrences (all)</p> <p>0</p>	<p>0 / 21 (0.00%)</p> <p>0</p>	<p>0 / 29 (0.00%)</p> <p>0</p>	<p>1 / 19 (5.26%)</p> <p>1</p>
<p>vulvovaginal pruritus</p> <p>alternative dictionary used: MedDRA 17.0</p> <p>subjects affected / exposed^[4]</p> <p>occurrences (all)</p> <p>0</p>	<p>0 / 21 (0.00%)</p> <p>0</p>	<p>0 / 29 (0.00%)</p> <p>0</p>	<p>1 / 19 (5.26%)</p> <p>1</p>
<p>Respiratory, thoracic and mediastinal disorders</p> <p>cough</p> <p>alternative dictionary used: MedDRA 17.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>7</p>	<p>7 / 105 (6.67%)</p> <p>7</p>	<p>5 / 103 (4.85%)</p> <p>6</p>	<p>9 / 105 (8.57%)</p> <p>10</p>
<p>dyspnoea</p> <p>alternative dictionary used: MedDRA 17.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>4</p>	<p>4 / 105 (3.81%)</p> <p>4</p>	<p>2 / 103 (1.94%)</p> <p>2</p>	<p>6 / 105 (5.71%)</p> <p>6</p>
<p>Musculoskeletal and connective tissue disorders</p> <p>arthralgia</p> <p>alternative dictionary used: MedDRA 17.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>8</p>	<p>7 / 105 (6.67%)</p> <p>8</p>	<p>6 / 103 (5.83%)</p> <p>7</p>	<p>3 / 105 (2.86%)</p> <p>3</p>
<p>back pain</p>			

alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	8 / 105 (7.62%) 8	9 / 103 (8.74%) 9	5 / 105 (4.76%) 5
muscle spasms alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	6 / 105 (5.71%) 6	4 / 103 (3.88%) 5	4 / 105 (3.81%) 4
pain in extremity alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	8 / 105 (7.62%) 11	4 / 103 (3.88%) 4	5 / 105 (4.76%) 6
Infections and infestations bronchitis alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	8 / 105 (7.62%) 8	4 / 103 (3.88%) 4	6 / 105 (5.71%) 6
influenza alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	6 / 105 (5.71%) 8	4 / 103 (3.88%) 4	2 / 105 (1.90%) 2
nasopharyngitis alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	6 / 105 (5.71%) 6	3 / 103 (2.91%) 5	2 / 105 (1.90%) 2
upper respiratory tract infection alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	11 / 105 (10.48%) 11	13 / 103 (12.62%) 16	11 / 105 (10.48%) 13
urinary tract infection alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	10 / 105 (9.52%) 11	1 / 103 (0.97%) 2	3 / 105 (2.86%) 3
Metabolism and nutrition disorders			

hyperkalaemia alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	6 / 105 (5.71%) 6	8 / 103 (7.77%) 8	4 / 105 (3.81%) 4
hypoglycaemia alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	13 / 105 (12.38%) 20	9 / 103 (8.74%) 25	7 / 105 (6.67%) 15

Non-serious adverse events	Placebo		
Total subjects affected by non-serious adverse events subjects affected / exposed	57 / 103 (55.34%)		
Vascular disorders hypertension alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	6 / 103 (5.83%) 6		
Nervous system disorders dizziness alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all) headache alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	8 / 103 (7.77%) 9 3 / 103 (2.91%) 5		
Blood and lymphatic system disorders anaemia alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	7 / 103 (6.80%) 7		
General disorders and administration site conditions fatigue alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	8 / 103 (7.77%) 9		

local swelling alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	7 / 103 (6.80%) 7		
oedema peripheral alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	15 / 103 (14.56%) 15		
Gastrointestinal disorders constipation alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	4 / 103 (3.88%) 4		
diarrhoea alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	4 / 103 (3.88%) 8		
nausea alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	5 / 103 (4.85%) 5		
vomiting alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	4 / 103 (3.88%) 4		
Reproductive system and breast disorders uterine polyp alternative dictionary used: MedDRA 17.0 subjects affected / exposed ^[2] occurrences (all)	0 / 27 (0.00%) 0		
vaginal discharge alternative dictionary used: MedDRA 17.0 subjects affected / exposed ^[3] occurrences (all)	0 / 27 (0.00%) 0		
vulvovaginal pruritus			

alternative dictionary used: MedDRA 17.0 subjects affected / exposed ^[4] occurrences (all)	0 / 27 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders cough alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all) dyspnoea alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	2 / 103 (1.94%) 2 4 / 103 (3.88%) 4		
Musculoskeletal and connective tissue disorders arthralgia alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all) back pain alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all) muscle spasms alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all) pain in extremity alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	4 / 103 (3.88%) 5 6 / 103 (5.83%) 6 3 / 103 (2.91%) 3 4 / 103 (3.88%) 4		
Infections and infestations bronchitis alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	5 / 103 (4.85%) 5		

influenza alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	4 / 103 (3.88%) 4		
nasopharyngitis alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	8 / 103 (7.77%) 8		
upper respiratory tract infection alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	10 / 103 (9.71%) 11		
urinary tract infection alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	6 / 103 (5.83%) 6		
Metabolism and nutrition disorders hyperkalaemia alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	1 / 103 (0.97%) 1		
hypoglycaemia alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	10 / 103 (9.71%) 16		

Notes:

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 April 2012	Lowering the proteinuria threshold for study entry from 1200 mg/g to 800 mg/g and a change in the planned interim analysis that in turn allowed for the early termination of the study for efficacy futility.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Study was stopped early for efficacy futility per recommendation by the independent Data Safety Monitoring Committee.

Notes: