



Clinical trial results:

A Randomized, Open-Label, Comparative Evaluation of Conversion From Calcineurin Inhibitors to Sirolimus Versus Continued Use of Calcineurin Inhibitors in Renal Allograft Recipients

Summary

EudraCT number	2006-005687-44
Trial protocol	Outside EU/EEA
Global end of trial date	21 May 2008

Results information

Result version number	v1 (current)
This version publication date	30 May 2016
First version publication date	31 July 2015

Trial information

Trial identification

Sponsor protocol code	0468H1-316
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00038948
WHO universal trial number (UTN)	-
Other trial identifiers	Alias: B1741186

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Clinical Trials.gov Call Center, Pfizer Inc, 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Clinical Trials.gov Call Center, Pfizer Inc, 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	12 December 2008
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	21 May 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the effect of conversion from calcineurin inhibitor (CNI)- to sirolimus (SRL)-based therapy on renal function 52 weeks after randomization, as indicated by the change from baseline calculated glomerular filtration rate (GFR) (Nankivell method), and to demonstrate:

a) superiority of the SRL conversion versus CNI continuation regimens in subjects with baseline Nankivell GFRs greater than ($>$) 40 milliliter per minute (mL/min). OR

b) noninferiority of the SRL conversion versus CNI continuation regimens in subjects with baseline Nankivell GFRs of 20 to 40 mL/min, and to establish superiority in this group if the results are consistent with this conclusion.

To assess equivalence 52 weeks after randomization between treatment groups in the composite endpoint of the incidence of the first occurrence of biopsy-confirmed acute rejection, graft loss, or death.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 February 2002
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	1 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Singapore: 7
Country: Number of subjects enrolled	France: 25
Country: Number of subjects enrolled	South Africa: 31
Country: Number of subjects enrolled	Denmark: 3
Country: Number of subjects enrolled	Czech Republic: 33
Country: Number of subjects enrolled	Portugal: 21
Country: Number of subjects enrolled	Mexico: 126
Country: Number of subjects enrolled	Italy: 46
Country: Number of subjects enrolled	Argentina: 68
Country: Number of subjects enrolled	Sweden: 2
Country: Number of subjects enrolled	Poland: 37
Country: Number of subjects enrolled	Brazil: 80

Country: Number of subjects enrolled	Chile: 9
Country: Number of subjects enrolled	Germany: 10
Country: Number of subjects enrolled	Saudi Arabia: 2
Country: Number of subjects enrolled	Spain: 59
Country: Number of subjects enrolled	Austria: 13
Country: Number of subjects enrolled	Belgium: 7
Country: Number of subjects enrolled	Australia: 38
Country: Number of subjects enrolled	Canada: 37
Country: Number of subjects enrolled	United States: 176
Worldwide total number of subjects	830
EEA total number of subjects	256

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)	38
Adults (18-64 years)	751
From 65 to 84 years	41
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited worldwide from January 2002 to September 2003.

Pre-assignment

Screening details:

Subjects were screened for two weeks.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
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Arm title	SRL Conversion in Stable Renal Transplant Recipients
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Arm description:

Conversion from calcineurin inhibitor immunosuppression therapy to Sirolimus-based immunosuppression therapy.

Arm type	Experimental
Investigational medicinal product name	Sirolimus
Investigational medicinal product code	
Other name	Rapamune
Pharmaceutical forms	Oral solution, Tablet
Routes of administration	Oral use

Dosage and administration details:

SRL was concentration-controlled and adjusted to achieve a whole blood trough level in the range of 8 to 20 nanogram per milliliter (ng/mL). SRL was administered for the entire 208-weeks treatment period.

Arm title	CNI Continuation in Stable Renal Transplant Recipients
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Arm description:

Continued calcineurin inhibitor immunosuppression therapy. Subjects in this arm will receive either CsA or TAC.

Arm type	Active comparator
Investigational medicinal product name	Cyclosporine (cyclosporin A):CsA
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution, Tablet
Routes of administration	Oral use

Dosage and administration details:

CsA trough concentrations was monitored at designated intervals and the CsA dose adjusted to maintain the following trough concentration ranges: CsA 50-250 ng/mL. Subjects continue to receive CsA for the entire 208-week treatment period. The investigators supplied CNIs in the appropriate formulation available in their region.

Investigational medicinal product name	Tacrolimus
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet, Oral solution
Routes of administration	Oral use

Dosage and administration details:

Tacrolimus (TAC) trough concentrations was monitored at designated intervals and the TAC dose adjusted to maintain the following trough concentration ranges: TAC 4-10 ng/mL. Subjects continue to

receive tacrolimus for the entire 208-week treatment period. The investigators supplied TAC in the appropriate formulation available in their region.

Number of subjects in period 1	SRL Conversion in Stable Renal Transplant Recipients	CNI Continuation in Stable Renal Transplant Recipients
Started	555	275
Completed	441	222
Not completed	114	53
Randomized, but not treated	4	2
No longer willing to participate in study	31	19
Adverse event	19	6
Lost to follow-up	35	18
Subject Died	25	8

Baseline characteristics

Reporting groups

Reporting group title	SRL Conversion in Stable Renal Transplant Recipients
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Reporting group description:

Conversion from calcineurin inhibitor immunosuppression therapy to Sirolimus-based immunosuppression therapy.

Reporting group title	CNI Continuation in Stable Renal Transplant Recipients
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Reporting group description:

Continued calcineurin inhibitor immunosuppression therapy. Subjects in this arm will receive either CsA or TAC.

Reporting group values	SRL Conversion in Stable Renal Transplant Recipients	CNI Continuation in Stable Renal Transplant Recipients	Total
Number of subjects	555	275	830
Age categorical Units: Subjects			
Age continuous Units: years median full range (min-max)	45 13.2 to 75.1	43.5 12.8 to 74	-
Gender categorical Units: Subjects			
Female	170	81	251
Male	385	194	579

End points

End points reporting groups

Reporting group title	SRL Conversion in Stable Renal Transplant Recipients
Reporting group description: Conversion from calcineurin inhibitor immunosuppression therapy to Sirolimus-based immunosuppression therapy.	
Reporting group title	CNI Continuation in Stable Renal Transplant Recipients
Reporting group description: Continued calcineurin inhibitor immunosuppression therapy. Subjects in this arm will receive either CsA or TAC.	
Subject analysis set title	SRL Conversion Strata 20.0-40.0 milliliter/minute (mL/Min)
Subject analysis set type	Intention-to-treat
Subject analysis set description: Conversion from calcineurin inhibitor immunosuppression therapy to Sirolimus-based immunosuppression therapy in stable renal transplant recipients.	
Subject analysis set title	CNI Continuation Strata 20.0-40.0 mL/Min
Subject analysis set type	Intention-to-treat
Subject analysis set description: Continued calcineurin inhibitor immunosuppression therapy in renal transplant recipients.	
Subject analysis set title	SRL Conversion Strata >40.0 mL/Min
Subject analysis set type	Intention-to-treat
Subject analysis set description: Conversion from calcineurin inhibitor immunosuppression therapy to Sirolimus-based immunosuppression therapy in renal transplant recipients.	
Subject analysis set title	CNI Continuation Strata >40.0 mL/Min
Subject analysis set type	Intention-to-treat
Subject analysis set description: Continued calcineurin inhibitor immunosuppression therapy in renal transplant recipients.	

Primary: Nankivell Glomerular Filtration Rate (GFR) at Week 52

End point title	Nankivell Glomerular Filtration Rate (GFR) at Week 52
End point description: Nankivell GFR: subjects with baseline GFR of 20.0 to 40.0 mL/min and subjects with baseline GFR of greater than 40.0 mL/min. GFR is an index of kidney function. A higher value means better kidney function. Subjects were stratified by GFR at baseline. GFR 20-40 mL/min and GFR >40 mL/min. Arithmetic mean as from ANCOVA model adjusted for center and baseline.	
End point type	Primary
End point timeframe: 52 weeks	

End point values	SRL Conversion Strata 20.0-40.0 milliliter/minute (mL/Min)	CNI Continuation Strata 20.0-40.0 mL/Min	SRL Conversion Strata >40.0 mL/Min	CNI Continuation Strata >40.0 mL/Min
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	58	29	496	245
Units: mL/min				
arithmetic mean (standard error)	24.56 (± 2.42)	27.24 (± 3.71)	59.04 (± 0.89)	57.73 (± 1.1)

Statistical analyses

Statistical analysis title	Baseline GFR of 20.0 to 40.0 mL/min
Statistical analysis description: Data was adjusted for baseline and center.	
Comparison groups	SRL Conversion Strata 20.0-40.0 milliliter/minute (mL/Min) v CNI Continuation Strata 20.0-40.0 mL/Min
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.575 ^[1]
Method	ANCOVA
Parameter estimate	Weighted difference
Point estimate	-2.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.27
upper limit	6.91

Notes:

[1] - Analysis of covariance P-value for testing the equality of mean GFR at week 52 between treatments.

Statistical analysis title	Baseline GFR of >40.0 mL/min
Statistical analysis description: Data was adjusted for baseline and center.	
Comparison groups	CNI Continuation Strata >40.0 mL/Min v SRL Conversion Strata >40.0 mL/Min
Number of subjects included in analysis	741
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.278 ^[2]
Method	ANCOVA
Parameter estimate	Weighted difference
Point estimate	1.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.06
upper limit	3.69

Notes:

[2] - Analysis of covariance P-value for testing the equality of mean GFR at week 52 between treatments.

Primary: First Occurrence of Biopsy-confirmed Acute Rejection, Graft Loss, or Death

End point title	First Occurrence of Biopsy-confirmed Acute Rejection, Graft Loss, or Death
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End point description:

Number of subjects who experienced for the first time either biopsy-confirmed acute rejection, graft loss, or death by weeks 52 and 104. Assessed by individual endpoint and as composite endpoint (all combined). Subjects were stratified by GFR at baseline. GFR 20-40 mL/min and GFR >40 mL/min. The outcome measure was primary safety endpoint.

End point type	Primary
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End point timeframe:

52 and 104 weeks

End point values	SRL Conversion Strata 20.0- 40.0 milliliter/minute (mL/Min)	CNI Continuation Strata 20.0- 40.0 mL/Min	SRL Conversion Strata >40.0 mL/Min	CNI Continuation Strata >40.0 mL/Min
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	58	29	497	246
Units: subjects				
52 weeks - Acute rejection	4	0	8	3
52 weeks - Graft loss	7	3	3	3
52 weeks - Death	3	0	6	1
52 weeks - Missing	0	0	5	1
104 weeks - Acute rejection	5	1	27	9
104 weeks - Graft loss	12	9	12	8
104 weeks - Death	7	0	13	3
104 weeks - Missing	0	2	13	8

Statistical analyses

Statistical analysis title	52 Weeks Statistical Analysis Across Strata
Comparison groups	SRL Conversion Strata 20.0-40.0 milliliter/minute (mL/Min) v CNI Continuation Strata 20.0-40.0 mL/Min v SRL Conversion Strata >40.0 mL/Min v CNI Continuation Strata >40.0 mL/Min
Number of subjects included in analysis	830
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.135 ^[3]
Method	Cochran-Mantel-Haenszel

Notes:

[3] - P-value for testing the equality of rates between treatments across strata at 52 weeks.

Statistical analysis title	104 Weeks Statistical Analysis Across Strata
Comparison groups	SRL Conversion Strata 20.0-40.0 milliliter/minute (mL/Min) v CNI Continuation Strata 20.0-40.0 mL/Min v SRL Conversion Strata >40.0 mL/Min v CNI Continuation Strata >40.0 mL/Min

Number of subjects included in analysis	830
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.559 ^[4]
Method	Cochran-Mantel-Haenszel

Notes:

[4] - P-value for testing the equality of rates between treatments across strata at 104 weeks.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to 212 weeks

Adverse event reporting additional description:

The same event may appear as both an AE and a SAE. However, what is presented are distinct events. An event may be categorized as serious in 1 subject and as non-serious in another, or 1 subject may have experienced both serious, non-serious event during study. EU BR specific AE tables were generated separately as per EU format using latest coding.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.1
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Reporting groups

Reporting group title	SRL Conversion in Stable Renal Transplant Recipients
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Reporting group description:

Conversion from calcineurin inhibitor immunosuppression therapy to Sirolimus-based immunosuppression therapy.

Reporting group title	CNI Continuation in Stable Renal Transplant Recipients
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Reporting group description:

Continued calcineurin inhibitor immunosuppression therapy.

Serious adverse events	SRL Conversion in Stable Renal Transplant Recipients	CNI Continuation in Stable Renal Transplant Recipients	
Total subjects affected by serious adverse events			
subjects affected / exposed	364 / 551 (66.06%)	152 / 273 (55.68%)	
number of deaths (all causes)	33	11	
number of deaths resulting from adverse events	11	4	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of the cervix			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenoma benign			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anogenital warts			

subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bowen's disease			
subjects affected / exposed	1 / 551 (0.18%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	1 / 1	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			
subjects affected / exposed	9 / 551 (1.63%)	12 / 273 (4.40%)	
occurrences causally related to treatment / all	7 / 13	20 / 24	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basosquamous carcinoma			
subjects affected / exposed	1 / 551 (0.18%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Astrocytoma malignant			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic myeloid leukaemia			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clear cell renal cell carcinoma			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cancer			

subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal stromal tumour			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glioblastoma multiforme			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric cancer			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal squamous cell carcinoma			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lip squamous cell carcinoma			

subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Keratoacanthoma			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphoproliferative disorder			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma			
subjects affected / exposed	2 / 551 (0.36%)	3 / 273 (1.10%)	
occurrences causally related to treatment / all	1 / 2	7 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Papilloma			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuroendocrine carcinoma of the skin			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian adenoma			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasm skin			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post transplant lymphoproliferative disorder			

subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal cancer			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	4 / 551 (0.73%)	3 / 273 (1.10%)	
occurrences causally related to treatment / all	5 / 9	6 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cell carcinoma			
subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin papilloma			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin cancer			
subjects affected / exposed	2 / 551 (0.36%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	2 / 2	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seminoma			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			
subjects affected / exposed	8 / 551 (1.45%)	13 / 273 (4.76%)	
occurrences causally related to treatment / all	9 / 15	20 / 48	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of head and neck			

subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine cancer			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of the tongue			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of skin			
subjects affected / exposed	3 / 551 (0.54%)	5 / 273 (1.83%)	
occurrences causally related to treatment / all	2 / 4	3 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine leiomyoma			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma of colon			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Breast cancer metastatic			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Vascular disorders			
Aortic disorder			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic aneurysm			

subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angiopathy			
subjects affected / exposed	1 / 551 (0.18%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	3 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aneurysm			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Accelerated hypertension			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	14 / 551 (2.54%)	4 / 273 (1.47%)	
occurrences causally related to treatment / all	7 / 16	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous fistula			
subjects affected / exposed	1 / 551 (0.18%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial thrombosis			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic stenosis			

subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic vascular disorder			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive emergency			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	2 / 551 (0.36%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	9 / 551 (1.63%)	4 / 273 (1.47%)	
occurrences causally related to treatment / all	0 / 9	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extremity necrosis			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolism			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	1 / 551 (0.18%)	3 / 273 (1.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphocele			

subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic venous thrombosis			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iliac vein occlusion			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intermittent claudication			
subjects affected / exposed	1 / 551 (0.18%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemia			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery stenosis			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral venous disease			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral ischaemia			

subjects affected / exposed	4 / 551 (0.73%)	3 / 273 (1.10%)	
occurrences causally related to treatment / all	4 / 7	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral vascular disorder			
subjects affected / exposed	1 / 551 (0.18%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral embolism			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vena cava thrombosis			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis			
subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis limb			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Phlebitis			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shock haemorrhagic			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis			

subjects affected / exposed	2 / 551 (0.36%)	3 / 273 (1.10%)	
occurrences causally related to treatment / all	1 / 2	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	2 / 551 (0.36%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Incisional hernia repair			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cancer surgery			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Unintended pregnancy			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy			
subjects affected / exposed	1 / 551 (0.18%)	3 / 273 (1.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chills			

subjects affected / exposed	6 / 551 (1.09%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 7	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest discomfort			
subjects affected / exposed	1 / 551 (0.18%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	9 / 551 (1.63%)	4 / 273 (1.47%)	
occurrences causally related to treatment / all	2 / 10	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device malfunction			
subjects affected / exposed	3 / 551 (0.54%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cyst			
subjects affected / exposed	1 / 551 (0.18%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device dislocation			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic cyst			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised oedema			
subjects affected / exposed	4 / 551 (0.73%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Granuloma			

subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	3 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Face oedema			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug intolerance			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device occlusion			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperpyrexia			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hernia			
subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired healing			
subjects affected / exposed	5 / 551 (0.91%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	3 / 7	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated hernia			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza like illness			

subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Serositis			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	48 / 551 (8.71%)	15 / 273 (5.49%)	
occurrences causally related to treatment / all	31 / 73	1 / 16	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral swelling			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mass			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema			
subjects affected / exposed	6 / 551 (1.09%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	2 / 8	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	1 / 551 (0.18%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multi-organ failure			
subjects affected / exposed	4 / 551 (0.73%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 4	0 / 0	
deaths causally related to treatment / all	1 / 3	0 / 0	
Oedema peripheral			

subjects affected / exposed	7 / 551 (1.27%)	3 / 273 (1.10%)	
occurrences causally related to treatment / all	0 / 7	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sudden death			
subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Immune system disorders			
Transplant rejection			
subjects affected / exposed	16 / 551 (2.90%)	7 / 273 (2.56%)	
occurrences causally related to treatment / all	4 / 17	4 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney transplant rejection			
subjects affected / exposed	2 / 551 (0.36%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	0 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug hypersensitivity			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amyloidosis			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Endometrial hyperplasia			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metrorrhagia			
subjects affected / exposed	4 / 551 (0.73%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	2 / 4	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Menorrhagia			
subjects affected / exposed	3 / 551 (0.54%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic ovarian cyst			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst			
subjects affected / exposed	4 / 551 (0.73%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	2 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian mass			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatitis			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	6 / 551 (1.09%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	8 / 8	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infiltration			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasal congestion			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleuritic pain			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oropharyngeal pain			

subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	5 / 551 (0.91%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	5 / 6	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary hypertension			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	2 / 551 (0.36%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sleep apnoea syndrome			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillar haemorrhage			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillar hypertrophy			

subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vocal cord disorder			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	17 / 551 (3.09%)	4 / 273 (1.47%)	
occurrences causally related to treatment / all	5 / 24	0 / 6	
deaths causally related to treatment / all	0 / 2	0 / 0	
Epistaxis			
subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Lung disorder			
subjects affected / exposed	8 / 551 (1.45%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	0 / 12	0 / 2	
deaths causally related to treatment / all	1 / 1	0 / 0	
Pleural effusion			
subjects affected / exposed	7 / 551 (1.27%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	6 / 8	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumothorax			
subjects affected / exposed	1 / 551 (0.18%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory acidosis			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory failure			

subjects affected / exposed	1 / 551 (0.18%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 1	
Psychiatric disorders			
Agitation			
subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug abuse			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional state			
subjects affected / exposed	1 / 551 (0.18%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	3 / 551 (0.54%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood glucose abnormal			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood parathyroid hormone			

increased			
subjects affected / exposed	1 / 551 (0.18%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood pressure increased			
subjects affected / exposed	1 / 551 (0.18%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood triglycerides increased			
subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alanine aminotransferase increased			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biopsy site unspecified abnormal			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood urea increased			
subjects affected / exposed	4 / 551 (0.73%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	1 / 6	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
C-reactive protein increased			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carbohydrate antigen 125 increased			

subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug level increased			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium test positive			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coagulation time prolonged			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus test positive			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carbon dioxide decreased			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric occult blood positive			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glomerular filtration rate decreased			

subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematology test abnormal			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic enzyme increased			
subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
International normalised ratio increased			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test abnormal			
subjects affected / exposed	4 / 551 (0.73%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	3 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transaminases abnormal			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcus test			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight decreased			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatinine increased			

subjects affected / exposed	38 / 551 (6.90%)	15 / 273 (5.49%)	
occurrences causally related to treatment / all	16 / 53	5 / 20	
deaths causally related to treatment / all	0 / 1	0 / 0	
Injury, poisoning and procedural complications			
Accident			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Accidental overdose			
subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous fistula site complication			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Complications of transplant surgery			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic allograft nephropathy			
subjects affected / exposed	13 / 551 (2.36%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	3 / 16	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous fistula thrombosis			
subjects affected / exposed	0 / 551 (0.00%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous fistula site haemorrhage			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Arteriovenous fistula aneurysm subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft thrombosis subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand fracture subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture subjects affected / exposed	3 / 551 (0.54%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Complications of transplanted kidney subjects affected / exposed	18 / 551 (3.27%)	8 / 273 (2.93%)	
occurrences causally related to treatment / all	9 / 29	2 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft complication			

subjects affected / exposed	4 / 551 (0.73%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft loss			
subjects affected / exposed	1 / 551 (0.18%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb traumatic amputation			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laceration			
subjects affected / exposed	1 / 551 (0.18%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incision site complication			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb injury			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incisional hernia			
subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	2 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury			

subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis chemical			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			
subjects affected / exposed	4 / 551 (0.73%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	1 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle strain			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Medication error			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural complication			
subjects affected / exposed	3 / 551 (0.54%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haematoma			
subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			

subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal haematoma			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal transplant failure			
subjects affected / exposed	21 / 551 (3.81%)	20 / 273 (7.33%)	
occurrences causally related to treatment / all	6 / 27	4 / 23	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seroma			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural pain			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural complication			
subjects affected / exposed	1 / 551 (0.18%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound complication			
subjects affected / exposed	0 / 551 (0.00%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin injury			

subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haemorrhage			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic haemothorax			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular procedure complication			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular pseudoaneurysm			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound complication			

subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	2 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound dehiscence			
subjects affected / exposed	3 / 551 (0.54%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound necrosis			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound secretion			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Congenital cystic kidney disease			
subjects affected / exposed	2 / 551 (0.36%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertrophic cardiomyopathy			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	2 / 551 (0.36%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Atrial fibrillation			
subjects affected / exposed	3 / 551 (0.54%)	4 / 273 (1.47%)	
occurrences causally related to treatment / all	0 / 4	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial thrombosis			
subjects affected / exposed	0 / 551 (0.00%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac tamponade			
subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure acute			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiomyopathy			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	3 / 551 (0.54%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	3 / 8	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Palpitations			

subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve incompetence			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cyanosis			
subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	5 / 551 (0.91%)	3 / 273 (1.10%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis constrictive			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular tachycardia			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Right ventricular failure			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			
subjects affected / exposed	1 / 551 (0.18%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Acute myocardial infarction			

subjects affected / exposed	2 / 551 (0.36%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac arrest			
subjects affected / exposed	4 / 551 (0.73%)	3 / 273 (1.10%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 2	0 / 1	
Cardiac failure			
subjects affected / exposed	6 / 551 (1.09%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 8	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	7 / 551 (1.27%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	2 / 13	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cor pulmonale			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Myocardial infarction			
subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nervous system disorders			
Anosmia			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arachnoid cyst			

subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	3 / 551 (0.54%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	1 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain mass			
subjects affected / exposed	1 / 551 (0.18%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			
subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
IVth nerve paralysis			

subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive encephalopathy			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lethargy			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningism			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyneuropathy			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurological decompensation			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuropathy peripheral			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nerve compression			

subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uraemic encephalopathy			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post herpetic neuralgia			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	1 / 551 (0.18%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 551 (0.00%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trigeminal neuralgia			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VIIth nerve paralysis			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vocal cord paralysis			

subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Subarachnoid haemorrhage			
subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Haemorrhagic stroke			
subjects affected / exposed	3 / 551 (0.54%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	27 / 551 (4.90%)	5 / 273 (1.83%)	
occurrences causally related to treatment / all	15 / 34	2 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemolytic uraemic syndrome			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron deficiency anaemia			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudolymphoma			

subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenopathy			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Microangiopathic haemolytic anaemia			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukocytosis			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	4 / 551 (0.73%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	3 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	3 / 551 (0.54%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	4 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombotic microangiopathy			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			

subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal discomfort			
subjects affected / exposed	0 / 551 (0.00%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal adhesions			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	20 / 551 (3.63%)	5 / 273 (1.83%)	
occurrences causally related to treatment / all	8 / 25	1 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain lower			
subjects affected / exposed	1 / 551 (0.18%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	2 / 551 (0.36%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fissure			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aphthous stomatitis			

subjects affected / exposed	3 / 551 (0.54%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic gastritis			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute abdomen			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	6 / 551 (1.09%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	2 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	36 / 551 (6.53%)	6 / 273 (2.20%)	
occurrences causally related to treatment / all	21 / 45	1 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea haemorrhagic			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticular perforation			
subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum			

subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenitis			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspepsia			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ulcerative			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faecal incontinence			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faeces discoloured			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Flatulence			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric polyps			

subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	4 / 551 (0.73%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal angiodysplasia haemorrhagic			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorder			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal necrosis			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal pain			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematochezia			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hernial eventration			

subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	2 / 551 (0.36%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal perforation			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Irritable bowel syndrome			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	1 / 551 (0.18%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal ulcer			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mechanical ileus			

subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mouth ulceration			
subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	9 / 551 (1.63%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	1 / 10	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal ulcer			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis haemorrhagic			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic cyst			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic necrosis			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			

subjects affected / exposed	2 / 551 (0.36%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	2 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peptic ulcer perforation			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	3 / 551 (0.54%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	2 / 551 (0.36%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			
subjects affected / exposed	3 / 551 (0.54%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	11 / 551 (2.00%)	4 / 273 (1.47%)	
occurrences causally related to treatment / all	2 / 13	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			

subjects affected / exposed	3 / 551 (0.54%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	1 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proctitis ulcerative			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	4 / 551 (0.73%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ascites			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Oesophageal rupture			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	2 / 551 (0.36%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary colic			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			

subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-alcoholic steatohepatitis			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatosplenomegaly			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatocellular injury			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis chronic active			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis acute			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic pain			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	2 / 551 (0.36%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cirrhosis			

subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hepatic failure			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angioedema			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decubitus ulcer			
subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis exfoliative			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatosis			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ulcer			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Exfoliative rash			

subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Granuloma skin			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperhidrosis			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pruritus			
subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash			
subjects affected / exposed	4 / 551 (0.73%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	4 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin disorder			
subjects affected / exposed	0 / 551 (0.00%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin exfoliation			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin lesion			
subjects affected / exposed	1 / 551 (0.18%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	2 / 2	1 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin necrosis			

subjects affected / exposed	4 / 551 (0.73%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 7	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin ulcer			
subjects affected / exposed	7 / 551 (1.27%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	5 / 10	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxic skin eruption			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	17 / 551 (3.09%)	4 / 273 (1.47%)	
occurrences causally related to treatment / all	1 / 23	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anuria			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Azotaemia			
subjects affected / exposed	7 / 551 (1.27%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	1 / 10	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic kidney disease			
subjects affected / exposed	5 / 551 (0.91%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	2 / 7	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysuria			
subjects affected / exposed	3 / 551 (0.54%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Focal segmental glomerulosclerosis			

subjects affected / exposed	5 / 551 (0.91%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	6 / 9	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glomerulonephritis			
subjects affected / exposed	0 / 551 (0.00%)	3 / 273 (1.10%)	
occurrences causally related to treatment / all	0 / 0	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glomerulonephritis membranous			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glomerulonephritis rapidly progressive			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
IgA nephropathy			
subjects affected / exposed	3 / 551 (0.54%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	2 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	3 / 551 (0.54%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	3 / 551 (0.54%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Micturition urgency			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			

subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephropathy			
subjects affected / exposed	2 / 551 (0.36%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrotic syndrome			
subjects affected / exposed	9 / 551 (1.63%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	12 / 16	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oliguria			
subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pollakiuria			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cyst			
subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal artery stenosis			
subjects affected / exposed	3 / 551 (0.54%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proteinuria			
subjects affected / exposed	7 / 551 (1.27%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	4 / 7	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cyst haemorrhage			

subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal impairment			
subjects affected / exposed	14 / 551 (2.54%)	7 / 273 (2.56%)	
occurrences causally related to treatment / all	6 / 20	3 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	4 / 551 (0.73%)	4 / 273 (1.47%)	
occurrences causally related to treatment / all	2 / 6	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal disorder			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal infarct			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal mass			
subjects affected / exposed	1 / 551 (0.18%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal tubular acidosis			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal tubular necrosis			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tubulointerstitial nephritis			

subjects affected / exposed	2 / 551 (0.36%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	2 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteric obstruction			
subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteric stenosis			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral stenosis			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vesicoureteric reflux			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract obstruction			
subjects affected / exposed	1 / 551 (0.18%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hyperparathyroidism tertiary			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperparathyroidism			
subjects affected / exposed	3 / 551 (0.54%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperthyroidism			

subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthralgia			
subjects affected / exposed	5 / 551 (0.91%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	4 / 7	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthropathy			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	2 / 551 (0.36%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chondrocalcinosis pyrophosphate			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chondropathy			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fasciitis			

subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gouty arthritis			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Costochondritis			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal stiffness			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myopathy			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	7 / 551 (1.27%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	3 / 8	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteochondrosis			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoporosis			

subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	2 / 551 (0.36%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon disorder			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhabdomyolysis			
subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abscess			
subjects affected / exposed	1 / 551 (0.18%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute hepatitis B			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute sinusitis			
subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial infection			

subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	6 / 551 (1.09%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	4 / 7	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical pneumonia			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous fistula site infection			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis perforated			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	2 / 551 (0.36%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary tract infection			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colonic abscess			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheter site infection			

subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Candida infection			
subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis viral			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	8 / 551 (1.45%)	3 / 273 (1.10%)	
occurrences causally related to treatment / all	5 / 8	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain abscess			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus infection			
subjects affected / exposed	2 / 551 (0.36%)	3 / 273 (1.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus colitis			

subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related sepsis			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disseminated tuberculosis			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	2 / 551 (0.36%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear infection			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	1 / 551 (0.18%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gangrene			
subjects affected / exposed	3 / 551 (0.54%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	2 / 6	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fungal sepsis			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft infection			

subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	5 / 551 (0.91%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis salmonella			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	2 / 551 (0.36%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	27 / 551 (4.90%)	6 / 273 (2.20%)	
occurrences causally related to treatment / all	9 / 32	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis Escherichia coli			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Legionella infection			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	2 / 551 (0.36%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			

subjects affected / exposed	6 / 551 (1.09%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	3 / 7	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster disseminated			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes simplex			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	7 / 551 (1.27%)	3 / 273 (1.10%)	
occurrences causally related to treatment / all	6 / 7	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cyst infection			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes oesophagitis			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis bacterial			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis tuberculous			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised infection			

subjects affected / exposed	3 / 551 (0.54%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	2 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	2 / 551 (0.36%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	3 / 4	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymph gland infection			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver abscess			
subjects affected / exposed	1 / 551 (0.18%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lobar pneumonia			
subjects affected / exposed	3 / 551 (0.54%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ophthalmic herpes zoster			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral herpes			
subjects affected / exposed	3 / 551 (0.54%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic abscess			
subjects affected / exposed	1 / 551 (0.18%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media chronic			

subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrotising fasciitis			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis bacterial			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis externa			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia haemophilus			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	64 / 551 (11.62%)	12 / 273 (4.40%)	
occurrences causally related to treatment / all	35 / 75	6 / 15	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			

subjects affected / exposed	1 / 551 (0.18%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngeal abscess			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis infective			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	3 / 551 (0.54%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative abscess			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	4 / 551 (0.73%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	2 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary mycosis			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary tuberculosis			
subjects affected / exposed	4 / 551 (0.73%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	4 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			

subjects affected / exposed	11 / 551 (2.00%)	6 / 273 (2.20%)	
occurrences causally related to treatment / all	5 / 13	2 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	11 / 551 (2.00%)	4 / 273 (1.47%)	
occurrences causally related to treatment / all	9 / 13	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyuria			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal abscess			
subjects affected / exposed	1 / 551 (0.18%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal abscess			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	7 / 551 (1.27%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	8 / 10	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salmonellosis			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			
subjects affected / exposed	3 / 551 (0.54%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic abscess			

subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal bacteraemia			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tinea pedis			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	2 / 551 (0.36%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	2 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculous pleurisy			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	3 / 551 (0.54%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	1 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth infection			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculosis			
subjects affected / exposed	0 / 551 (0.00%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicella			

subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral diarrhoea			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	6 / 551 (1.09%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	3 / 8	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	4 / 551 (0.73%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	4 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	42 / 551 (7.62%)	14 / 273 (5.13%)	
occurrences causally related to treatment / all	17 / 54	1 / 15	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	6 / 551 (1.09%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	6 / 7	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 0	
Septic shock			
subjects affected / exposed	4 / 551 (0.73%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	1 / 5	1 / 1	
deaths causally related to treatment / all	3 / 3	0 / 0	
Bronchopneumonia			

subjects affected / exposed	8 / 551 (1.45%)	3 / 273 (1.10%)	
occurrences causally related to treatment / all	5 / 8	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cellulitis			
subjects affected / exposed	14 / 551 (2.54%)	4 / 273 (1.47%)	
occurrences causally related to treatment / all	9 / 25	1 / 4	
deaths causally related to treatment / all	1 / 1	0 / 0	
Sepsis			
subjects affected / exposed	17 / 551 (3.09%)	6 / 273 (2.20%)	
occurrences causally related to treatment / all	14 / 28	4 / 8	
deaths causally related to treatment / all	2 / 3	0 / 0	
Metabolism and nutrition disorders			
Calciphylaxis			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrolyte imbalance			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyslipidaemia			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	2 / 551 (0.36%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus			
subjects affected / exposed	5 / 551 (0.91%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	1 / 7	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			

subjects affected / exposed	15 / 551 (2.72%)	3 / 273 (1.10%)	
occurrences causally related to treatment / all	6 / 19	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decreased appetite			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fluid overload			
subjects affected / exposed	3 / 551 (0.54%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	2 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
subjects affected / exposed	0 / 551 (0.00%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	2 / 551 (0.36%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	0 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	1 / 551 (0.18%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypervolaemia			
subjects affected / exposed	2 / 551 (0.36%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypocalcaemia			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			

subjects affected / exposed	1 / 551 (0.18%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemia			
subjects affected / exposed	4 / 551 (0.73%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic acidosis			
subjects affected / exposed	1 / 551 (0.18%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 551 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	SRL Conversion in Stable Renal Transplant Recipients	CNI Continuation in Stable Renal Transplant Recipients	
Total subjects affected by non-serious adverse events subjects affected / exposed	542 / 551 (98.37%)	258 / 273 (94.51%)	
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	120 / 551 (21.78%) 215	67 / 273 (24.54%) 125	
General disorders and administration site conditions Chest pain subjects affected / exposed occurrences (all) Asthenia subjects affected / exposed occurrences (all) Oedema peripheral subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) Oedema subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all)	36 / 551 (6.53%) 43 39 / 551 (7.08%) 55 196 / 551 (35.57%) 551 51 / 551 (9.26%) 80 67 / 551 (12.16%) 119 120 / 551 (21.78%) 173	20 / 273 (7.33%) 34 13 / 273 (4.76%) 16 52 / 273 (19.05%) 111 21 / 273 (7.69%) 35 23 / 273 (8.42%) 35 26 / 273 (9.52%) 40	
Reproductive system and breast disorders Amenorrhoea subjects affected / exposed occurrences (all) Erectile dysfunction subjects affected / exposed occurrences (all) Menorrhagia	15 / 551 (2.72%) 24 25 / 551 (4.54%) 52	1 / 273 (0.37%) 1 8 / 273 (2.93%) 15	

subjects affected / exposed occurrences (all)	11 / 551 (2.00%) 19	2 / 273 (0.73%) 2	
Ovarian cyst subjects affected / exposed occurrences (all)	13 / 551 (2.36%) 33	2 / 273 (0.73%) 4	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	116 / 551 (21.05%) 170	42 / 273 (15.38%) 66	
Dyspnoea subjects affected / exposed occurrences (all)	51 / 551 (9.26%) 79	21 / 273 (7.69%) 36	
Epistaxis subjects affected / exposed occurrences (all)	53 / 551 (9.62%) 82	6 / 273 (2.20%) 7	
Oropharyngeal pain subjects affected / exposed occurrences (all)	42 / 551 (7.62%) 45	11 / 273 (4.03%) 13	
Psychiatric disorders Depression subjects affected / exposed occurrences (all)	34 / 551 (6.17%) 66	14 / 273 (5.13%) 25	
Insomnia subjects affected / exposed occurrences (all)	42 / 551 (7.62%) 81	17 / 273 (6.23%) 27	
Investigations Blood cholesterol increased subjects affected / exposed occurrences (all)	61 / 551 (11.07%) 152	6 / 273 (2.20%) 14	
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	44 / 551 (7.99%) 81	2 / 273 (0.73%) 2	
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	50 / 551 (9.07%) 83	4 / 273 (1.47%) 7	
Blood lactate dehydrogenase			

increased subjects affected / exposed occurrences (all)	72 / 551 (13.07%) 129	6 / 273 (2.20%) 9	
Blood triglycerides increased subjects affected / exposed occurrences (all)	68 / 551 (12.34%) 161	8 / 273 (2.93%) 15	
Low density lipoprotein increased subjects affected / exposed occurrences (all)	37 / 551 (6.72%) 73	8 / 273 (2.93%) 19	
Weight decreased subjects affected / exposed occurrences (all)	32 / 551 (5.81%) 41	11 / 273 (4.03%) 19	
Blood creatinine increased subjects affected / exposed occurrences (all)	109 / 551 (19.78%) 239	48 / 273 (17.58%) 96	
Nervous system disorders Headache subjects affected / exposed occurrences (all)	117 / 551 (21.23%) 253	45 / 273 (16.48%) 70	
Dizziness subjects affected / exposed occurrences (all)	38 / 551 (6.90%) 49	16 / 273 (5.86%) 26	
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	213 / 551 (38.66%) 582	68 / 273 (24.91%) 147	
Leukopenia subjects affected / exposed occurrences (all)	70 / 551 (12.70%) 134	17 / 273 (6.23%) 21	
Thrombocytopenia subjects affected / exposed occurrences (all)	71 / 551 (12.89%) 124	12 / 273 (4.40%) 22	
Gastrointestinal disorders Dyspepsia subjects affected / exposed occurrences (all)	32 / 551 (5.81%) 46	21 / 273 (7.69%) 27	
Diarrhoea			

subjects affected / exposed	234 / 551 (42.47%)	83 / 273 (30.40%)	
occurrences (all)	530	140	
Gastritis			
subjects affected / exposed	20 / 551 (3.63%)	17 / 273 (6.23%)	
occurrences (all)	30	23	
Abdominal pain			
subjects affected / exposed	54 / 551 (9.80%)	28 / 273 (10.26%)	
occurrences (all)	67	37	
Abdominal pain upper			
subjects affected / exposed	27 / 551 (4.90%)	16 / 273 (5.86%)	
occurrences (all)	36	23	
Aphthous stomatitis			
subjects affected / exposed	70 / 551 (12.70%)	6 / 273 (2.20%)	
occurrences (all)	154	12	
Constipation			
subjects affected / exposed	38 / 551 (6.90%)	17 / 273 (6.23%)	
occurrences (all)	52	24	
Mouth ulceration			
subjects affected / exposed	39 / 551 (7.08%)	1 / 273 (0.37%)	
occurrences (all)	66	1	
Nausea			
subjects affected / exposed	72 / 551 (13.07%)	27 / 273 (9.89%)	
occurrences (all)	101	44	
Stomatitis			
subjects affected / exposed	69 / 551 (12.52%)	7 / 273 (2.56%)	
occurrences (all)	87	8	
Vomiting			
subjects affected / exposed	73 / 551 (13.25%)	37 / 273 (13.55%)	
occurrences (all)	106	50	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	29 / 551 (5.26%)	4 / 273 (1.47%)	
occurrences (all)	37	6	
Rash			
subjects affected / exposed	62 / 551 (11.25%)	12 / 273 (4.40%)	
occurrences (all)	103	17	

Skin lesion subjects affected / exposed occurrences (all)	23 / 551 (4.17%) 34	17 / 273 (6.23%) 62	
Acne subjects affected / exposed occurrences (all)	95 / 551 (17.24%) 214	10 / 273 (3.66%) 18	
Renal and urinary disorders Renal impairment subjects affected / exposed occurrences (all)	30 / 551 (5.44%) 60	23 / 273 (8.42%) 54	
Dysuria subjects affected / exposed occurrences (all)	30 / 551 (5.44%) 44	12 / 273 (4.40%) 16	
Haematuria subjects affected / exposed occurrences (all)	35 / 551 (6.35%) 59	11 / 273 (4.03%) 15	
Proteinuria subjects affected / exposed occurrences (all)	159 / 551 (28.86%) 365	43 / 273 (15.75%) 92	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	91 / 551 (16.52%) 180	54 / 273 (19.78%) 113	
Back pain subjects affected / exposed occurrences (all)	51 / 551 (9.26%) 73	37 / 273 (13.55%) 71	
Muscle spasms subjects affected / exposed occurrences (all)	21 / 551 (3.81%) 25	18 / 273 (6.59%) 24	
Myalgia subjects affected / exposed occurrences (all)	38 / 551 (6.90%) 43	12 / 273 (4.40%) 16	
Pain in extremity subjects affected / exposed occurrences (all)	64 / 551 (11.62%) 101	32 / 273 (11.72%) 50	
Infections and infestations			

Sinusitis			
subjects affected / exposed	40 / 551 (7.26%)	21 / 273 (7.69%)	
occurrences (all)	63	30	
Pneumonia			
subjects affected / exposed	34 / 551 (6.17%)	9 / 273 (3.30%)	
occurrences (all)	42	10	
Pharyngitis			
subjects affected / exposed	54 / 551 (9.80%)	24 / 273 (8.79%)	
occurrences (all)	97	43	
Oral herpes			
subjects affected / exposed	39 / 551 (7.08%)	9 / 273 (3.30%)	
occurrences (all)	63	13	
Nasopharyngitis			
subjects affected / exposed	69 / 551 (12.52%)	37 / 273 (13.55%)	
occurrences (all)	114	65	
Influenza			
subjects affected / exposed	70 / 551 (12.70%)	36 / 273 (13.19%)	
occurrences (all)	96	58	
Gastroenteritis			
subjects affected / exposed	42 / 551 (7.62%)	18 / 273 (6.59%)	
occurrences (all)	51	21	
Bronchitis			
subjects affected / exposed	56 / 551 (10.16%)	21 / 273 (7.69%)	
occurrences (all)	71	27	
Upper respiratory tract infection			
subjects affected / exposed	109 / 551 (19.78%)	54 / 273 (19.78%)	
occurrences (all)	214	100	
Urinary tract infection			
subjects affected / exposed	126 / 551 (22.87%)	55 / 273 (20.15%)	
occurrences (all)	281	114	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	37 / 551 (6.72%)	13 / 273 (4.76%)	
occurrences (all)	45	19	
Hypercholesterolaemia			

subjects affected / exposed	196 / 551 (35.57%)	41 / 273 (15.02%)
occurrences (all)	583	94
Gout		
subjects affected / exposed	29 / 551 (5.26%)	16 / 273 (5.86%)
occurrences (all)	49	34
Dyslipidaemia		
subjects affected / exposed	58 / 551 (10.53%)	12 / 273 (4.40%)
occurrences (all)	154	19
Diabetes mellitus		
subjects affected / exposed	30 / 551 (5.44%)	9 / 273 (3.30%)
occurrences (all)	56	17
Hyperglycaemia		
subjects affected / exposed	63 / 551 (11.43%)	19 / 273 (6.96%)
occurrences (all)	128	34
Hypertriglyceridaemia		
subjects affected / exposed	169 / 551 (30.67%)	57 / 273 (20.88%)
occurrences (all)	546	152
Hyperlipidaemia		
subjects affected / exposed	69 / 551 (12.52%)	21 / 273 (7.69%)
occurrences (all)	151	44
Hyperkalaemia		
subjects affected / exposed	16 / 551 (2.90%)	18 / 273 (6.59%)
occurrences (all)	20	29
Hyperuricaemia		
subjects affected / exposed	47 / 551 (8.53%)	46 / 273 (16.85%)
occurrences (all)	90	104
Hypokalaemia		
subjects affected / exposed	57 / 551 (10.34%)	9 / 273 (3.30%)
occurrences (all)	97	12

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 August 2003	Closed further study enrollment in the prospectively defined stratum of subjects with baseline Nankivell GFR of 20.0 to 40.0 mL/min.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
19 August 2003	Following the recommendations of the DSMB, enrollment of high risk subjects (GFR of 20.0 to 40.0 ml/min) was stopped. Beginning 19 Aug 2003, only subjects with baseline Nankivell GFR >40.0 mL/min could be randomly assigned to receive treatment.	-

Notes:

Limitations and caveats

None reported