Clinical trial results:
A 24-month, multi-center, open-label, randomized, controlled trial to investigate efficacy, safety and evolution of cardiovascular parameters in de novo renal transplant recipients after early calcineurin inhibitor to everolimus conversion

Summary

EudraCT number	2009-015918-22
Trial protocol	PT ES AT BE GR LV EE LT DE IT
Global end of trial date	30 October 2014

Results information

Result version number	v1 (current)
This version publication date	23 July 2016
First version publication date	23 July 2016

Trial information

Trial identification

Sponsor protocol code	CRAD001A2429

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01114529
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111,
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111,

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	31 July 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 October 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study was to determine whether an early Calcineurin Inhibitor (CNI) to everolimus conversion at 10-14 weeks post transplantation improves renal allograft function without compromising efficacy compared to standard CNI treatment in de novo renal allograft recipients. In addition, the study was designed to evaluate the impact of a CNI-free regimen on evolution of cardiovascular parameters in de novo renal allograft recipients

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 August 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 55
Country: Number of subjects enrolled	Australia: 50
Country: Number of subjects enrolled	Austria: 25
Country: Number of subjects enrolled	Belgium: 6
Country: Number of subjects enrolled	France: 34
Country: Number of subjects enrolled	Germany: 67
Country: Number of subjects enrolled	Greece: 12
Country: Number of subjects enrolled	India: 71
Country: Number of subjects enrolled	Italy: 17
Country: Number of subjects enrolled	Latvia: 8
Country: Number of subjects enrolled	Mexico: 32
Country: Number of subjects enrolled	Netherlands: 93
Country: Number of subjects enrolled	Norway: 47
Country: Number of subjects enrolled	Portugal: 4
Country: Number of subjects enrolled	Romania: 2
Country: Number of subjects enrolled	Russian Federation: 43
Country: Number of subjects enrolled	Spain: 75

Country: Number of subjects enrolled	Thailand: 48
Country: Number of subjects enrolled	Turkey: 19
Country: Number of subjects enrolled	Estonia: 1
Worldwide total number of subjects	709
EEA total number of subjects	391

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	619
From 65 to 84 years	90
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Full analysis set (24 month analysis)

Pre-assignment

Screening details:

Full analysis set (24 month analysis)

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Everolimus

Arm description:

Conversion from Calcineurin inhibitor (CNI) to everolimus in combination with Myfortic (mycophenolic acid) and steroids

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

Dosage and administration details:

(0.25 mg, 0.5 mg, 0.75 mg or 1.0 mg).

Arm title	Standard CNI (Tac)

Arm description:

Calcineurin inhibitor (CNI), Prograf: CNI continuation with Prograf (tacrolimus) in combination with Myfortic (mycophenolic acid), and steroids

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

Dosage and administration details:

(0.5 mg, 1 mg, or 5 mg). twice a Day each 12-hours

Arm title	Standard CNI (CsA)

Arm description:

Calcineurin inhibitor (CNI), Neoral: CNI continuation with Neoral(cyclosporine) in combination with Myfortic (mycophenolic acid), and steroids

Arm type	Experimental

Investigational medicinal product name	Neoral
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

(10, 25, 50, or 100 mg). twice a Day each 12-hour

Number of subjects in period 1	Everolimus	Standard CNI (Tac)	Standard CNI (CsA)
Started	353	231	125
Completed	229	190	93
Not completed	124	41	32
Abnormal laboratory value(s)	6	-	1
Adverse event, serious fatal	2	1	2
Consent withdrawn by subject	18	8	2
Graft loss	-	2	-
Adverse event, non-fatal	87	18	17
Administrative problems	2	1	2
Subject's no longer required drug	1	1	1
Lost to follow-up	1	4	2
Abnormal test procedure result(s)	3	-	1
Missing	2	-	-
Lack of efficacy	2	1	2
Protocol deviation	-	5	2

Baseline characteristics

Reporting groups	
Reporting group title	Everolimus
Reporting group description:	
Conversion from Calcineurin inhibitor (CNI) to everolimus in combination with Myfortic (mycophenolic acid) and steroids	
Reporting group title	Standard CNI (Tac)
Reporting group description:	
Calcineurin inhibitor (CNI), Prograf: CNI continuation with Prograf (tacrolimus) in combination with Myfortic (mycophenolic acid), and steroids	
Reporting group title	Standard CNI (CsA)
Reporting group description:	
Calcineurin inhibitor (CNI), Neoral: CNI continuation with Neoral(cyclosporine) in combination with Myfortic (mycophenolic acid), and steroids	

Reporting group values	Everolimus	Standard CNI (Tac)	Standard CNI (CsA)
Number of subjects	353	231	125
Age categorical Units: Subjects			
Adults (18-64 years)	313	200	106
From 65-84 years	40	31	19
Age Continuous			
Age			
Units: years			
arithmetic mean	46	47.3	45.4
standard deviation	± 14.4	± 14.5	± 15.6
Gender, Male/Female Units: participants			
Male	242	160	92
Female	111	71	33
Race/Ethnicity, Customized Units: Subjects			
Caucasian	246	173	97
Black	4	5	0
Asian	66	41	20
Native American	1	0	0
Pacific Islander	0	1	1
Other	36	11	7

Reporting group values	Total		
Number of subjects	709		
Age categorical Units: Subjects			
Adults (18-64 years)	619		
From 65-84 years	90		
Age Continuous			
Age			
Units: years			
arithmetic mean			

standard deviation	-		

Gender, Male/Female Units: participants			
Male	494		
Female	215		
Race/Ethnicity, Customized Units: Subjects			
Caucasian	516		
Black	9		
Asian	127		
Native American	1		
Pacific Islander	2		
Other	54		

Subject analysis sets

Subject analysis set title	Difference (Everolimus - Standard CNI)
Subject analysis set type	Full analysis
Subject analysis set description: Least Squares Mean vs Standard Error(Change in eGFR)	
Subject analysis set title	Difference (Everolimus - Standard CNI)
Subject analysis set type	Full analysis
Subject analysis set description: Least Squares Mean vs Standard Error(Change in eGFR)	
Subject analysis set title	Standard CNI (Tac and CsA)
Subject analysis set type	Full analysis
Subject analysis set description: Conversion from Calcineurin inhibitor (CNI) to Standard CNI (Tac or CsA) in combination with Myfortic (mycophenolic acid) and steroidsRisk diff (%)	

Reporting group values	Difference (Everolimus - Standard CNI)	Difference (Everolimus - Standard CNI)	Standard CNI (Tac and CsA)
Number of subjects	321	353	356
Age categorical Units: Subjects			
Adults (18-64 years)	113	207	320
From 65-84 years	9	21	30
Age Continuous			
Age			
Units: years arithmetic mean standard deviation	±	±	±
Gender, Male/Female Units: participants			
Male			
Female			
Race/Ethnicity, Customized Units: Subjects			
Caucasian			

Black Asian Native American Pacific Islander Other			

End points

End points reporting groups

Reporting group title	Everolimus
Reporting group description:	
Conversion from Calcineurin inhibitor (CNI) to everolimus in combination with Myfortic (mycophenolic acid) and steroids	
Reporting group title	Standard CNI (Tac)
Reporting group description:	
Calcineurin inhibitor (CNI), Prograf: CNI continuation with Prograf (tacrolimus) in combination with Myfortic (mycophenolic acid), and steroids	
Reporting group title	Standard CNI (CsA)
Reporting group description:	
Calcineurin inhibitor (CNI), Neoral: CNI continuation with Neoral(cyclosporine) in combination with Myfortic (mycophenolic acid), and steroids	
Subject analysis set title	Difference (Everolimus - Standard CNI)
Subject analysis set type	Full analysis
Subject analysis set description:	
Least Squares Mean vs Standard Error(Change in eGFR)	
Subject analysis set title	Difference (Everolimus - Standard CNI)
Subject analysis set type	Full analysis
Subject analysis set description:	
Least Squares Mean vs Standard Error(Change in eGFR)	
Subject analysis set title	Standard CNI (Tac and CsA)
Subject analysis set type	Full analysis
Subject analysis set description:	
Conversion from Calcineurin inhibitor (CNI) to Standard CNI (Tac or CsA) in combination with Myfortic (mycophenolic acid) and steroidsRisk diff (%)	

Primary: Change in eGFR from randomization to Month 24: Difference (Everolimus-Standard CNI)

End point title	Change in eGFR from randomization to Month 24: Difference (Everolimus-Standard CNI)
End point description:	
Difference (Everolimus-Standard CNI): Assessment of renal function by comparing change from randomization to Month 24 in eGFR (MDRD4) between treatment arms	
End point type	Primary
End point timeframe:	
Change in eGFR (MDRD4) from randomization to Month 24	

End point values	Everolimus	Standard CNI (Tac)	Standard CNI (CsA)	Standard CNI (Tac and CsA)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	321	213	116	321
Units: participants				
least squares mean (standard error)				
Difference (Everolimus - Standard CNI)	1.61 (± 1.48)	1.93 (± 0.25)	1.98 (± 0.1)	1.9 (± 1.1)

Statistical analyses

Statistical analysis title	Difference (Everolimus - Standard CNI)

Statistical analysis description:

Change in eGFR (MDRD4) from randomization to month 12

Comparison groups	Everolimus v Standard CNI (Tac and CsA)
Number of subjects included in analysis	642
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0847 [1]
Method	ANCOVA

Notes:

[1] - Comparison between treatment arms by change from randomization to Month 12 in estimated Glomerular Filtration Rate (eGFR) (MDRD4)

Statistical analysis title	Difference (Everolimus - Standard CNI: TAC)

Statistical analysis description:

Everolimus vs Standard CNI

Comparison groups	Standard CNI (Tac) v Everolimus
Number of subjects included in analysis	534
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1963
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	1.68
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.87
upper limit	4.24
Variability estimate	Standard error of the mean
Dispersion value	1.3

Statistical analysis title	Difference (Everolimus - Standard CNI CsA)

Statistical analysis description:

Difference (Everolimus - Standard CNI CsA)

Comparison groups	Everolimus v Standard CNI (CsA)

Number of subjects included in analysis	437
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1963
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	2.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.05
upper limit	5.22
Variability estimate	Standard error of the mean
Dispersion value	1.59

Secondary: Comparison of Kaplan-Meier incidence rates of composite efficacy endpoint for each arm at Month 24 (Full analysis set)

End point title	Comparison of Kaplan-Meier incidence rates of composite efficacy endpoint for each arm at Month 24 (Full analysis set)

End point description:

To demonstrate non-inferior efficacy (defined by a composite efficacy endpoint of treated Biopsy Proven Acute Rejection (tBPAR) ≥ IB, graft loss or death) at month 24.

End point type	Secondary

End point timeframe:

at 24 months post-transplantation

End point values	Everolimus	Standard CNI (Tac)	Standard CNI (CsA)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	353	231	125	
Units: KM estimate of incidence rate				
number (not applicable)				
Number of composite endpoint *	21	8	8	
KM estimate of incidence rate (%)	6.2	3.5	6.4	
Difference in KM estimate (%)	3.6	4.6	1.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Comparison between treatment arms' change from randomization to Month 24 in left ventricular mass index (LVMi)

End point title	Comparison between treatment arms' change from randomization to Month 24 in left ventricular mass index (LVMi)

End point description:

Comparison between treatment arms for change from randomization to Month 12 in left ventricular mass index (LVMi) (FAS - 12 month analysis)

End point type	Secondary

End point timeframe:

baseline to 24 months

End point values	Difference (Everolimus - Standard CNI)			
Subject group type	Subject analysis set			
Number of subjects analysed	353			
Units: participants				
least squares mean (standard error)				
Everolimus (N=247)	0.05 (± 0)			
Standard CNI (N=284)	-1.14 (± 1.19)			
Tac (N=187)	-1.76 (± 1.81)			
CsA (N=97)	0.06 (± 0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Comparison of incidence rates of efficacy endpoints between treatment arms (Full analysis set - 24 month analysis)

End point title	Comparison of incidence rates of efficacy endpoints between treatment arms (Full analysis set - 24 month analysis)[2]

End point description:

Incidence, time to event and severity of treated BPAR ≥ IB; incidence of BPAR that need antibody treatment; incidence of humoral rejection; incidence of treated BPAR ≥ IB

End point type	Secondary

End point timeframe:

at 24 months post-transplantation

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: See primary end point

End point values	Everolimus	Standard CNI (Tac and CsA)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	353	356		
Units: participants				
number (not applicable)				
Composite failure: tBPAR>=IB, graft loss, death	27	3.2		
Composite tBPAR>=IB, graft loss, death, loss f/u	35	1.8		
Composite of graft loss or Death	10	0		

tBPAR>=IB	18	2.9		
Graft loss	4	0		
Death	8	-0.3		
Suspected Acute rejection	61	4.4		
Subclinical Acute rejection	0	0		
Acute rejection (AR)	52	6.6		
Treated Acute rejection (tAR)	40	4.9		
biopsy proven acute rejection (BPAR)	37	4.6		
treated biopsy proven acute rejection (tBPAR)	32	3.4		
tBPAR=IA	16	1.4		
tBPAR=IB	14	1.7		
tBPAR=IIA	3	0.6		
tBPAR=IIB	2	0.6		
tBPAR=III	0	0		
Antibody tBPAR	0	0		
Antibody mediated rejection (AMR)	16	2.6		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All adverse events reported in this record are from date of First Patient First Treatment until Last Patient Last Visit.

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Standard CNI

Reporting group description:

Standard CNI

Reporting group title	Everolimus

Reporting group description:

Everolimus

Serious adverse events	Standard CNI	Everolimus	
Total subjects affected by serious adverse events			
subjects affected / exposed	176 / 359 (49.03%)	188 / 346 (54.34%)	
number of deaths (all causes)	9	8	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma gastric			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Basal cell carcinoma			
subjects affected / exposed	3 / 359 (0.84%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	3 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bowen's disease			

subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain neoplasm malignant			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Bronchial carcinoma			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric cancer			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glioblastoma			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cancer			
subjects affected / exposed	2 / 359 (0.56%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hepatic cancer metastatic			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive ductal breast carcinoma			

subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lentigo maligna			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	2 / 359 (0.56%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to spine			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Papillary thyroid cancer			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (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	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parathyroid tumour benign			
subjects affected / exposed	1 / 359 (0.28%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal neoplasm			

subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cancer			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cell carcinoma			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small cell lung cancer			
subjects affected / exposed	1 / 359 (0.28%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Squamous cell carcinoma			
subjects affected / exposed	3 / 359 (0.84%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	6 / 6	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Arteriovenous fistula			
subjects affected / exposed	2 / 359 (0.56%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	2 / 359 (0.56%)	6 / 346 (1.73%)	
occurrences causally related to treatment / all	0 / 2	4 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma			

subjects affected / exposed	2 / 359 (0.56%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemodynamic instability			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	2 / 359 (0.56%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphocele			
subjects affected / exposed	2 / 359 (0.56%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphoedema			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrosis ischaemic			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic hypotension			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery thrombosis			

subjects affected / exposed	2 / 359 (0.56%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery stenosis			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral vascular disorder			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis			
subjects affected / exposed	1 / 359 (0.28%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vena cava thrombosis			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	2 / 359 (0.56%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis limb			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			
subjects affected / exposed	2 / 359 (0.56%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device leakage			

subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gait disturbance			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised oedema			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired healing			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	0 / 359 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	3 / 359 (0.84%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 3	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			

subjects affected / exposed	9 / 359 (2.51%)	25 / 346 (7.23%)	
occurrences causally related to treatment / all	3 / 10	7 / 28	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	0 / 359 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Surgical failure			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney transplant rejection			
subjects affected / exposed	13 / 359 (3.62%)	19 / 346 (5.49%)	
occurrences causally related to treatment / all	5 / 15	8 / 20	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transplant rejection			
subjects affected / exposed	14 / 359 (3.90%)	23 / 346 (6.65%)	
occurrences causally related to treatment / all	3 / 15	11 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 359 (0.28%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epididymitis			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Ovarian cyst			
subjects affected / exposed	1 / 359 (0.28%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic haematoma			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatitis			
subjects affected / exposed	0 / 359 (0.00%)	4 / 346 (1.16%)	
occurrences causally related to treatment / all	0 / 0	2 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 359 (0.00%)	5 / 346 (1.45%)	
occurrences causally related to treatment / all	0 / 0	2 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung disorder			
subjects affected / exposed	1 / 359 (0.28%)	3 / 346 (0.87%)	
occurrences causally related to treatment / all	0 / 1	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive airways disorder			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 359 (0.28%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pneumonia aspiration			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 359 (0.00%)	3 / 346 (0.87%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary alveolar haemorrhage			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 359 (0.00%)	3 / 346 (0.87%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	3 / 359 (0.84%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			

subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychotic disorder			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Biopsy			
subjects affected / exposed	0 / 359 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatine increased			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatinine abnormal			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
C-reactive protein increased			
subjects affected / exposed	1 / 359 (0.28%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatinine increased			
subjects affected / exposed	11 / 359 (3.06%)	17 / 346 (4.91%)	
occurrences causally related to treatment / all	1 / 13	4 / 18	
deaths causally related to treatment / all	0 / 0	0 / 0	
Creatinine renal clearance decreased			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoglobin decreased			

subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoglobin urine present			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (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	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test abnormal			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Protein urine present			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight decreased			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Abdominal wound dehiscence			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Animal bite			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous fistula thrombosis			

subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carbon monoxide poisoning			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cervical vertebral fracture			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon injury			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (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	5 / 359 (1.39%)	5 / 346 (1.45%)	
occurrences causally related to treatment / all	1 / 7	2 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Face injury			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft dysfunction			
subjects affected / exposed	5 / 359 (1.39%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft loss			
subjects affected / exposed	3 / 359 (0.84%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	1 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			

subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incisional hernia			
subjects affected / exposed	0 / 359 (0.00%)	3 / 346 (0.87%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb traumatic amputation			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haematuria			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound complication			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal graft loss			
subjects affected / exposed	2 / 359 (0.56%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	1 / 359 (0.28%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shunt aneurysm			

subjects affected / exposed	2 / 359 (0.56%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	0 / 359 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shunt thrombosis			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	2 / 359 (0.56%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transplant dysfunction			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transplant failure			
subjects affected / exposed	3 / 359 (0.84%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic arthritis			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteric anastomosis complication			

subjects affected / exposed	1 / 359 (0.28%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular pseudoaneurysm			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound necrosis			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Congenital cystic kidney disease			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	2 / 359 (0.56%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	4 / 359 (1.11%)	3 / 346 (0.87%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

Atrial flutter			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	2 / 359 (0.56%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Cardiac failure			
subjects affected / exposed	3 / 359 (0.84%)	4 / 346 (1.16%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cyanosis			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (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 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	4 / 359 (1.11%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Myocardial ischaemia			

subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Palpitations			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			
subjects affected / exposed	2 / 359 (0.56%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	0 / 359 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dementia Alzheimer's type			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dementia with Lewy bodies			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			

subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	0 / 359 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	0 / 359 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multifocal motor neuropathy			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Agranulocytosis			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	1 / 359 (0.28%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coagulopathy			

subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	1 / 359 (0.28%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypochromic anaemia			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	6 / 359 (1.67%)	4 / 346 (1.16%)	
occurrences causally related to treatment / all	2 / 6	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenopathy			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphocytic infiltration			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	2 / 359 (0.56%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 2	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Normochromic normocytic anaemia			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			

subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombotic microangiopathy			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 359 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	2 / 359 (0.56%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	2 / 359 (0.56%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	0 / 359 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fistula			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	3 / 359 (0.84%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			

subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Crohn's disease			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	13 / 359 (3.62%)	15 / 346 (4.34%)	
occurrences causally related to treatment / all	5 / 13	4 / 15	
deaths causally related to treatment / all	0 / 0	0 / 0	
Food poisoning			
subjects affected / exposed	1 / 359 (0.28%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer haemorrhage			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal obstruction			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal toxicity			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (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	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileal fistula			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal ischaemia			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine perforation			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mouth ulceration			
subjects affected / exposed	0 / 359 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 359 (0.28%)	3 / 346 (0.87%)	
occurrences causally related to treatment / all	1 / 1	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedematous pancreatitis			

subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	1 / 359 (0.28%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	2 / 359 (0.56%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			
subjects affected / exposed	0 / 359 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			

subjects affected / exposed	0 / 359 (0.00%)	3 / 346 (0.87%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis chronic			
subjects affected / exposed	2 / 359 (0.56%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocholecystis			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver disorder			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	0 / 359 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin ulcer			

subjects affected / exposed	1 / 359 (0.28%)	3 / 346 (0.87%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute prerenal failure			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder obstruction			
subjects affected / exposed	1 / 359 (0.28%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus urinary			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis haemorrhagic			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysuria			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	4 / 359 (1.11%)	5 / 346 (1.45%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	3 / 359 (0.84%)	3 / 346 (0.87%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney fibrosis			

subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephritis haemorrhagic			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephropathy toxic			
subjects affected / exposed	2 / 359 (0.56%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive uropathy			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oliguria			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prerenal failure			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proteinuria			
subjects affected / exposed	0 / 359 (0.00%)	8 / 346 (2.31%)	
occurrences causally related to treatment / all	0 / 0	3 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal artery stenosis			
subjects affected / exposed	2 / 359 (0.56%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cyst			

subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cyst haemorrhage			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	1 / 359 (0.28%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Renal failure acute			
subjects affected / exposed	10 / 359 (2.79%)	7 / 346 (2.02%)	
occurrences causally related to treatment / all	4 / 11	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure chronic			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Renal impairment			
subjects affected / exposed	8 / 359 (2.23%)	6 / 346 (1.73%)	
occurrences causally related to treatment / all	2 / 12	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal tubular atrophy			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal tubular necrosis			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tubulointerstitial nephritis			

subjects affected / exposed	0 / 359 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteric obstruction			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (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	2 / 359 (0.56%)	4 / 346 (1.16%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral obstruction			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral stenosis			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary fistula			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
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	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hyperparathyroidism			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (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			

Arthralgia			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (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	1 / 359 (0.28%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	2 / 359 (0.56%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar spinal stenosis			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle haemorrhage			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myopathy			
subjects affected / exposed	0 / 359 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	2 / 359 (0.56%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	1 / 359 (0.28%)	3 / 346 (0.87%)	
occurrences causally related to treatment / all	0 / 1	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			

subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal osteoarthritis			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess limb			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute sinusitis			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis bacterial			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asymptomatic bacteriuria			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
BK virus infection			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial infection			

subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial pyelonephritis			
subjects affected / exposed	1 / 359 (0.28%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial sepsis			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 359 (0.28%)	3 / 346 (0.87%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			
subjects affected / exposed	2 / 359 (0.56%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheter site abscess			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 359 (0.28%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			

subjects affected / exposed	0 / 359 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Corona virus infection			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus colitis			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus infection			
subjects affected / exposed	7 / 359 (1.95%)	4 / 346 (1.16%)	
occurrences causally related to treatment / all	2 / 9	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus viraemia			
subjects affected / exposed	2 / 359 (0.56%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dengue fever			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea infectious			
subjects affected / exposed	1 / 359 (0.28%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis			

subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia urinary tract infection			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis norovirus			
subjects affected / exposed	0 / 359 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	14 / 359 (3.90%)	11 / 346 (3.18%)	
occurrences causally related to treatment / all	1 / 15	3 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal infection			
subjects affected / exposed	1 / 359 (0.28%)	3 / 346 (0.87%)	
occurrences causally related to treatment / all	1 / 1	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gingivitis			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft infection			

subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
H1N1 influenza			
subjects affected / exposed	0 / 359 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes simplex			
subjects affected / exposed	0 / 359 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	1 / 359 (0.28%)	3 / 346 (0.87%)	
occurrences causally related to treatment / all	0 / 1	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected lymphocele			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious pleural effusion			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (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	1 / 359 (0.28%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral discitis			

subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney infection			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver abscess			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lobar pneumonia			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised infection			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 359 (0.28%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mastitis			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metapneumovirus infection			

subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ophthalmic herpes zoster			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	0 / 359 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritoneal tuberculosis			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonsillar abscess			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			
subjects affected / exposed	2 / 359 (0.56%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	9 / 359 (2.51%)	14 / 346 (4.05%)	
occurrences causally related to treatment / all	5 / 10	9 / 22	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia cytomegaloviral			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia klebsiella			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia mycoplasmal			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyomavirus-associated nephropathy			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural infection			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	1 / 359 (0.28%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary tuberculosis			
subjects affected / exposed	1 / 359 (0.28%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary sepsis			

subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	1 / 359 (0.28%)	4 / 346 (1.16%)	
occurrences causally related to treatment / all	1 / 1	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	9 / 359 (2.51%)	13 / 346 (3.76%)	
occurrences causally related to treatment / all	6 / 16	13 / 19	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis chronic			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cyst infection			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhinitis			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhinovirus infection			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salmonellosis			

subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scrub typhus			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 359 (0.28%)	6 / 346 (1.73%)	
occurrences causally related to treatment / all	0 / 1	1 / 6	
deaths causally related to treatment / all	0 / 0	0 / 1	
Septic necrosis			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 359 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Shunt infection			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic candida			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculosis			
subjects affected / exposed	1 / 359 (0.28%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			

subjects affected / exposed	2 / 359 (0.56%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	1 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	27 / 359 (7.52%)	25 / 346 (7.23%)	
occurrences causally related to treatment / all	9 / 35	3 / 36	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection bacterial			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection fungal			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (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	9 / 359 (2.51%)	9 / 346 (2.60%)	
occurrences causally related to treatment / all	1 / 12	2 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vestibular neuronitis			
subjects affected / exposed	1 / 359 (0.28%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Zygomycosis			

subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 359 (0.28%)	3 / 346 (0.87%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus			
subjects affected / exposed	6 / 359 (1.67%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	4 / 6	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 359 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes with hyperosmolarity			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fluid retention			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
subjects affected / exposed	0 / 359 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			

subjects affected / exposed	1 / 359 (0.28%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	1 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperosmolar state			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypocalcaemia			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypophosphataemia			
subjects affected / exposed	0 / 359 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obesity			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 1 diabetes mellitus			
subjects affected / exposed	1 / 359 (0.28%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Standard CNI	Everolimus	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	246 / 359 (68.52%)	254 / 346 (73.41%)	
Investigations			
Blood creatinine increased			
subjects affected / exposed	34 / 359 (9.47%)	18 / 346 (5.20%)	
occurrences (all)	39	19	
Vascular disorders			
Hypertension			
subjects affected / exposed	35 / 359 (9.75%)	35 / 346 (10.12%)	
occurrences (all)	37	37	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	25 / 359 (6.96%)	40 / 346 (11.56%)	
occurrences (all)	28	44	
Leukopenia			
subjects affected / exposed	41 / 359 (11.42%)	46 / 346 (13.29%)	
occurrences (all)	52	51	
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	31 / 359 (8.64%)	60 / 346 (17.34%)	
occurrences (all)	38	77	
Pyrexia			
subjects affected / exposed	25 / 359 (6.96%)	41 / 346 (11.85%)	
occurrences (all)	30	49	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	57 / 359 (15.88%)	70 / 346 (20.23%)	
occurrences (all)	71	79	
Mouth ulceration			
subjects affected / exposed	3 / 359 (0.84%)	24 / 346 (6.94%)	
occurrences (all)	3	31	
Nausea			

subjects affected / exposed	17 / 359 (4.74%)	18 / 346 (5.20%)	
occurrences (all)	20	19	
Vomiting			
subjects affected / exposed	12 / 359 (3.34%)	18 / 346 (5.20%)	
occurrences (all)	13	20	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	19 / 359 (5.29%)	29 / 346 (8.38%)	
occurrences (all)	21	31	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	11 / 359 (3.06%)	19 / 346 (5.49%)	
occurrences (all)	12	23	
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	13 / 359 (3.62%)	46 / 346 (13.29%)	
occurrences (all)	15	51	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	19 / 359 (5.29%)	18 / 346 (5.20%)	
occurrences (all)	22	26	
Nasopharyngitis			
subjects affected / exposed	33 / 359 (9.19%)	31 / 346 (8.96%)	
occurrences (all)	45	40	
Urinary tract infection			
subjects affected / exposed	51 / 359 (14.21%)	62 / 346 (17.92%)	
occurrences (all)	87	114	
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	18 / 359 (5.01%)	14 / 346 (4.05%)	
occurrences (all)	18	16	
Dyslipidaemia			
subjects affected / exposed	15 / 359 (4.18%)	26 / 346 (7.51%)	
occurrences (all)	17	27	
Hypercholesterolaemia			

subjects affected / exposed	22 / 359 (6.13%)	40 / 346 (11.56%)	
occurrences (all)	22	40	
Hyperlipidaemia			
subjects affected / exposed	20 / 359 (5.57%)	17 / 346 (4.91%)	
occurrences (all)	21	17	
Hypokalaemia			
subjects affected / exposed	14 / 359 (3.90%)	23 / 346 (6.65%)	
occurrences (all)	15	27	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 November 2010	Investigational drug and concomitant medication definitions were further clarified

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported