



Clinical trial results:

A Randomized, Multicountry, Multicenter, Double-Blind, Parallel, Placebo-Controlled Study of the Effects of Atrasentan on Renal Outcomes in Subjects with Type 2 Diabetes and Nephropathy. SONAR: Study Of Diabetic Nephropathy with Atrasentan

Summary

EudraCT number	2012-005848-21
Trial protocol	SE DE CZ BE GB IE PT DK NL IT GR SK FI ES PL AT
Global end of trial date	29 March 2018

Results information

Result version number	v1 (current)
This version publication date	14 April 2019
First version publication date	14 April 2019

Trial information

Trial identification

Sponsor protocol code	M11-352
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01858532
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie Deutschland GmbH & Co. KG
Sponsor organisation address	AbbVie House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6-4UB
Public contact	Global Medical Services, AbbVie, 001 800-633-9110,
Scientific contact	Melissa Wigderson, AbbVie, melissa.wigderson@abbvie.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	29 March 2018
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	29 March 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The study objective was to evaluate the effect of atrasentan compared with placebo on time to doubling of serum creatinine (DBSC) or the onset of end-stage renal disease (ESRD) in adults with type 2 diabetes and nephropathy who were treated with the maximum tolerated labeled daily dose (MTLDD) of a renin-angiotensin system (RAS) inhibitor. The study also assessed cardiovascular (CV) morbidity and mortality, urine albumin excretion, and changes in estimated glomerular filtration rate (eGFR). There was an optional Pre-Screening Period, Screening Period, Run-In Period (up to 12 weeks), Enrichment Period (6 weeks of atrasentan Tx), Double-Blind Treatment Period (randomization to final Tx visit), and Follow-Up Period (Final Tx to F1 visit [45 days post Tx] and other post-treatment visits). The study was prematurely discontinued because of a lower than expected event rate for the renal composite endpoint, which was adjudicated by a blinded independent events adjudication committee.

Protection of trial subjects:

Prior to the initiation of any screening or study-specific procedures, the investigator or his or her representative explained the nature of the study to the subject or his or her representative and answered all questions regarding this study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 May 2013
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	Argentina: 62
Country: Number of subjects enrolled	Australia: 56
Country: Number of subjects enrolled	Austria: 14
Country: Number of subjects enrolled	Belgium: 22
Country: Number of subjects enrolled	Brazil: 259
Country: Number of subjects enrolled	Canada: 74
Country: Number of subjects enrolled	Chile: 40
Country: Number of subjects enrolled	China: 283
Country: Number of subjects enrolled	Czech Republic: 66
Country: Number of subjects enrolled	Denmark: 28
Country: Number of subjects enrolled	Finland: 12
Country: Number of subjects enrolled	France: 48
Country: Number of subjects enrolled	Germany: 79
Country: Number of subjects enrolled	Greece: 38

Country: Number of subjects enrolled	Hong Kong: 135
Country: Number of subjects enrolled	Ireland: 25
Country: Number of subjects enrolled	Israel: 82
Country: Number of subjects enrolled	Italy: 166
Country: Number of subjects enrolled	Japan: 386
Country: Number of subjects enrolled	Korea, Republic of: 234
Country: Number of subjects enrolled	Malaysia: 195
Country: Number of subjects enrolled	Mexico: 149
Country: Number of subjects enrolled	Netherlands: 41
Country: Number of subjects enrolled	New Zealand: 45
Country: Number of subjects enrolled	Peru: 111
Country: Number of subjects enrolled	Poland: 56
Country: Number of subjects enrolled	Portugal: 38
Country: Number of subjects enrolled	Puerto Rico: 132
Country: Number of subjects enrolled	Romania: 49
Country: Number of subjects enrolled	Russian Federation: 164
Country: Number of subjects enrolled	Singapore: 33
Country: Number of subjects enrolled	Slovakia: 65
Country: Number of subjects enrolled	South Africa: 64
Country: Number of subjects enrolled	Spain: 315
Country: Number of subjects enrolled	Sweden: 8
Country: Number of subjects enrolled	Switzerland: 1
Country: Number of subjects enrolled	Taiwan: 141
Country: Number of subjects enrolled	Turkey: 19
Country: Number of subjects enrolled	Ukraine: 111
Country: Number of subjects enrolled	United Kingdom: 24
Country: Number of subjects enrolled	United States: 1237
Worldwide total number of subjects	5107
EEA total number of subjects	1094

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)	2473
From 65 to 84 years	2621
85 years and over	13

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

5107 participants dosed in the Enrichment Period (EP); 1441 prematurely discontinued Tx or did not proceed to the Double-Blind Treatment Period per criteria. 3666 participants completed EP and proceeded to Double-Blind Treatment Period, along with 2 additional participants who discontinued study drug in EP but were randomized in error.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Intent-to-Treat (ITT) Responder atrasentan

Arm description:

Participants who achieved at least 30% reduction in their albumin to creatinine ratio (UACR) in the Enrichment Period and were randomized to receive atrasentan in the Double-Blind Treatment Period

Arm type	Experimental
Investigational medicinal product name	Atrasentan
Investigational medicinal product code	
Other name	ABT-627
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

0.75 mg atrasentan once daily by mouth for 48 months

Arm title	Intent-to-Treat (ITT) Responder placebo
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Arm description:

Participants who achieved at least 30% reduction in their albumin to creatinine ratio (UACR) in the Enrichment Period and were randomized to receive placebo in the Double-Blind Treatment Period

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo once daily by mouth for 48 months

Arm title	Intent-to-Treat (ITT) Non-responder atrasentan
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Arm description:

Participants who achieved < 30% reduction in their urinary albumin to creatinine ratio (UACR) in the Enrichment Period and were randomized to receive atrasentan in the Double-Blind Treatment Period

Arm type	Experimental
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Investigational medicinal product name	Atrasentan
Investigational medicinal product code	
Other name	ABT-627
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details:	
0.75 mg atrasentan once daily by mouth for 48 months	
Arm title	Intent-to-Treat (ITT) Non-responder placebo

Arm description:

Participants who achieved < 30% reduction in their urinary albumin to creatinine ratio (UACR) in the Enrichment Period and were randomized to receive placebo in the Double-Blind Treatment Period

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo once daily by mouth for 48 months

Number of subjects in period 1 ^[1]	Intent-to-Treat (ITT) Responder atrasentan	Intent-to-Treat (ITT) Responder placebo	Intent-to-Treat (ITT) Non-responder atrasentan
Started	1325	1323	509
Completed	1144	1131	411
Not completed	181	192	98
Adverse event, non-fatal	58	50	23
Other, not specified	29	15	13
Withdrew consent	71	93	46
Lost to follow-up	17	26	11
Deterioration of medical status	3	4	3
Investigator request	3	4	2

Number of subjects in period 1 ^[1]	Intent-to-Treat (ITT) Non-responder placebo
Started	511
Completed	418
Not completed	93
Adverse event, non-fatal	28
Other, not specified	11
Withdrew consent	27
Lost to follow-up	14
Deterioration of medical status	7
Investigator request	6

Notes:

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

Justification: 5107 subjects dosed in the open-label Enrichment Period (EP). Of these, 1441 either prematurely discontinued study treatment during the EP or were unable to proceed to the Double-Blind Treatment Period per protocol-specified criteria. 3,666 subjects completed the EP and proceeded into the Double-Blind Treatment Period, along with 2 additional subjects who discontinued study drug in the EP but were randomized in error, for a total of 3,668 subjects.

Baseline characteristics

Reporting groups

Reporting group title	Intent-to-Treat (ITT) Responder atrasentan
Reporting group description: Participants who achieved at least 30% reduction in their albumin to creatinine ratio (UACR) in the Enrichment Period and were randomized to receive atrasentan in the Double-Blind Treatment Period	
Reporting group title	Intent-to-Treat (ITT) Responder placebo
Reporting group description: Participants who achieved at least 30% reduction in their albumin to creatinine ratio (UACR) in the Enrichment Period and were randomized to receive placebo in the Double-Blind Treatment Period	
Reporting group title	Intent-to-Treat (ITT) Non-responder atrasentan
Reporting group description: Participants who achieved < 30% reduction in their urinary albumin to creatinine ratio (UACR) in the Enrichment Period and were randomized to receive atrasentan in the Double-Blind Treatment Period	
Reporting group title	Intent-to-Treat (ITT) Non-responder placebo
Reporting group description: Participants who achieved < 30% reduction in their urinary albumin to creatinine ratio (UACR) in the Enrichment Period and were randomized to receive placebo in the Double-Blind Treatment Period	

Reporting group values	Intent-to-Treat (ITT) Responder atrasentan	Intent-to-Treat (ITT) Responder placebo	Intent-to-Treat (ITT) Non-responder atrasentan
Number of subjects	1325	1323	509
Age categorical			
Units: Subjects			

Age continuous			
Intent-to-Treat (ITT) Responders (participants who achieved at least 30% reduction in their albumin to creatinine ratio (UACR) in the Enrichment Period [EP]) and ITT Non-responders (Participants who achieved < 30% reduction in their UACR in the EP)			
Units: years			
arithmetic mean	64.9	64.7	63.8
standard deviation	± 8.64	± 8.66	± 9.12
Gender categorical			
Intent-to-Treat (ITT) Responders (participants who achieved at least 30% reduction in their albumin to creatinine ratio (UACR) in the Enrichment Period [EP]) and ITT Non-responders (Participants who achieved < 30% reduction in their UACR in the EP)			
Units: Subjects			
Female	331	352	127
Male	994	971	382

Reporting group values	Intent-to-Treat (ITT) Non-responder placebo	Total	
Number of subjects	511	3668	
Age categorical			
Units: Subjects			

Age continuous			
Intent-to-Treat (ITT) Responders (participants who achieved at least 30% reduction in their albumin to creatinine ratio (UACR) in the Enrichment Period [EP]) and ITT Non-responders (Participants who achieved < 30% reduction in their UACR in the EP)			

Units: years			
arithmetic mean	63.6		
standard deviation	± 8.93	-	
Gender categorical			
Intent-to-Treat (ITT) Responders (participants who achieved at least 30% reduction in their albumin to creatinine ratio (UACR) in the Enrichment Period [EP]) and ITT Non-responders (Participants who achieved < 30% reduction in their UACR in the EP)			
Units: Subjects			
Female	136	946	
Male	375	2722	

End points

End points reporting groups

Reporting group title	Intent-to-Treat (ITT) Responder atrasentan
Reporting group description: Participants who achieved at least 30% reduction in their albumin to creatinine ratio (UACR) in the Enrichment Period and were randomized to receive atrasentan in the Double-Blind Treatment Period	
Reporting group title	Intent-to-Treat (ITT) Responder placebo
Reporting group description: Participants who achieved at least 30% reduction in their albumin to creatinine ratio (UACR) in the Enrichment Period and were randomized to receive placebo in the Double-Blind Treatment Period	
Reporting group title	Intent-to-Treat (ITT) Non-responder atrasentan
Reporting group description: Participants who achieved < 30% reduction in their urinary albumin to creatinine ratio (UACR) in the Enrichment Period and were randomized to receive atrasentan in the Double-Blind Treatment Period	
Reporting group title	Intent-to-Treat (ITT) Non-responder placebo
Reporting group description: Participants who achieved < 30% reduction in their urinary albumin to creatinine ratio (UACR) in the Enrichment Period and were randomized to receive placebo in the Double-Blind Treatment Period	
Subject analysis set title	Intent-to-Treat (ITT) Atrasentan
Subject analysis set type	Intention-to-treat
Subject analysis set description: All randomized participants who entered the Double-Blind Treatment Period and were randomized to receive atrasentan	
Subject analysis set title	Intent-to-Treat Placebo
Subject analysis set type	Intention-to-treat
Subject analysis set description: All randomized participants who entered the Double-Blind Treatment Period and were randomized to receive placebo	

Primary: Time to the first occurrence of a component of the composite renal endpoint in the Intent-to-Treat (ITT) Responder Set (as randomized)

End point title	Time to the first occurrence of a component of the composite renal endpoint in the Intent-to-Treat (ITT) Responder Set (as randomized) ^[1]
End point description: Time to the first occurrence of a component of the composite renal endpoint was defined as doubling of serum creatinine (confirmed by a 30-day serum creatinine measurement) or the onset of end stage renal disease (estimated glomerular filtration rate [eGFR] less than 15 ml/min/1.73 m ² confirmed by a 90-day eGFR measurement, receiving chronic dialysis, renal transplantation, or renal death). Only events adjudicated by the Events Adjudication Committee (EAC) were considered in defining this endpoint. Data are presented as number of participants with a primary renal composite event (first event per participant).	
Analysis population: Intent-to-Treat (ITT) Responders (participants who achieved at least 30% reduction in their albumin to creatinine ratio [UACR] in the Enrichment Period [EP])	
End point type	Primary
End point timeframe: From randomization to individual end of observation, up to 53 months	

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The Intent-to-Treat Responder Set (as randomized) is the primary analysis for this endpoint.

End point values	Intent-to-Treat (ITT) Responder atrasentan	Intent-to-Treat (ITT) Responder placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1325	1323		
Units: Number of participants	79	105		

Statistical analyses

Statistical analysis title	Stratified log-rank test
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Statistical analysis description:

The endpoint was analyzed using the stratified log-rank test for treatment comparison.

Comparison groups	Intent-to-Treat (ITT) Responder atrasentan v Intent-to-Treat (ITT) Responder placebo
Number of subjects included in analysis	2648
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.029
Method	Stratified log-rank test

Statistical analysis title	Cox Proportional Hazard Ratio
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Statistical analysis description:

A Cox Proportional Hazards regression model with pre-specified covariates adjusted was used to estimate the hazard ratio of atrasentan to placebo and its 95% confidence interval.

Comparison groups	Intent-to-Treat (ITT) Responder atrasentan v Intent-to-Treat (ITT) Responder placebo
Number of subjects included in analysis	2648
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.005
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.654
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.488
upper limit	0.878

Secondary: Time to First Occurrence of a Component of Composite Renal Endpoint for All Randomized Participants (Pooled)

End point title	Time to First Occurrence of a Component of Composite Renal Endpoint for All Randomized Participants (Pooled)
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End point description:

Time to the first occurrence of a component of the composite renal endpoint was defined as doubling of serum creatinine (confirmed by a 30-day serum creatinine measurement) or the onset of end stage renal disease (estimated glomerular filtration rate [eGFR] less than 15 ml/min/1.73 m² confirmed by a 90-day eGFR measurement, receiving chronic dialysis, renal transplantation, or renal death). Data for all randomized participants were pooled by treatment and analyzed. Data are presented as number of participants with a renal composite event (first event per participant).

Analysis Population: Intent-to-treat population: participants who were randomized to receive either atrasentan or placebo during the Double-Blind Treatment Period

End point type	Secondary
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End point timeframe:

From randomization to individual end of observation, up to 53 months

End point values	Intent-to-Treat (ITT) Atrasentan	Intent-to-Treat Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	1834	1834		
Units: Number of participants	152	192		

Statistical analyses

Statistical analysis title	Cox Proportional Hazard Ratio
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Statistical analysis description:

A Cox Proportional Hazards regression model with pre-specified covariates adjusted was used to estimate the hazard ratio of atrasentan to placebo and its 95% confidence interval.

Comparison groups	Intent-to-Treat Placebo v Intent-to-Treat (ITT) Atrasentan
Number of subjects included in analysis	3668
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.002
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.58
upper limit	0.89

Secondary: Time to Cardio-renal Composite Endpoint in the Intent-to-Treat (ITT) Responder Set (as randomized)

End point title	Time to Cardio-renal Composite Endpoint in the Intent-to-Treat (ITT) Responder Set (as randomized) ^[2]
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End point description:

The composite event of interest for this outcome consisted of doubling of serum creatinine, end-stage renal disease (ESRD), cardiovascular (CV) death (including CV death and presumed CV death), nonfatal myocardial infarction (MI; heart attack) and nonfatal stroke. Presumed sudden cardiac death was included as a subcategory of presumed CV death. Only events adjudicated by the Events Adjudication Committee (EAC) were considered in defining this endpoint. Data are presented as number of participants with a cardio-renal composite event (first event per participant).

Analysis Population: Intent-to-Treat (ITT) Responders (participants who achieved at least 30% reduction in their albumin to creatinine ratio [UACR] in the Enrichment Period [EP])

End point type	Secondary
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End point timeframe:

From randomization to individual end of observation, up to 53 months

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The Intent-to-Treat Responder Set (as randomized) is the primary analysis for this endpoint.

End point values	Intent-to-Treat (ITT) Responder atrasentan	Intent-to-Treat (ITT) Responder placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1325	1323		
Units: Number of participants	147	172		

Statistical analyses

Statistical analysis title	Stratified log-rank test
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Statistical analysis description:

The endpoint was analyzed using the stratified log-rank test for treatment comparison.

Comparison groups	Intent-to-Treat (ITT) Responder atrasentan v Intent-to-Treat (ITT) Responder placebo
Number of subjects included in analysis	2648
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.089
Method	Stratified log-rank test

Statistical analysis title	Cox Proportional Hazard Ratio
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Statistical analysis description:

A Cox Proportional Hazards regression model with pre-specified covariates adjusted was used to estimate the hazard ratio of atrasentan to placebo and its 95% confidence interval.

Comparison groups	Intent-to-Treat (ITT) Responder atrasentan v Intent-to-Treat
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	(ITT) Responder placebo
Number of subjects included in analysis	2648
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.049
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.801
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.642
upper limit	0.999

Secondary: Time to a 50% Estimated Glomerular Filtration Rate Reduction in the Intent-to-Treat (ITT) Responder Set (as randomized)

End point title	Time to a 50% Estimated Glomerular Filtration Rate Reduction in the Intent-to-Treat (ITT) Responder Set (as randomized) ^[3]
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End point description:

The event of interest for this outcome was a 50% reduction in a participant's estimated glomerular filtration rate (eGFR) value as compared to baseline, confirmed by a repeated value at least 20 days apart. The event time was defined as the first time that a 50% reduction in eGFR was observed. Data are presented as number of participants with a 50% reduction in eGFR (first event per participant).

Analysis Population Description

Intent-to-Treat (ITT) Responders (participants who achieved at least 30% reduction in their albumin to creatinine ratio [UACR] in the Enrichment Period [EP])

End point type	Secondary
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End point timeframe:

From randomization to individual end of observation, up to 53 months

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The Intent-to-Treat Responder Set (as randomized) is the primary analysis for this endpoint.

End point values	Intent-to-Treat (ITT) Responder atrasentan	Intent-to-Treat (ITT) Responder placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1325	1323		
Units: Number of participants	78	88		

Statistical analyses

Statistical analysis title	Stratified log-rank test
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Statistical analysis description:

The endpoint was analyzed using the stratified log-rank test for treatment comparison.

Comparison groups	Intent-to-Treat (ITT) Responder atrasentan v Intent-to-Treat (ITT) Responder placebo
Number of subjects included in analysis	2648
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.289
Method	Stratified log-rank test

Statistical analysis title	Cox Proportional Hazard Ratio
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Statistical analysis description:

A Cox Proportional Hazards regression model with pre-specified covariates adjusted was used to estimate the hazard ratio of atrasentan to placebo and its 95% confidence interval.

Comparison groups	Intent-to-Treat (ITT) Responder atrasentan v Intent-to-Treat (ITT) Responder placebo
Number of subjects included in analysis	2648
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.112
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.779
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.573
upper limit	1.06

Secondary: Time to the Cardiovascular Composite Endpoint in the Intent-to-Treat (ITT) Responder Set (as randomized)

End point title	Time to the Cardiovascular Composite Endpoint in the Intent-to-Treat (ITT) Responder Set (as randomized) ^[4]
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End point description:

The composite event of interest for this outcome was cardiovascular (CV) death (CV death, presumed CV death), nonfatal myocardial infarction (MI; heart attack), and nonfatal stroke. Presumed sudden cardiac death was included as a sub-category of presumed CV death. Only events adjudicated by the Events Adjudication Committee (EAC) were used. Data are presented as number of participants with a cardiovascular composite event (first event per participant).

End point type	Secondary
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End point timeframe:

From randomization to individual end of observation, up to 53 months

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The Intent-to-Treat Responder Set (as randomized) is the primary analysis for this endpoint.

End point values	Intent-to-Treat (ITT) Responder atrasentan	Intent-to-Treat (ITT) Responder placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1325	1323		
Units: Number of participants	72	81		

Statistical analyses

Statistical analysis title	Stratified log-rank test
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Statistical analysis description:

The endpoint was analyzed using the stratified log-rank test for treatment comparison.

Comparison groups	Intent-to-Treat (ITT) Responder atrasentan v Intent-to-Treat (ITT) Responder placebo
Number of subjects included in analysis	2648
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.446
Method	Stratified log-rank test

Statistical analysis title	Cox Proportional Hazard Ratio
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Statistical analysis description:

A Cox Proportional Hazards regression model with pre-specified covariates adjusted was used to estimate the hazard ratio of atrasentan to placebo and its 95% confidence interval.

Comparison groups	Intent-to-Treat (ITT) Responder placebo v Intent-to-Treat (ITT) Responder atrasentan
Number of subjects included in analysis	2648
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.447
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.884
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.643
upper limit	1.215

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events (TEAEs) and serious adverse events (TESAEs) reported from time of study drug administration until 45 d after last dose (up to 24 wks for All Atrasentan Set in EP; 54 mos for ITT sets in Double-Blind period)

Adverse event reporting additional description:

TEAEs and TESAEs are defined as any adverse event (AE) with an onset date that is after the first dose of study drug until 45 days after the last dose of study drug and were collected whether elicited or spontaneously reported by the participant.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.0
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Reporting groups

Reporting group title	All Atrasentan Set
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Reporting group description:

Participants who received at least one dose of atrasentan, including both Enrichment and Double-Blind Treatment Periods

Reporting group title	Double-Blind Placebo
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Reporting group description:

All participants who received at least one dose of placebo during the Double-Blind Treatment Period

Reporting group title	Double-Blind Atrasentan
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Reporting group description:

All participants who received at least one dose of atrasentan during the Double-Blind Treatment Period

Serious adverse events	All Atrasentan Set	Double-Blind Placebo	Double-Blind Atrasentan
Total subjects affected by serious adverse events			
subjects affected / exposed	292 / 5107 (5.72%)	626 / 1830 (34.21%)	685 / 1829 (37.45%)
number of deaths (all causes)	25	79	84
number of deaths resulting from adverse events	23	64	65
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ACUTE MYELOID LEUKAEMIA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
ADENOCARCINOMA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

ADENOCARCINOMA GASTRIC			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
ADENOCARCINOMA OF COLON			
subjects affected / exposed	2 / 5107 (0.04%)	1 / 1830 (0.05%)	3 / 1829 (0.16%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ADENOCARCINOMA PANCREAS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ADRENAL NEOPLASM			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
ATYPICAL FIBROXANTHOMA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BASAL CELL CARCINOMA			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
BENIGN NEOPLASM OF BLADDER			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
BENIGN NEOPLASM OF THYROID GLAND			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
BENIGN RENAL NEOPLASM			

subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
BILE DUCT CANCER			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
BLADDER CANCER			
subjects affected / exposed	1 / 5107 (0.02%)	3 / 1830 (0.16%)	3 / 1829 (0.16%)
occurrences causally related to treatment / all	0 / 1	0 / 3	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BLADDER CANCER RECURRENT			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BLADDER CANCER STAGE I, WITH CANCER IN SITU			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BLADDER NEOPLASM			
subjects affected / exposed	1 / 5107 (0.02%)	3 / 1830 (0.16%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BLADDER TRANSITIONAL CELL CARCINOMA			
subjects affected / exposed	0 / 5107 (0.00%)	3 / 1830 (0.16%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BONE NEOPLASM			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRAIN NEOPLASM			

subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
BRAIN NEOPLASM BENIGN			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BREAST CANCER			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BREAST CANCER RECURRENT			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BREAST NEOPLASM			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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
BRONCHIAL CARCINOMA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARCINOID TUMOUR PULMONARY			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
CHOLANGIOCARCINOMA			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
CHRONIC LYMPHOCYTIC LEUKAEMIA			

subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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
COLON ADENOMA			
subjects affected / exposed	1 / 5107 (0.02%)	1 / 1830 (0.05%)	7 / 1829 (0.38%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COLON CANCER			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	3 / 1829 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 2	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COLON NEOPLASM			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
COLORECTAL CANCER			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
DIFFUSE LARGE B-CELL LYMPHOMA			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GALLBLADDER CANCER METASTATIC			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
ENDOMETRIAL CANCER			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRIC ADENOMA			

subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRIC CANCER			
subjects affected / exposed	0 / 5107 (0.00%)	6 / 1830 (0.33%)	3 / 1829 (0.16%)
occurrences causally related to treatment / all	0 / 0	1 / 6	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GLIOBLASTOMA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROINTESTINAL TRACT ADENOMA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEPATIC CANCER			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
HEPATOCELLULAR CARCINOMA			
subjects affected / exposed	0 / 5107 (0.00%)	3 / 1830 (0.16%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HUERTHLE CELL CARCINOMA			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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
INFLAMMATORY PSEUDOTUMOUR			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTESTINAL ADENOCARCINOMA			

subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
LANGERHANS CELL SARCOMA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTRADUCTAL PROLIFERATIVE BREAST LESION			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LIPOSARCOMA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LIPOMA			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LARYNGEAL SQUAMOUS CELL CARCINOMA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
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 ADENOCARCINOMA STAGE IV			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
LUNG ADENOCARCINOMA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
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 NEOPLASM MALIGNANT			

subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LUNG NEOPLASM			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
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 CANCER METASTATIC			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
MALIGNANT PALATE NEOPLASM			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
LYMPHOMA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
METASTATIC CARCINOMA OF THE BLADDER			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
METASTATIC MALIGNANT MELANOMA			
subjects affected / exposed	1 / 5107 (0.02%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
METASTATIC NEOPLASM			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MUCINOUS ADENOCARCINOMA OF APPENDIX			

subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NASOPHARYNGEAL CANCER			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUROENDOCRINE CARCINOMA			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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
OESOPHAGEAL CARCINOMA			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUROENDOCRINE TUMOUR OF THE LUNG			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OESOPHAGEAL SQUAMOUS CELL CARCINOMA			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
OROPHARYNGEAL NEOPLASM			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OSTEOSARCOMA			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
OVARIAN CANCER			

subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
OVARIAN ADENOMA			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
PITUITARY TUMOUR BENIGN			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
PANCREATIC CARCINOMA METASTATIC			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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
PANCREATIC CARCINOMA			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
PROSTATE CANCER			
subjects affected / exposed	0 / 5107 (0.00%)	7 / 1830 (0.38%)	3 / 1829 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 7	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PLASMA CELL MYELOMA			
subjects affected / exposed	2 / 5107 (0.04%)	0 / 1830 (0.00%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
PROSTATE CANCER RECURRENT			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PSEUDOMYXOMA PERITONEI			

subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PROSTATIC ADENOMA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RECTAL ADENOCARCINOMA			
subjects affected / exposed	0 / 5107 (0.00%)	3 / 1830 (0.16%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RENAL CANCER			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RENAL CELL CARCINOMA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RENAL CANCER METASTATIC			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RENAL ONCOCYTOMA			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
SINONASAL PAPILLOMA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SQUAMOUS CELL CARCINOMA			

subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SMALL CELL LUNG CANCER METASTATIC			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
SQUAMOUS CELL CARCINOMA OF THE HYPOPHARYNX			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
SQUAMOUS CELL CARCINOMA OF LUNG			
subjects affected / exposed	2 / 5107 (0.04%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
SQUAMOUS CELL CARCINOMA OF THE ORAL CAVITY			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TRANSITIONAL CELL CARCINOMA			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
THYROID NEOPLASM			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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
TRANSITIONAL CELL CARCINOMA RECURRENT			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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

UTERINE LEIOMYOMA			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
ANEURYSM			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
AORTIC ANEURYSM			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	0 / 1829 (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
AORTIC STENOSIS			
subjects affected / exposed	1 / 5107 (0.02%)	3 / 1830 (0.16%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
AORTIC ANEURYSM RUPTURE			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
ARTERIOSCLEROSIS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
ARTERIAL STENOSIS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
ARTERIAL DISORDER			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BLOOD PRESSURE INADEQUATELY			

CONTROLLED			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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
ARTERITIS			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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 VASCULAR DISORDER			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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
DEEP VEIN THROMBOSIS			
subjects affected / exposed	0 / 5107 (0.00%)	4 / 1830 (0.22%)	4 / 1829 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DRY GANGRENE			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EXTREMITY NECROSIS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	3 / 1829 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMATOMA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERTENSION			
subjects affected / exposed	0 / 5107 (0.00%)	9 / 1830 (0.49%)	9 / 1829 (0.49%)
occurrences causally related to treatment / all	0 / 0	1 / 9	0 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERTENSIVE CRISIS			

subjects affected / exposed	2 / 5107 (0.04%)	4 / 1830 (0.22%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	1 / 2	1 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERTENSIVE EMERGENCY			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOVOLAEMIC SHOCK			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOTENSION			
subjects affected / exposed	4 / 5107 (0.08%)	4 / 1830 (0.22%)	4 / 1829 (0.22%)
occurrences causally related to treatment / all	4 / 5	1 / 4	1 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERIPHERAL ARTERIAL OCCLUSIVE DISEASE			
subjects affected / exposed	1 / 5107 (0.02%)	7 / 1830 (0.38%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 10	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MALIGNANT HYPERTENSION			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	0 / 1829 (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
ORTHOSTATIC HYPOTENSION			
subjects affected / exposed	1 / 5107 (0.02%)	2 / 1830 (0.11%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 1	1 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERIPHERAL ARTERY STENOSIS			
subjects affected / exposed	1 / 5107 (0.02%)	2 / 1830 (0.11%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERIPHERAL ARTERY OCCLUSION			

subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERIPHERAL ARTERY THROMBOSIS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERIPHERAL VASCULAR DISORDER			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	3 / 1829 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERIPHERAL ISCHAEMIA			
subjects affected / exposed	2 / 5107 (0.04%)	2 / 1830 (0.11%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SHOCK HAEMORRHAGIC			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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
PERIPHERAL VENOUS DISEASE			
subjects affected / exposed	1 / 5107 (0.02%)	1 / 1830 (0.05%)	0 / 1829 (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
SUBCLAVIAN ARTERY OCCLUSION			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
THROMBOPHLEBITIS			
subjects affected / exposed	1 / 5107 (0.02%)	1 / 1830 (0.05%)	0 / 1829 (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
VASCULAR OCCLUSION			

subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
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			
BRAIN DEATH			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
ASTHENIA			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHEST DISCOMFORT			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
CHEST PAIN			
subjects affected / exposed	1 / 5107 (0.02%)	4 / 1830 (0.22%)	7 / 1829 (0.38%)
occurrences causally related to treatment / all	0 / 1	1 / 4	1 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHILLS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
DEATH			
subjects affected / exposed	3 / 5107 (0.06%)	4 / 1830 (0.22%)	5 / 1829 (0.27%)
occurrences causally related to treatment / all	2 / 3	0 / 4	1 / 5
deaths causally related to treatment / all	2 / 3	0 / 4	1 / 5
DISEASE COMPLICATION			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
FACE OEDEMA			

subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FATIGUE			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEELING ABNORMAL			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
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 PHYSICAL HEALTH DETERIORATION			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GENERALISED OEDEMA			
subjects affected / exposed	2 / 5107 (0.04%)	3 / 1830 (0.16%)	3 / 1829 (0.16%)
occurrences causally related to treatment / all	2 / 2	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOTHERMIA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
IMPAIRED HEALING			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	3 / 1829 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MULTIPLE ORGAN DYSFUNCTION SYNDROME			

subjects affected / exposed	0 / 5107 (0.00%)	3 / 1830 (0.16%)	5 / 1829 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 3	0 / 4
NECROSIS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	0 / 5107 (0.00%)	3 / 1830 (0.16%)	4 / 1829 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OEDEMA PERIPHERAL			
subjects affected / exposed	4 / 5107 (0.08%)	3 / 1830 (0.16%)	6 / 1829 (0.33%)
occurrences causally related to treatment / all	3 / 4	3 / 3	3 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERIPHERAL SWELLING			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYREXIA			
subjects affected / exposed	1 / 5107 (0.02%)	2 / 1830 (0.11%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUDDEN CARDIAC DEATH			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
SUDDEN DEATH			
subjects affected / exposed	1 / 5107 (0.02%)	5 / 1830 (0.27%)	8 / 1829 (0.44%)
occurrences causally related to treatment / all	0 / 1	2 / 5	1 / 8
deaths causally related to treatment / all	0 / 1	2 / 5	1 / 8
SYSTEMIC INFLAMMATORY RESPONSE SYNDROME			

subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ULCER HAEMORRHAGE			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VASCULAR STENT STENOSIS			
subjects affected / exposed	1 / 5107 (0.02%)	1 / 1830 (0.05%)	0 / 1829 (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
Immune system disorders			
ALLERGY TO ARTHROPOD BITE			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
ANAPHYLACTIC SHOCK			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DRUG HYPERSENSITIVITY			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERSENSITIVITY			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Social circumstances			
OVERWORK			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast			

disorders			
BENIGN PROSTATIC HYPERPLASIA			
subjects affected / exposed	0 / 5107 (0.00%)	7 / 1830 (0.38%)	3 / 1829 (0.16%)
occurrences causally related to treatment / all	0 / 0	1 / 7	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EPIDIDYMAL CYST			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GYNAECOMASTIA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PROSTATITIS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SCROTAL OEDEMA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UTERINE PROLAPSE			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
ACUTE PULMONARY OEDEMA			
subjects affected / exposed	1 / 5107 (0.02%)	6 / 1830 (0.33%)	5 / 1829 (0.27%)
occurrences causally related to treatment / all	0 / 1	2 / 6	3 / 5
deaths causally related to treatment / all	0 / 0	0 / 2	1 / 2
ACUTE RESPIRATORY DISTRESS SYNDROME			

subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ACUTE RESPIRATORY FAILURE			
subjects affected / exposed	0 / 5107 (0.00%)	9 / 1830 (0.49%)	11 / 1829 (0.60%)
occurrences causally related to treatment / all	0 / 0	1 / 9	0 / 11
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ASPIRATION			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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
ASTHMA			
subjects affected / exposed	3 / 5107 (0.06%)	3 / 1830 (0.16%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
BRONCHOSPASM			
subjects affected / exposed	1 / 5107 (0.02%)	1 / 1830 (0.05%)	0 / 1829 (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
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	3 / 5107 (0.06%)	6 / 1830 (0.33%)	9 / 1829 (0.49%)
occurrences causally related to treatment / all	0 / 3	0 / 7	0 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COUGH			
subjects affected / exposed	1 / 5107 (0.02%)	1 / 1830 (0.05%)	0 / 1829 (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
DYSPNOEA			
subjects affected / exposed	1 / 5107 (0.02%)	3 / 1830 (0.16%)	5 / 1829 (0.27%)
occurrences causally related to treatment / all	0 / 1	0 / 3	2 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DYSPNOEA EXERTIONAL			

subjects affected / exposed	1 / 5107 (0.02%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EPISTAXIS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMOPTYSIS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
HAEMOTHORAX			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYDROTHORAX			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERCAPNIA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOVENTILATION			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOXIA			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTERSTITIAL LUNG DISEASE			

subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	3 / 1829 (0.16%)
occurrences causally related to treatment / all	0 / 0	1 / 1	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MEDIASTINAL CYST			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OBSTRUCTIVE AIRWAYS DISORDER			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PLEURAL EFFUSION			
subjects affected / exposed	2 / 5107 (0.04%)	2 / 1830 (0.11%)	7 / 1829 (0.38%)
occurrences causally related to treatment / all	0 / 2	0 / 2	1 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMOMEDIASTINUM			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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			
subjects affected / exposed	1 / 5107 (0.02%)	1 / 1830 (0.05%)	6 / 1829 (0.33%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMOTHORAX			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PULMONARY CONGESTION			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PULMONARY EMBOLISM			

subjects affected / exposed	2 / 5107 (0.04%)	2 / 1830 (0.11%)	4 / 1829 (0.22%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
PULMONARY HYPERTENSION			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PULMONARY MASS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PULMONARY OEDEMA			
subjects affected / exposed	6 / 5107 (0.12%)	4 / 1830 (0.22%)	7 / 1829 (0.38%)
occurrences causally related to treatment / all	1 / 6	0 / 5	2 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY ARREST			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
RESPIRATORY DISTRESS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	5 / 1829 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
RESPIRATORY FAILURE			
subjects affected / exposed	3 / 5107 (0.06%)	8 / 1830 (0.44%)	6 / 1829 (0.33%)
occurrences causally related to treatment / all	0 / 3	1 / 8	0 / 6
deaths causally related to treatment / all	0 / 2	1 / 4	0 / 1
RESTRICTIVE PULMONARY DISEASE			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SLEEP APNOEA SYNDROME			

subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
AGITATION			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANXIETY			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BIPOLAR DISORDER			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CONFUSIONAL STATE			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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
DELIRIUM			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
DELUSIONAL DISORDER, SOMATIC TYPE			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
DEPRESSION			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DISORIENTATION			

subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
DRUG ABUSE			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INSOMNIA			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MENTAL STATUS CHANGES			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MAJOR DEPRESSION			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
SUICIDAL IDEATION			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
Product issues			
Device capturing issue			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
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 dislocation			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			

BILE DUCT STONE			
subjects affected / exposed	1 / 5107 (0.02%)	3 / 1830 (0.16%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BILIARY COLIC			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHOLANGITIS			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHOLECYSTITIS			
subjects affected / exposed	2 / 5107 (0.04%)	2 / 1830 (0.11%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHOLECYSTITIS ACUTE			
subjects affected / exposed	0 / 5107 (0.00%)	3 / 1830 (0.16%)	6 / 1829 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHOLECYSTITIS CHRONIC			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHOLELITHIASIS			
subjects affected / exposed	0 / 5107 (0.00%)	3 / 1830 (0.16%)	5 / 1829 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DRUG-INDUCED LIVER INJURY			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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
GALLBLADDER PERFORATION			

subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEPATIC CIRRHOSIS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEPATIC LESION			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEPATIC STEATOSIS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
HEPATITIS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
HEPATITIS ACUTE			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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
Investigations			
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BLOOD BICARBONATE DECREASED			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BLOOD CREATININE INCREASED			

subjects affected / exposed	1 / 5107 (0.02%)	7 / 1830 (0.38%)	5 / 1829 (0.27%)
occurrences causally related to treatment / all	1 / 1	1 / 8	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BLOOD GLUCOSE DECREASED			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
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 POTASSIUM INCREASED			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BLOOD UREA INCREASED			
subjects affected / exposed	1 / 5107 (0.02%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRAIN NATRIURETIC PEPTIDE INCREASED			
subjects affected / exposed	2 / 5107 (0.04%)	0 / 1830 (0.00%)	0 / 1829 (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
ELECTROCARDIOGRAM Q WAVE ABNORMAL			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
GLOMERULAR FILTRATION RATE DECREASED			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
HAEMOGLOBIN DECREASED			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HELICOBACTER TEST POSITIVE			

subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
HEPATIC ENZYME INCREASED			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LIPASE INCREASED			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTRAOCULAR PRESSURE INCREASED			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PROSTATIC SPECIFIC ANTIGEN INCREASED			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PROTEIN URINE PRESENT			
subjects affected / exposed	1 / 5107 (0.02%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TROPONIN INCREASED			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINE CYTOLOGY ABNORMAL			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WEIGHT INCREASED			

subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
ABDOMINAL INJURY			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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
ANKLE FRACTURE			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	3 / 1829 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ABDOMINAL WOUND DEHISCENCE			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
BRAIN CONTUSION			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BLADDER INJURY			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
BURNS SECOND DEGREE			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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
CERVICAL VERTEBRAL FRACTURE			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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
CLAVICLE FRACTURE			

subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CONCUSSION			
subjects affected / exposed	0 / 5107 (0.00%)	3 / 1830 (0.16%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CONTUSION			
subjects affected / exposed	1 / 5107 (0.02%)	2 / 1830 (0.11%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CYSTITIS RADIATION			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CRANIOCEREBRAL INJURY			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
DISLOCATION OF VERTEBRA			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
FACIAL BONES FRACTURE			
subjects affected / exposed	1 / 5107 (0.02%)	1 / 1830 (0.05%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FALL			
subjects affected / exposed	7 / 5107 (0.14%)	5 / 1830 (0.27%)	12 / 1829 (0.66%)
occurrences causally related to treatment / all	0 / 7	0 / 6	0 / 12
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEMORAL NECK FRACTURE			

subjects affected / exposed	0 / 5107 (0.00%)	3 / 1830 (0.16%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
FIBULA FRACTURE			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
FEMUR FRACTURE			
subjects affected / exposed	1 / 5107 (0.02%)	3 / 1830 (0.16%)	3 / 1829 (0.16%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FOOT FRACTURE			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FOREIGN BODY IN GASTROINTESTINAL TRACT			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GRAFT THROMBOSIS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
HAND FRACTURE			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEAD INJURY			
subjects affected / exposed	1 / 5107 (0.02%)	3 / 1830 (0.16%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HIP FRACTURE			

subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	0 / 1829 (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
HUMERUS FRACTURE			
subjects affected / exposed	2 / 5107 (0.04%)	2 / 1830 (0.11%)	3 / 1829 (0.16%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ILIUM FRACTURE			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	0 / 1829 (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
INCISIONAL HERNIA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
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			
subjects affected / exposed	1 / 5107 (0.02%)	1 / 1830 (0.05%)	0 / 1829 (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
JAW FRACTURE			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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
JOINT DISLOCATION			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LACERATION			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LIGAMENT SPRAIN			

subjects affected / exposed	1 / 5107 (0.02%)	1 / 1830 (0.05%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LIMB INJURY			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LIMB TRAUMATIC AMPUTATION			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
LISFRANC FRACTURE			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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
LOWER LIMB FRACTURE			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	3 / 1829 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LUMBAR VERTEBRAL FRACTURE			
subjects affected / exposed	0 / 5107 (0.00%)	4 / 1830 (0.22%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MENISCUS INJURY			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MULTIPLE FRACTURES			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MUSCLE RUPTURE			

subjects affected / exposed	1 / 5107 (0.02%)	1 / 1830 (0.05%)	0 / 1829 (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
OVERDOSE			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATIC LEAK			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
PATELLA FRACTURE			
subjects affected / exposed	1 / 5107 (0.02%)	1 / 1830 (0.05%)	0 / 1829 (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
PELVIC FRACTURE			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
POST CONCUSSION SYNDROME			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
POST PROCEDURAL DISCHARGE			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
POST PROCEDURAL HAEMATOMA			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
POST PROCEDURAL HAEMORRHAGE			

subjects affected / exposed	1 / 5107 (0.02%)	2 / 1830 (0.11%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
POST PROCEDURAL SWELLING			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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 WOUND COMPLICATION			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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
PROCEDURAL PAIN			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
PUBIS FRACTURE			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
RADIUS FRACTURE			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RIB FRACTURE			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	3 / 1829 (0.16%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ROAD TRAFFIC ACCIDENT			
subjects affected / exposed	1 / 5107 (0.02%)	1 / 1830 (0.05%)	3 / 1829 (0.16%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
SPINAL COMPRESSION FRACTURE			

subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SKIN ABRASION			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SPINAL CORD INJURY CERVICAL			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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
SPINAL FRACTURE			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
SUBARACHNOID HAEMORRHAGE			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUBDURAL HAEMATOMA			
subjects affected / exposed	2 / 5107 (0.04%)	2 / 1830 (0.11%)	3 / 1829 (0.16%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUBDURAL HAEMORRHAGE			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TENDON RUPTURE			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
THERMAL BURN			

subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
THORACIC VERTEBRAL FRACTURE			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TIBIA FRACTURE			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TOXICITY TO VARIOUS AGENTS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
TRAUMATIC FRACTURE			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TRAUMATIC HAEMATOMA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TRAUMATIC HAEMOTHORAX			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TRAUMATIC LUNG INJURY			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ULNA FRACTURE			

subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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
ULNAR NERVE INJURY			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY RETENTION POSTOPERATIVE			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VASCULAR PSEUDOANEURYSM			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	0 / 1829 (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
WOUND			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	3 / 1829 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WOUND COMPLICATION			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WOUND DEHISCENCE			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WOUND HAEMORRHAGE			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WOUND NECROSIS			

subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
Congenital, familial and genetic disorders			
GLUCOSE-6-PHOSPHATE DEHYDROGENASE DEFICIENCY			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
ACUTE CORONARY SYNDROME			
subjects affected / exposed	1 / 5107 (0.02%)	2 / 1830 (0.11%)	5 / 1829 (0.27%)
occurrences causally related to treatment / all	1 / 1	0 / 2	1 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ACUTE LEFT VENTRICULAR FAILURE			
subjects affected / exposed	1 / 5107 (0.02%)	3 / 1830 (0.16%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	1 / 1	1 / 4	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ACUTE MYOCARDIAL INFARCTION			
subjects affected / exposed	7 / 5107 (0.14%)	28 / 1830 (1.53%)	34 / 1829 (1.86%)
occurrences causally related to treatment / all	1 / 7	1 / 29	4 / 40
deaths causally related to treatment / all	0 / 1	0 / 4	0 / 2
ADAMS-STOKES SYNDROME			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANGINA PECTORIS			
subjects affected / exposed	4 / 5107 (0.08%)	10 / 1830 (0.55%)	10 / 1829 (0.55%)
occurrences causally related to treatment / all	0 / 5	0 / 10	0 / 11
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANGINA UNSTABLE			
subjects affected / exposed	4 / 5107 (0.08%)	3 / 1830 (0.16%)	7 / 1829 (0.38%)
occurrences causally related to treatment / all	0 / 4	0 / 3	1 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

AORTIC VALVE STENOSIS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ARRHYTHMIA SUPRAVENTRICULAR			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ARRHYTHMIA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
ARTERIOSCLEROSIS CORONARY ARTERY			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
ATRIAL FIBRILLATION			
subjects affected / exposed	2 / 5107 (0.04%)	10 / 1830 (0.55%)	16 / 1829 (0.87%)
occurrences causally related to treatment / all	0 / 2	0 / 11	4 / 17
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ATRIAL FLUTTER			
subjects affected / exposed	2 / 5107 (0.04%)	2 / 1830 (0.11%)	5 / 1829 (0.27%)
occurrences causally related to treatment / all	0 / 2	0 / 2	2 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ATRIAL TACHYCARDIA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ATRIOVENTRICULAR BLOCK			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ATRIOVENTRICULAR BLOCK COMPLETE			

subjects affected / exposed	1 / 5107 (0.02%)	2 / 1830 (0.11%)	7 / 1829 (0.38%)
occurrences causally related to treatment / all	1 / 1	0 / 2	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ATRIOVENTRICULAR BLOCK FIRST DEGREE			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ATRIOVENTRICULAR BLOCK SECOND DEGREE			
subjects affected / exposed	1 / 5107 (0.02%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRADYARRHYTHMIA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRADYCARDIA			
subjects affected / exposed	3 / 5107 (0.06%)	2 / 1830 (0.11%)	4 / 1829 (0.22%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BUNDLE BRANCH BLOCK BILATERAL			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BUNDLE BRANCH BLOCK RIGHT			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	0 / 1829 (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
BUNDLE BRANCH BLOCK LEFT			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIAC ARREST			

subjects affected / exposed	3 / 5107 (0.06%)	5 / 1830 (0.27%)	4 / 1829 (0.22%)
occurrences causally related to treatment / all	1 / 3	1 / 5	1 / 4
deaths causally related to treatment / all	1 / 3	1 / 5	1 / 3
CARDIAC FAILURE			
subjects affected / exposed	5 / 5107 (0.10%)	11 / 1830 (0.60%)	19 / 1829 (1.04%)
occurrences causally related to treatment / all	4 / 5	5 / 11	6 / 20
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
CARDIAC FAILURE ACUTE			
subjects affected / exposed	4 / 5107 (0.08%)	4 / 1830 (0.22%)	5 / 1829 (0.27%)
occurrences causally related to treatment / all	2 / 4	0 / 5	4 / 6
deaths causally related to treatment / all	1 / 2	0 / 1	1 / 1
CARDIAC FAILURE CHRONIC			
subjects affected / exposed	3 / 5107 (0.06%)	2 / 1830 (0.11%)	5 / 1829 (0.27%)
occurrences causally related to treatment / all	2 / 3	1 / 2	1 / 5
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
CARDIAC FAILURE CONGESTIVE			
subjects affected / exposed	22 / 5107 (0.43%)	22 / 1830 (1.20%)	37 / 1829 (2.02%)
occurrences causally related to treatment / all	17 / 22	7 / 23	15 / 41
deaths causally related to treatment / all	0 / 0	0 / 3	0 / 1
CARDIO-RESPIRATORY ARREST			
subjects affected / exposed	1 / 5107 (0.02%)	1 / 1830 (0.05%)	3 / 1829 (0.16%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 3
deaths causally related to treatment / all	1 / 1	0 / 1	0 / 3
CARDIOGENIC SHOCK			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
CARDIOMYOPATHY			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
CARDIOPULMONARY FAILURE			

subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
CARDIORENAL SYNDROME			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIOVASCULAR DISORDER			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
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 LEFT VENTRICULAR FAILURE			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CORONARY ARTERY DISEASE			
subjects affected / exposed	6 / 5107 (0.12%)	19 / 1830 (1.04%)	29 / 1829 (1.59%)
occurrences causally related to treatment / all	1 / 6	1 / 20	3 / 31
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
CORONARY ARTERY OCCLUSION			
subjects affected / exposed	0 / 5107 (0.00%)	3 / 1830 (0.16%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CORONARY ARTERY STENOSIS			
subjects affected / exposed	3 / 5107 (0.06%)	2 / 1830 (0.11%)	5 / 1829 (0.27%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CORONARY ARTERY THROMBOSIS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
CYANOSIS			

subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIASTOLIC DYSFUNCTION			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERTENSIVE CARDIOMYOPATHY			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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
HYPERTENSIVE HEART DISEASE			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
ISCHAEMIC CARDIOMYOPATHY			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
LEFT VENTRICULAR FAILURE			
subjects affected / exposed	3 / 5107 (0.06%)	1 / 1830 (0.05%)	4 / 1829 (0.22%)
occurrences causally related to treatment / all	2 / 3	0 / 1	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MITRAL VALVE INCOMPETENCE			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
MYOCARDIAL INFARCTION			
subjects affected / exposed	7 / 5107 (0.14%)	8 / 1830 (0.44%)	13 / 1829 (0.71%)
occurrences causally related to treatment / all	3 / 7	0 / 8	4 / 15
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 2
MYOCARDIAL ISCHAEMIA			

subjects affected / exposed	1 / 5107 (0.02%)	4 / 1830 (0.22%)	9 / 1829 (0.49%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 11
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PALPITATIONS			
subjects affected / exposed	1 / 5107 (0.02%)	2 / 1830 (0.11%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERICARDIAL EFFUSION			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	4 / 1829 (0.22%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
SINOATRIAL BLOCK			
subjects affected / exposed	1 / 5107 (0.02%)	1 / 1830 (0.05%)	0 / 1829 (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
SINUS ARREST			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SINUS NODE DYSFUNCTION			
subjects affected / exposed	1 / 5107 (0.02%)	2 / 1830 (0.11%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 1	1 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUPRAVENTRICULAR TACHYCARDIA			
subjects affected / exposed	2 / 5107 (0.04%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TACHYCARDIA			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VENTRICULAR EXTRASYSTOLES			

subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VENTRICULAR FIBRILLATION			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
VENTRICULAR TACHYCARDIA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
ALTERED STATE OF CONSCIOUSNESS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ACUTE MOTOR AXONAL NEUROPATHY			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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
APHASIA			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
BALANCE DISORDER			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
CAROTID ARTERY OCCLUSION			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRAIN STEM INFARCTION			

subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CAROTID ARTERY STENOSIS			
subjects affected / exposed	0 / 5107 (0.00%)	3 / 1830 (0.16%)	3 / 1829 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 3	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARPAL TUNNEL SYNDROME			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
CEREBELLAR HAEMATOMA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CEREBELLAR INFARCTION			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
CEREBRAL HAEMORRHAGE			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
CEREBRAL INFARCTION			
subjects affected / exposed	1 / 5107 (0.02%)	8 / 1830 (0.44%)	3 / 1829 (0.16%)
occurrences causally related to treatment / all	0 / 1	1 / 9	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
CEREBRAL ISCHAEMIA			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CEREBRAL THROMBOSIS			

subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CEREBROVASCULAR ACCIDENT			
subjects affected / exposed	5 / 5107 (0.10%)	14 / 1830 (0.77%)	13 / 1829 (0.71%)
occurrences causally related to treatment / all	0 / 5	0 / 14	0 / 14
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 1
CEREBROVASCULAR DISORDER			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	0 / 1829 (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
CERVICOBACHIAL SYNDROME			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
COMA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
DEMENTIA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
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 COMA			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIABETIC HYPERGLYCAEMIC COMA			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIABETIC HYPEROSMOLAR COMA			

subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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 NEUROPATHY			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
DIZZINESS			
subjects affected / exposed	0 / 5107 (0.00%)	3 / 1830 (0.16%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EMBOLIC CEREBRAL INFARCTION			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
ENCEPHALOPATHY			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FACIAL PARALYSIS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEADACHE			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMORRHAGIC STROKE			
subjects affected / exposed	0 / 5107 (0.00%)	3 / 1830 (0.16%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
HEMIPARESIS			

subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYDROCEPHALUS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERTENSIVE ENCEPHALOPATHY			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOGLYCAEMIC SEIZURE			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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			
subjects affected / exposed	3 / 5107 (0.06%)	9 / 1830 (0.49%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	1 / 3	0 / 10	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 1
ISCHAEMIC CEREBRAL INFARCTION			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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
IVTH NERVE PARALYSIS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
LACUNAR INFARCTION			
subjects affected / exposed	1 / 5107 (0.02%)	2 / 1830 (0.11%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LOSS OF CONSCIOUSNESS			

subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
LUMBAR RADICULOPATHY			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
METABOLIC ENCEPHALOPATHY			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MIGRAINE			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MONONEUROPATHY MULTIPLEX			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYELOPATHY			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYOCLONUS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUROPATHY PERIPHERAL			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PARAESTHESIA			

subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
PRESYNCOPE			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
QUADRIPLEGIA			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
RADICULOPATHY			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SCIATICA			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEIZURE			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	4 / 1829 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SENILE DEMENTIA			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
SPINAL CORD DISORDER			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
SPONDYLITIC MYELOPATHY			

subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
STATUS EPILEPTICUS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYNCOPE			
subjects affected / exposed	3 / 5107 (0.06%)	11 / 1830 (0.60%)	6 / 1829 (0.33%)
occurrences causally related to treatment / all	1 / 3	0 / 11	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
THALAMIC INFARCTION			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TRANSIENT ISCHAEMIC ATTACK			
subjects affected / exposed	2 / 5107 (0.04%)	7 / 1830 (0.38%)	7 / 1829 (0.38%)
occurrences causally related to treatment / all	0 / 2	0 / 7	1 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VASCULAR DEMENTIA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	7 / 5107 (0.14%)	11 / 1830 (0.60%)	27 / 1829 (1.48%)
occurrences causally related to treatment / all	2 / 7	1 / 15	3 / 28
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANAEMIA OF CHRONIC DISEASE			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
AUTOIMMUNE HAEMOLYTIC ANAEMIA			

subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COAGULOPATHY			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DISSEMINATED INTRAVASCULAR COAGULATION			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMORRHAGIC ANAEMIA			
subjects affected / exposed	1 / 5107 (0.02%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
IRON DEFICIENCY ANAEMIA			
subjects affected / exposed	1 / 5107 (0.02%)	2 / 1830 (0.11%)	4 / 1829 (0.22%)
occurrences causally related to treatment / all	1 / 1	0 / 2	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LEUKOCYTOSIS			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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
MICROCYTIC ANAEMIA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEPHROGENIC ANAEMIA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUTROPENIA			

subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
PANCYTOPENIA			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
THROMBOCYTOPENIA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
MENIERE'S DISEASE			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VERTIGO			
subjects affected / exposed	1 / 5107 (0.02%)	7 / 1830 (0.38%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VERTIGO POSITIONAL			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
AGE-RELATED MACULAR DEGENERATION			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
ANGLE CLOSURE GLAUCOMA			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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

BLINDNESS TRANSIENT			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CATARACT			
subjects affected / exposed	3 / 5107 (0.06%)	10 / 1830 (0.55%)	19 / 1829 (1.04%)
occurrences causally related to treatment / all	0 / 3	0 / 12	0 / 19
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CATARACT DIABETIC			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CATARACT NUCLEAR			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CORNEAL EPITHELIUM DEFECT			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
CORNEAL OPACITY			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DACRYOSTENOSIS ACQUIRED			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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 RETINOPATHY			
subjects affected / exposed	2 / 5107 (0.04%)	0 / 1830 (0.00%)	3 / 1829 (0.16%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIPLOPIA			

subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EYE HAEMORRHAGE			
subjects affected / exposed	1 / 5107 (0.02%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EYELID PTOSIS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
GLAUCOMA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	3 / 1829 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LAGOPHTHALMOS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
MACULAR FIBROSIS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
MACULAR OEDEMA			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OPTIC ISCHAEMIC NEUROPATHY			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERIORBITAL OEDEMA			

subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RETINAL DETACHMENT			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RETINAL HAEMORRHAGE			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RETINOPATHY PROLIFERATIVE			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RHEGMATOGENOUS RETINAL DETACHMENT			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TRACTIONAL RETINAL DETACHMENT			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
VISUAL IMPAIRMENT			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
VITREOUS ADHESIONS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
VITREOUS HAEMORRHAGE			

subjects affected / exposed	4 / 5107 (0.08%)	5 / 1830 (0.27%)	9 / 1829 (0.49%)
occurrences causally related to treatment / all	0 / 4	0 / 7	0 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
ABDOMINAL DISTENSION			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ABDOMINAL HERNIA			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	0 / 1829 (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
ABDOMINAL PAIN			
subjects affected / exposed	1 / 5107 (0.02%)	2 / 1830 (0.11%)	3 / 1829 (0.16%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANAL INCONTINENCE			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANORECTAL ULCER			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ASCITES			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHRONIC GASTRITIS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COLITIS			

subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	0 / 1829 (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
COLITIS ULCERATIVE			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CONSTIPATION			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DENTAL CARIES			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIABETIC GASTROPARESIS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIABETIC GASTROPATHY			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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
DIARRHOEA			
subjects affected / exposed	0 / 5107 (0.00%)	3 / 1830 (0.16%)	4 / 1829 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIVERTICULUM			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
DIVERTICULUM INTESTINAL HAEMORRHAGIC			

subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DUODENAL ULCER			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DUODENAL ULCER HAEMORRHAGE			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DUODENITIS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DYSPHAGIA			
subjects affected / exposed	1 / 5107 (0.02%)	2 / 1830 (0.11%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENTEROVESICAL FISTULA			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
EROSIVE DUODENITIS			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	0 / 1829 (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
GASTRIC DISORDER			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRIC FISTULA			

subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRIC MUCOSAL HYPERTROPHY			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRIC POLYPS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRIC ULCER			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	3 / 1829 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRIC ULCER HAEMORRHAGE			
subjects affected / exposed	2 / 5107 (0.04%)	3 / 1830 (0.16%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRITIS			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRITIS HAEMORRHAGIC			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	1 / 5107 (0.02%)	3 / 1830 (0.16%)	6 / 1829 (0.33%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROINTESTINAL MUCOSAL DISORDER			

subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	1 / 5107 (0.02%)	2 / 1830 (0.11%)	3 / 1829 (0.16%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMORRHOIDS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HIATUS HERNIA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ILEUS			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	1 / 2	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
IMPAIRED GASTRIC EMPTYING			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INGUINAL HERNIA			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	3 / 1829 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTESTINAL OBSTRUCTION			

subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	3 / 1829 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTESTINAL PERFORATION			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
IRRITABLE BOWEL SYNDROME			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LARGE INTESTINE PERFORATION			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LARGE INTESTINE POLYP			
subjects affected / exposed	1 / 5107 (0.02%)	2 / 1830 (0.11%)	7 / 1829 (0.38%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LOWER GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LYMPHOCYTIC OESOPHAGITIS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MELAENA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NAUSEA			

subjects affected / exposed	2 / 5107 (0.04%)	1 / 1830 (0.05%)	4 / 1829 (0.22%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OBSTRUCTIVE PANCREATITIS			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
OESOPHAGEAL SPASM			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OESOPHAGEAL ULCER HAEMORRHAGE			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OESOPHAGITIS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATIC DISORDER			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATITIS			
subjects affected / exposed	2 / 5107 (0.04%)	4 / 1830 (0.22%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	1 / 2	0 / 5	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
PANCREATITIS ACUTE			
subjects affected / exposed	1 / 5107 (0.02%)	4 / 1830 (0.22%)	5 / 1829 (0.27%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PEPTIC ULCER HAEMORRHAGE			

subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PEPTIC ULCER			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
PROCTITIS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
RECTAL HAEMORRHAGE			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RECTAL ULCER HAEMORRHAGE			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RECTAL POLYP			
subjects affected / exposed	1 / 5107 (0.02%)	1 / 1830 (0.05%)	0 / 1829 (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
SMALL INTESTINAL OBSTRUCTION			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UMBILICAL HERNIA			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ULCERATIVE GASTRITIS			

subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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 GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 5107 (0.00%)	3 / 1830 (0.16%)	5 / 1829 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VOMITING			
subjects affected / exposed	3 / 5107 (0.06%)	5 / 1830 (0.27%)	7 / 1829 (0.38%)
occurrences causally related to treatment / all	0 / 3	1 / 5	0 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
ACTINIC KERATOSIS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANGIOEDEMA			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIABETIC CHEIROARTHROPATHY			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DECUBITUS ULCER			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIABETIC FOOT			
subjects affected / exposed	1 / 5107 (0.02%)	10 / 1830 (0.55%)	8 / 1829 (0.44%)
occurrences causally related to treatment / all	0 / 1	0 / 10	0 / 10
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ECZEMA			

subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INGROWING NAIL			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PRURITUS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SKIN DISCOLOURATION			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SKIN ULCER			
subjects affected / exposed	4 / 5107 (0.08%)	3 / 1830 (0.16%)	5 / 1829 (0.27%)
occurrences causally related to treatment / all	0 / 4	0 / 3	0 / 10
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	19 / 5107 (0.37%)	36 / 1830 (1.97%)	54 / 1829 (2.95%)
occurrences causally related to treatment / all	3 / 20	7 / 40	4 / 56
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
AZOTAEMIA			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	3 / 1829 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
BLADDER STENOSIS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CALCULUS URINARY			

subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
CHRONIC KIDNEY DISEASE			
subjects affected / exposed	1 / 5107 (0.02%)	13 / 1830 (0.71%)	9 / 1829 (0.49%)
occurrences causally related to treatment / all	1 / 1	2 / 13	0 / 11
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIABETIC NEPHROPATHY			
subjects affected / exposed	2 / 5107 (0.04%)	10 / 1830 (0.55%)	17 / 1829 (0.93%)
occurrences causally related to treatment / all	1 / 2	1 / 11	1 / 23
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
END STAGE RENAL DISEASE			
subjects affected / exposed	0 / 5107 (0.00%)	27 / 1830 (1.48%)	19 / 1829 (1.04%)
occurrences causally related to treatment / all	0 / 0	0 / 30	1 / 20
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GLOMERULONEPHRITIS MEMBRANOUS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMATURIA			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMORRHAGE URINARY TRACT			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYDRONEPHROSIS			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	0 / 1829 (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
HYDROURETER			

subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
NEPHROLITHIASIS			
subjects affected / exposed	1 / 5107 (0.02%)	1 / 1830 (0.05%)	4 / 1829 (0.22%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEPHROPATHY TOXIC			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PROTEINURIA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RENAL ARTERY STENOSIS			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RENAL FAILURE			
subjects affected / exposed	2 / 5107 (0.04%)	5 / 1830 (0.27%)	5 / 1829 (0.27%)
occurrences causally related to treatment / all	0 / 2	0 / 5	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
RENAL IMPAIRMENT			
subjects affected / exposed	3 / 5107 (0.06%)	13 / 1830 (0.71%)	10 / 1829 (0.55%)
occurrences causally related to treatment / all	1 / 3	0 / 14	1 / 11
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URETERIC OBSTRUCTION			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RENAL VASCULITIS			

subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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
URETHRAL STENOSIS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URETEROLITHIASIS			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	3 / 1829 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY BLADDER POLYP			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY RETENTION			
subjects affected / exposed	1 / 5107 (0.02%)	1 / 1830 (0.05%)	5 / 1829 (0.27%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT OBSTRUCTION			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
GOITRE			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERPARATHYROIDISM PRIMARY			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
Musculoskeletal and connective tissue disorders			

ARTHRALGIA			
subjects affected / exposed	0 / 5107 (0.00%)	3 / 1830 (0.16%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ARTHRITIS			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	4 / 1829 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ARTHROPATHY			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
CHRONIC KIDNEY DISEASE-MINERAL AND BONE DISORDER			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CERVICAL SPINAL STENOSIS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BACK PAIN			
subjects affected / exposed	0 / 5107 (0.00%)	4 / 1830 (0.22%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COMPARTMENT SYNDROME			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
COSTOCHONDRITIS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMARTHROSIS			

subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GOUTY ARTHRITIS			
subjects affected / exposed	0 / 5107 (0.00%)	4 / 1830 (0.22%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTERVERTEBRAL DISC DEGENERATION			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTERVERTEBRAL DISC DISORDER			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
INTERVERTEBRAL DISC DISPLACEMENT			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTERVERTEBRAL DISC PROTRUSION			
subjects affected / exposed	0 / 5107 (0.00%)	4 / 1830 (0.22%)	4 / 1829 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LUMBAR SPINAL STENOSIS			
subjects affected / exposed	0 / 5107 (0.00%)	3 / 1830 (0.16%)	5 / 1829 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
JOINT SWELLING			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
MENISCAL DEGENERATION			

subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MOBILITY DECREASED			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MUSCULAR WEAKNESS			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	0 / 1829 (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
MYALGIA			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	0 / 5107 (0.00%)	5 / 1830 (0.27%)	3 / 1829 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 5	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NECK PAIN			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUROPATHIC ARTHROPATHY			
subjects affected / exposed	1 / 5107 (0.02%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OSTEOARTHRITIS			
subjects affected / exposed	1 / 5107 (0.02%)	16 / 1830 (0.87%)	8 / 1829 (0.44%)
occurrences causally related to treatment / all	0 / 1	0 / 19	0 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OSTEITIS			

subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
OSTEOPOROSIS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PAIN IN EXTREMITY			
subjects affected / exposed	1 / 5107 (0.02%)	1 / 1830 (0.05%)	0 / 1829 (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
POLYARTHRITIS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
RHABDOMYOLYSIS			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ROTATOR CUFF SYNDROME			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
SACROILIITIS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
SOFT TISSUE NECROSIS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
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 COLUMN STENOSIS			

subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SPINAL INSTABILITY			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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
SPINAL LIGAMENT OSSIFICATION			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
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 OSTEOARTHRITIS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	3 / 1829 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SPONDYLITIS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SPONDYLOLISTHESIS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYMPATHETIC POSTERIOR CERVICAL SYNDROME			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
SYNOVIAL CYST			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYNOVITIS			

subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
THORACIC SPINAL STENOSIS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TORTICOLLIS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
ABDOMINAL ABSCESS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ABSCESS LIMB			
subjects affected / exposed	0 / 5107 (0.00%)	6 / 1830 (0.33%)	6 / 1829 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 7	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ABSCESS SOFT TISSUE			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
ACUTE SINUSITIS			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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
ANAL ABSCESS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
APPENDICITIS			

subjects affected / exposed	2 / 5107 (0.04%)	3 / 1830 (0.16%)	3 / 1829 (0.16%)
occurrences causally related to treatment / all	1 / 2	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ARTERIOSCLEROTIC GANGRENE			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ARTHRITIS BACTERIAL			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ARTHRITIS INFECTIVE			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
BACTERAEMIA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BACTERIAL DIARRHOEA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BACTERIAL SEPSIS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BILIARY SEPSIS			
subjects affected / exposed	1 / 5107 (0.02%)	1 / 1830 (0.05%)	0 / 1829 (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
BRAIN ABSCESS			

subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
BRONCHITIS			
subjects affected / exposed	1 / 5107 (0.02%)	4 / 1830 (0.22%)	9 / 1829 (0.49%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHITIS BACTERIAL			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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
CAMPYLOBACTER GASTROENTERITIS			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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
CAMPYLOBACTER INFECTION			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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
CELLULITIS			
subjects affected / exposed	5 / 5107 (0.10%)	22 / 1830 (1.20%)	14 / 1829 (0.77%)
occurrences causally related to treatment / all	0 / 5	0 / 24	0 / 15
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CELLULITIS GANGRENOUS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHOLECYSTITIS INFECTIVE			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CLOSTRIDIAL SEPSIS			

subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHRONIC TONSILLITIS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
CLOSTRIDIUM DIFFICILE INFECTION			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CLOSTRIDIUM DIFFICILE COLITIS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CYSTITIS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CYSTITIS KLEBSIELLA			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
DENGUE FEVER			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEVICE RELATED INFECTION			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIABETIC FOOT INFECTION			

subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIVERTICULITIS			
subjects affected / exposed	1 / 5107 (0.02%)	4 / 1830 (0.22%)	4 / 1829 (0.22%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIABETIC GANGRENE			
subjects affected / exposed	0 / 5107 (0.00%)	3 / 1830 (0.16%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EMPHYSEMATOUS PYELONEPHRITIS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
ENDOCARDITIS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	3 / 1829 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENDOPHTHALMITIS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENTERITIS INFECTIOUS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
ENTEROBACTER INFECTION			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
ERYSIPELAS			

subjects affected / exposed	1 / 5107 (0.02%)	3 / 1830 (0.16%)	3 / 1829 (0.16%)
occurrences causally related to treatment / all	0 / 1	0 / 3	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENTEROCOCCAL INFECTION			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	0 / 1829 (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
ESCHERICHIA INFECTION			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ESCHERICHIA BACTERAEMIA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ESCHERICHIA SEPSIS			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
ESCHERICHIA URINARY TRACT INFECTION			
subjects affected / exposed	1 / 5107 (0.02%)	1 / 1830 (0.05%)	0 / 1829 (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
GANGRENE			
subjects affected / exposed	1 / 5107 (0.02%)	7 / 1830 (0.38%)	4 / 1829 (0.22%)
occurrences causally related to treatment / all	0 / 3	0 / 7	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GAS GANGRENE			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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			

subjects affected / exposed	1 / 5107 (0.02%)	10 / 1830 (0.55%)	8 / 1829 (0.44%)
occurrences causally related to treatment / all	0 / 1	0 / 10	0 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROENTERITIS VIRAL			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GRAFT INFECTION			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
HELICOBACTER INFECTION			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
HEPATITIS B			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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
HEPATITIS C			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
HERPES ZOSTER			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFECTED SKIN ULCER			
subjects affected / exposed	1 / 5107 (0.02%)	1 / 1830 (0.05%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFECTION			

subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
INFECTIVE EXACERBATION OF BRONCHIECTASIS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFLUENZA			
subjects affected / exposed	2 / 5107 (0.04%)	1 / 1830 (0.05%)	0 / 1829 (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
INTERVERTEBRAL DISCITIS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
JOINT ABSCESS			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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
KLEBSIELLA INFECTION			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LEPTOSPIROSIS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
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 ABSCESS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LOCALISED INFECTION			

subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	3 / 1829 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	2 / 5107 (0.04%)	1 / 1830 (0.05%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LUNG INFECTION			
subjects affected / exposed	0 / 5107 (0.00%)	3 / 1830 (0.16%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MASTOIDITIS			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MEDICAL DEVICE SITE INFECTION			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
MORGANELLA INFECTION			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NASOPHARYNGITIS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
NECROTISING FASCIITIS			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUTROPENIC SEPSIS			

subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NOSOCOMIAL INFECTION			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ORCHITIS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
OSTEOMYELITIS			
subjects affected / exposed	1 / 5107 (0.02%)	10 / 1830 (0.55%)	9 / 1829 (0.49%)
occurrences causally related to treatment / all	0 / 1	0 / 11	0 / 11
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OSTEOMYELITIS ACUTE			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	0 / 1829 (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
OSTEOMYELITIS CHRONIC			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OTITIS EXTERNA			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
OTITIS MEDIA ACUTE			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
OTITIS MEDIA CHRONIC			

subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
PANCREATITIS BACTERIAL			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
PAROTID ABSCESS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERIODONTITIS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
PERIRECTAL ABSCESS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERITONITIS			
subjects affected / exposed	0 / 5107 (0.00%)	3 / 1830 (0.16%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
PERITONSILLAR ABSCESS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PHARYNGEAL ABSCESS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
PILONIDAL CYST			

subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
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			
subjects affected / exposed	14 / 5107 (0.27%)	41 / 1830 (2.24%)	54 / 1829 (2.95%)
occurrences causally related to treatment / all	0 / 14	3 / 43	2 / 63
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 1
PNEUMONIA BACTERIAL			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	4 / 1829 (0.22%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA LEGIONELLA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
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 PARAINFLUENZAE VIRAL			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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 PSEUDOMONAL			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA STAPHYLOCOCCAL			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
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 STREPTOCOCCAL			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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 VIRAL			

subjects affected / exposed	1 / 5107 (0.02%)	1 / 1830 (0.05%)	0 / 1829 (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
POST PROCEDURAL CELLULITIS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
POST PROCEDURAL INFECTION			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
POSTOPERATIVE ABSCESS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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 WOUND INFECTION			
subjects affected / exposed	1 / 5107 (0.02%)	1 / 1830 (0.05%)	0 / 1829 (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
PROSTATIC ABSCESS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PROSTATITIS ESCHERICHIA COLI			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
PSEUDOMONAS INFECTION			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PULMONARY TUBERCULOMA			

subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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
PYELONEPHRITIS			
subjects affected / exposed	3 / 5107 (0.06%)	4 / 1830 (0.22%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 3	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYELONEPHRITIS ACUTE			
subjects affected / exposed	0 / 5107 (0.00%)	4 / 1830 (0.22%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYELONEPHRITIS CHRONIC			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 5107 (0.02%)	1 / 1830 (0.05%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RHINITIS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEPSIS			
subjects affected / exposed	4 / 5107 (0.08%)	18 / 1830 (0.98%)	16 / 1829 (0.87%)
occurrences causally related to treatment / all	0 / 4	2 / 18	0 / 17
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 3
SEPSIS SYNDROME			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
SEPTIC EMBOLUS			

subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEPTIC ENCEPHALOPATHY			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEPTIC NECROSIS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEPTIC SHOCK			
subjects affected / exposed	1 / 5107 (0.02%)	6 / 1830 (0.33%)	5 / 1829 (0.27%)
occurrences causally related to treatment / all	0 / 1	0 / 6	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 2
SIALOADENITIS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STAPHYLOCOCCAL ABSCESS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STAPHYLOCOCCAL BACTERAEMIA			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STAPHYLOCOCCAL SEPSIS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STREPTOCOCCAL BACTERAEMIA			

subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYSTEMIC CANDIDA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TOOTH ABSCESS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
TOXIC SHOCK SYNDROME			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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 RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TUBERCULOSIS			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
URINARY TRACT INFECTION			
subjects affected / exposed	6 / 5107 (0.12%)	12 / 1830 (0.66%)	21 / 1829 (1.15%)
occurrences causally related to treatment / all	0 / 6	0 / 15	1 / 21
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT INFECTION ENTEROCOCCAL			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT INFECTION BACTERIAL			

subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UROSEPSIS			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VIRAL INFECTION			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	0 / 1829 (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
VULVAL ABSCESS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WOUND INFECTION			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	3 / 1829 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WOUND SEPSIS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WOUND INFECTION STAPHYLOCOCCAL			
subjects affected / exposed	1 / 5107 (0.02%)	0 / 1830 (0.00%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	1 / 5107 (0.02%)	1 / 1830 (0.05%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CACHEXIA			

subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEHYDRATION			
subjects affected / exposed	7 / 5107 (0.14%)	8 / 1830 (0.44%)	11 / 1829 (0.60%)
occurrences causally related to treatment / all	0 / 7	0 / 8	1 / 11
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIABETES MELLITUS			
subjects affected / exposed	1 / 5107 (0.02%)	4 / 1830 (0.22%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIABETES MELLITUS INADEQUATE CONTROL			
subjects affected / exposed	3 / 5107 (0.06%)	7 / 1830 (0.38%)	9 / 1829 (0.49%)
occurrences causally related to treatment / all	0 / 3	0 / 7	0 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIABETIC KETOACIDOSIS			
subjects affected / exposed	1 / 5107 (0.02%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIABETIC KETOSIS			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
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 METABOLIC DECOMPENSATION			
subjects affected / exposed	0 / 5107 (0.00%)	3 / 1830 (0.16%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ELECTROLYTE IMBALANCE			
subjects affected / exposed	0 / 5107 (0.00%)	2 / 1830 (0.11%)	0 / 1829 (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
FLUID OVERLOAD			

subjects affected / exposed	2 / 5107 (0.04%)	3 / 1830 (0.16%)	9 / 1829 (0.49%)
occurrences causally related to treatment / all	1 / 2	2 / 3	3 / 10
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FLUID RETENTION			
subjects affected / exposed	2 / 5107 (0.04%)	0 / 1830 (0.00%)	0 / 1829 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GOUT			
subjects affected / exposed	1 / 5107 (0.02%)	2 / 1830 (0.11%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	1 / 1	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERCALCAEMIA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERGLYCAEMIA			
subjects affected / exposed	2 / 5107 (0.04%)	9 / 1830 (0.49%)	8 / 1829 (0.44%)
occurrences causally related to treatment / all	1 / 2	0 / 11	1 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERGLYCAEMIC HYPEROSMOLAR NONKETOTIC SYNDROME			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERKALAEMIA			
subjects affected / exposed	5 / 5107 (0.10%)	16 / 1830 (0.87%)	16 / 1829 (0.87%)
occurrences causally related to treatment / all	1 / 6	3 / 19	2 / 18
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERURICAEMIA			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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
HYPOCALCAEMIA			

subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOALBUMINAEMIA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPONATRAEMIA			
subjects affected / exposed	2 / 5107 (0.04%)	2 / 1830 (0.11%)	3 / 1829 (0.16%)
occurrences causally related to treatment / all	1 / 2	0 / 2	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOMAGNESAEMIA			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOGLYCAEMIA			
subjects affected / exposed	13 / 5107 (0.25%)	12 / 1830 (0.66%)	22 / 1829 (1.20%)
occurrences causally related to treatment / all	0 / 13	0 / 14	0 / 24
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOVOLAEMIA			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOPHAGIA			
subjects affected / exposed	0 / 5107 (0.00%)	0 / 1830 (0.00%)	1 / 1829 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
METABOLIC ACIDOSIS			
subjects affected / exposed	0 / 5107 (0.00%)	6 / 1830 (0.33%)	5 / 1829 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 6	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
OBESITY			

subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	2 / 1829 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TYPE 2 DIABETES MELLITUS			
subjects affected / exposed	0 / 5107 (0.00%)	1 / 1830 (0.05%)	0 / 1829 (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

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

Non-serious adverse events	All Atrasentan Set	Double-Blind Placebo	Double-Blind Atrasentan
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1781 / 5107 (34.87%)	1038 / 1830 (56.72%)	1043 / 1829 (57.03%)
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	78 / 5107 (1.53%)	218 / 1830 (11.91%)	158 / 1829 (8.64%)
occurrences (all)	79	257	179
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	180 / 5107 (3.52%)	127 / 1830 (6.94%)	216 / 1829 (11.81%)
occurrences (all)	183	138	241
General disorders and administration site conditions			
OEDEMA PERIPHERAL			
subjects affected / exposed	1148 / 5107 (22.48%)	483 / 1830 (26.39%)	534 / 1829 (29.20%)
occurrences (all)	1273	666	765
Gastrointestinal disorders			
DIARRHOEA			
subjects affected / exposed	103 / 5107 (2.02%)	103 / 1830 (5.63%)	99 / 1829 (5.41%)
occurrences (all)	108	110	116
Musculoskeletal and connective tissue disorders			
BACK PAIN			
subjects affected / exposed	61 / 5107 (1.19%)	125 / 1830 (6.83%)	88 / 1829 (4.81%)
occurrences (all)	62	133	93
Infections and infestations			

UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	110 / 5107 (2.15%)	114 / 1830 (6.23%)	106 / 1829 (5.80%)
occurrences (all)	114	140	131
NASOPHARYNGITIS			
subjects affected / exposed	145 / 5107 (2.84%)	169 / 1830 (9.23%)	180 / 1829 (9.84%)
occurrences (all)	152	278	274
URINARY TRACT INFECTION			
subjects affected / exposed	50 / 5107 (0.98%)	93 / 1830 (5.08%)	93 / 1829 (5.08%)
occurrences (all)	51	135	126
Metabolism and nutrition disorders			
HYPERKALAEMIA			
subjects affected / exposed	77 / 5107 (1.51%)	143 / 1830 (7.81%)	132 / 1829 (7.22%)
occurrences (all)	77	165	159
HYPERURICAEMIA			
subjects affected / exposed	84 / 5107 (1.64%)	105 / 1830 (5.74%)	101 / 1829 (5.52%)
occurrences (all)	85	106	105
HYPOGLYCAEMIA			
subjects affected / exposed	126 / 5107 (2.47%)	120 / 1830 (6.56%)	114 / 1829 (6.23%)
occurrences (all)	189	212	193

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 October 2014	<ul style="list-style-type: none"> • ESRD for primary endpoint: confirmed eGFR < 15 mL/min/1.73 m² • Other endpoints: Changed time to 30% eGFR reduction after 2 mos post-random to 50% eGFR reduction; change from Baseline (BL) to 24 mo post-random on UACR new endpoint; made time to first occurrence of component of composite renal endpoint new endpoint; added endpoints about vascular events and laser photocoagulations • Inclusion criterion (IC) 3: antihyperglycemic meds and ACE inhibitor or angiotensin receptor blocker at least 4 wks prior to screening visit 2; latent autoimmune diabetes or insulin-treated w/o history of diabetic ketoacidosis who also have a negative anti-GAD test + an elevated post-prandial serum C-peptide level • IC 5: serum albumin criteria ≥ 2.5 g/dL (25 g/L); serum K upper limit =6.0 mEq/L; upper limit of systolic BP =180 mmHg; eligible BP at any time during screening • IC 7: remove acute kidney injury; subjects may not have a weight gain ≥ 3 kg AND brain natriuretic peptide (BNP) ≥ 300 pg/mL last visit of the enrichment period compared to BL • IC 8: dual contraception acceptable forms • Removed HbA1c IC • Exclusion criterion (EC) 1: removed moderate edema and pulmonary edema; updated time frame from 6 mos to 4 wks prior to screening. • EC 2: subject has history of pulmonary hypertension, pulmonary fibrosis or any lung disease requiring oxygen therapy (e.g., chronic obstructive pulmonary disease, emphysema) • EC 15: include atrasentan use • Removed EC for Hx of symptomatic hypotension, BMI, and pioglitazone • Added EC 22: subjects considered to be clinically unstable regarding general, metabolic or CV health determined by investigator • Removed UACR blind during Enrichment Period • Revised randomization strategy for non-responder to distribute non-responder chronologically throughout study in 1:3 proportion to # of responders randomized • Revised primary efficacy analysis from Cox proportional-hazard model analysis to stratified log-rank test
11 February 2015	<ul style="list-style-type: none"> • Updated HOMA-IR calculation for insulin resistance • Removed allowance for repeat of serum creatinine at an unscheduled visit (s) after E5 • Clarified that if during the Double-Blind Treatment Period the subject discontinued study drug, the investigator should only re-start if it was medically appropriate • Added statement regarding the maximum duration of atrasentan exposure and maximum atrasentan dose • Updated the number of study sites to 800 – 900 • Added additional clarification regarding the randomization strategy of the non-responder arm

19 May 2017	<ul style="list-style-type: none"> • Updated figures throughout protocol: Revised number of subjects to be enrolled from 4,148 to 3,500; revised responders (UACR reduction \geq 30% from Baseline) in the Study Diagram from 1,574 to 1,250; revised number of responders from 3,148 to 2,500; extended yearly treatment visits past T48 • Updated statistical methods: Sample size determination, definition of Baseline, primary efficacy analysis, derivation of safety endpoints, interim analysis • Updated duration of the Double-Blind Treatment Period from 48 months to approximately 6 years • Clarified exclusion criterion 19 to re-define premenopausal women are not eligible for study participation
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Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported