Clinical trial results:
A Phase III, Randomized, Open-Label, Comparative, Multi-Center Study to Assess the Safety and Efficacy of Prograf® (tacrolimus)/MMF, Modified Release (MR) Tacrolimus/MMF and Neoral® (cyclosporine) /MMF in De Novo Kidney Transplant Recipients

Summary

EudraCT number	2015-003288-12
Trial protocol	Outside EU/EEA
Global end of trial date	12 March 2009

Results information

Result version number	v1 (current)
This version publication date	11 May 2016
First version publication date	11 May 2016

Trial information

Trial identification

Sponsor protocol code	02-0-158

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00064701
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Astellas Pharma Global Development, Inc.
Sponsor organisation address	Three Parkway North, Deerfield, Illinois, United States, 60015
Public contact	Clinical Trial Disclosure, Astellas Pharma Global Development, Inc., Astellas.resultsdisclosure@astellas.com
Scientific contact	Clinical Trial Disclosure, Astellas Pharma Global Development, Inc., Astellas.resultsdisclosure@astellas.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 March 2009
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 March 2009
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to compare the safety and efficacy of Prograf/MMF and Neoral/MMF in de novo kidney transplant recipients, and to compare the safety and efficacy of MR4/MMF and Neoral/MMF in de novo kidney transplant recipients.

Protection of trial subjects:

This clinical study was written, conducted and reported in accordance with the protocol, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), Good Clinical Practice (GCP) Guidelines, and applicable local regulations, including the European Directive 2001/20/EC, on the protection of human rights, and with the ethical principles that have their origin in the Declaration of Helsinki. Astellas ensures that the use and disclosure of protected health information (PHI) obtained during a research study complies with the federal, national and/or regional legislation related to the privacy and protection of personal information.

Background therapy:

All participants were to have received mycophenolate mofetil (MMF) and corticosteroids concomitantly with the randomized study drug. Additionally, all participants were to have received induction therapy (basiliximab). Antibody induction with basiliximab 20 mg was administered intravenously on day 0 (first dose could have been administered before skin closure), a second dose was to have been administered between days 3 to 5. Corticosteroid administration was to be initiated on day 0 (500-1000 mg methylprednisolone intravenous bolus or equivalent dose) with oral administration of 200 mg methylprednisolone (or equivalent) on day 1 and subsequent tapering to achieve a targeted mean prednisone equivalent after the first 3 months of 5 to 10 mg/day.

Evidence for comparator: -

Actual start date of recruitment	29 June 2003
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	Brazil: 92
Country: Number of subjects enrolled	Canada: 28
Country: Number of subjects enrolled	United States: 548
Worldwide total number of subjects	668
EEA total number of subjects	0

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)	3
Adults (18-64 years)	594
From 65 to 84 years	71
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was a 3 arm randomized, open-label, comparative, multi-center study in de novo kidney transplant recipients at 60 centers in the U.S., Canada and Brazil. De novo kidney transplant recipients 12 years of age and older were randomized in a 1:1:1 ratio to 1 of 3 treatment arms.

Pre-assignment

Screening details:

The study consisted of a 1-year post-transplant efficacy and safety study with a clinical continuation phase of a minimum of 2 years or until commercial availability of tacrolimus modified release, unless the Data Safety Monitoring Board or sponsor specified otherwise. The sponsor discontinued the study in March 2009.

Period 1

Period 1 title	One year post-transplant
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

This was an open label study.

Arms

Are arms mutually exclusive?	Yes
Arm title	Tacrolimus

Arm description:

Participants received a first dose of tacrolimus between 0.075 and 0.10 mg/kg twice daily, orally prior to or within 48 hours of the completion of the transplant procedure, and subsequently as twice daily oral doses adjusted based on clinical evidence of efficacy, blood concentrations of tacrolimus and adverse events. Participants also received 1.0 g mycophenolate mofetil orally twice daily throughout the study.

Arm type	Experimental
Investigational medicinal product name	Tacrolimus
Investigational medicinal product code	FK506
Other name	Prograf
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received a first dose of tacrolimus between 0.075 and 0.10 mg/kg twice daily, orally prior to or within 48 hours of the completion of the transplant procedure, and subsequently as twice daily oral doses adjusted based on clinical evidence of efficacy, blood concentrations of tacrolimus and adverse events within a target whole blood tacrolimus trough level range of 7 to 16 ng/mL for the first 90 days post-transplant and 5 to 15 ng/mL thereafter. Participants unable to take the first dose of study drug orally or via a nasogastric tube within 48 hours following completion of the transplant procedure were discontinued from the study.

Investigational medicinal product name	Mycophenolate Mofetil
Investigational medicinal product code	
Other name	CellCept, MMF
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

The first dose of Mycophenolate Mofetil (MMF) was to be administered orally or intravenously prior to, or within 48 hours of, completion of the transplant procedure. Subsequent MMF was administered in 2 equal oral doses 12 hours apart (1 g); MMF up to 1.5 g twice daily was permitted in African American/black participants. Dose-equivalent 3 or 4 times daily was permitted at the investigator's discretion if clinically indicated. Dose changes for adverse events were permitted at the investigator's discretion if clinically indicated.

Arm title	Tacrolimus Modified Release (MR)

Arm description:

Participants received a first dose of tacrolimus modified release between 0.15 and 0.20 mg/kg/day, given as a single oral dose in the morning, prior to or within 48 hours following the completion of the transplant procedure, and subsequently as once daily oral doses adjusted based on clinical evidence of efficacy, blood concentrations of tacrolimus and adverse events. Participants also received 1.0 g mycophenolate mofetil orally twice daily throughout the study.

Arm type	Active comparator
Investigational medicinal product name	Tacrolimus Modified Release (MR)
Investigational medicinal product code	FK506
Other name	Advagraf, FKMR, MR4, Astagraf XL
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received a first dose of tacrolimus modified release (MR4) between 0.15 and 0.20 mg/kg/day, given as a single oral dose in the morning, prior to or within 48 hours following the completion of the transplant procedure, and subsequently as once daily oral doses adjusted based on clinical evidence of efficacy, blood concentrations of tacrolimus and adverse events within a target whole blood tacrolimus trough level range of 7 to 16 ng/mL for the first 90 days post-transplant and 5 to 15 ng/mL thereafter. Participants unable to take the first dose of study drug orally or via a nasogastric tube within 48 hours following completion of the transplant procedure were discontinued from the study.

Investigational medicinal product name	Mycophenolate Mofetil
Investigational medicinal product code	
Other name	CellCept, MMF
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

The first dose of Mycophenolate Mofetil (MMF) was to be administered orally or intravenously prior to, or within 48 hours of, completion of the transplant procedure. Subsequent MMF was administered in 2 equal oral doses 12 hours apart (1 g); MMF up to 1.5 g twice daily was permitted in African American/black participants. Dose-equivalent 3 or 4 times daily was permitted at the investigator's discretion if clinically indicated. Dose changes for adverse events were permitted at the investigator's discretion if clinically indicated.

Arm title	Cyclosporine

Arm description:

Participants received a first dose of cyclosporine between 4 to 5 mg/kg orally prior to or within 48 hours following the completion of the transplant procedure and subsequently as twice daily oral doses adjusted based on clinical evidence of efficacy, blood concentrations of tacrolimus and adverse events. Participants also received 1.0 g mycophenolate mofetil orally twice daily throughout the study.

Arm type	Active comparator
Investigational medicinal product name	Cyclosporine
Investigational medicinal product code	
Other name	Cyclosporine, Neoral, CsA
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Participants received a first dose of cyclosporine between 4 to 5 mg/kg orally prior to or within 48 hours following the completion of the transplant procedure and subsequently as twice daily oral doses adjusted based on clinical evidence of efficacy, blood concentrations of tacrolimus and adverse events within a target whole blood trough level range of 125 to 400 ng/mL for the first 90 days post-transplant and 100 to 300 ng/mL thereafter. Participants unable to take the first dose of study drug orally or via a nasogastric tube within 48 hours following completion of the transplant procedure were discontinued from the study.

Investigational medicinal product name	Mycophenolate Mofetil
Investigational medicinal product code	
Other name	CellCept, MMF
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

The first dose of Mycophenolate Mofetil (MMF) was to be administered orally or intravenously prior to, or within 48 hours of, completion of the transplant procedure. Subsequent MMF was administered in 2 equal oral doses 12 hours apart (1 g); MMF up to 1.5 g twice daily was permitted in African American/black participants. Dose-equivalent 3 or 4 times daily was permitted at the investigator's discretion if clinically indicated. Dose changes for adverse events were permitted at the investigator's discretion if clinically indicated.

Number of subjects in period 1	Tacrolimus	Tacrolimus Modified Release (MR)	Cyclosporine
Started	219	226	223
Received Study Drug	212	214	212
Completed	212	214	212
Not completed	7	12	11
Did not receive study drug	7	12	11

Period 2

Period 2 title	Full Analysis Set (FAS) for baseline
Is this the baseline period?	Yes[1]
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

This was an open label study. The FAS was defined as all randomized participants who received at least one dose of study drug, was part of the one year post-transplant period and was only added here for baseline characteristics reporting purposes.

Arms

Are arms mutually exclusive?	Yes
Arm title	Tacrolimus

Arm description:

Participants received a first dose of tacrolimus between 0.075 and 0.10 mg/kg twice daily, orally prior to or within 48 hours of the completion of the transplant procedure, and subsequently as twice daily oral doses adjusted based on clinical evidence of efficacy, blood concentrations of tacrolimus and adverse events. Participants also received 1.0 g mycophenolate mofetil orally twice daily throughout the study.

Arm type	Experimental
Investigational medicinal product name	Tacrolimus
Investigational medicinal product code	FK506
Other name	Prograf
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received a first dose of tacrolimus between 0.075 and 0.10 mg/kg twice daily, orally prior to or within 48 hours of the completion of the transplant procedure, and subsequently as twice daily oral doses adjusted based on clinical evidence of efficacy, blood concentrations of tacrolimus and adverse events within a target whole blood tacrolimus trough level range of 7 to 16 ng/mL for the first 90 days post-transplant and 5 to 15 ng/mL thereafter. Participants unable to take the first dose of study drug orally or via a nasogastric tube within 48 hours following completion of the transplant procedure were discontinued from the study.

Investigational medicinal product name	Mycophenolate Mofetil
Investigational medicinal product code	
Other name	CellCept, MMF
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

The first dose of Mycophenolate Mofetil (MMF) was to be administered orally or intravenously prior to, or within 48 hours of, completion of the transplant procedure. Subsequent MMF was administered in 2 equal oral doses 12 hours apart (1 g); MMF up to 1.5 g twice daily was permitted in African American/black participants. Dose-equivalent 3 or 4 times daily was permitted at the investigator's discretion if clinically indicated. Dose changes for adverse events were permitted at the investigator's discretion if clinically indicated.

Arm title	Tacrolimus Modified Release (MR)

Arm description:

Participants received a first dose of tacrolimus modified release between 0.15 and 0.20 mg/kg/day, given as a single oral dose in the morning, prior to or within 48 hours following the completion of the transplant procedure, and subsequently as once daily oral doses adjusted based on clinical evidence of efficacy, blood concentrations of tacrolimus and adverse events. Participants also received 1.0 g mycophenolate mofetil orally twice daily throughout the study.

Arm type	Active comparator
Investigational medicinal product name	Tacrolimus Modified Release (MR)
Investigational medicinal product code	FK506
Other name	Advagraf, FKMR, MR4, Astagraf XL
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received a first dose of tacrolimus modified release (MR4) between 0.15 and 0.20 mg/kg/day, given as a single oral dose in the morning, prior to or within 48 hours following the completion of the transplant procedure, and subsequently as once daily oral doses adjusted based on clinical evidence of efficacy, blood concentrations of tacrolimus and adverse events within a target whole blood tacrolimus trough level range of 7 to 16 ng/mL for the first 90 days post-transplant and 5 to 15 ng/mL thereafter. Participants unable to take the first dose of study drug orally or via a nasogastric tube within 48 hours following completion of the transplant procedure were discontinued from the study.

Investigational medicinal product name	Mycophenolate Mofetil
Investigational medicinal product code	
Other name	CellCept, MMF
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

The first dose of Mycophenolate Mofetil (MMF) was to be administered orally or intravenously prior to, or within 48 hours of, completion of the transplant procedure. Subsequent MMF was administered in 2 equal oral doses 12 hours apart (1 g); MMF up to 1.5 g twice daily was permitted in African American/black participants. Dose-equivalent 3 or 4 times daily was permitted at the investigator's discretion if clinically indicated. Dose changes for adverse events were permitted at the investigator's discretion if clinically indicated.

Arm title	Cyclosporine

Arm description:

Participants received a first dose of cyclosporine between 4 to 5 mg/kg orally prior to or within 48 hours following the completion of the transplant procedure and subsequently as twice daily oral doses adjusted based on clinical evidence of efficacy, blood concentrations of tacrolimus and adverse events. Participants also received 1.0 g mycophenolate mofetil orally twice daily throughout the study.

Arm type	Active comparator
Investigational medicinal product name	Cyclosporine
Investigational medicinal product code	
Other name	Cyclosporine, Neoral, CsA
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Participants received a first dose of cyclosporine between 4 to 5 mg/kg orally prior to or within 48 hours following the completion of the transplant procedure and subsequently as twice daily oral doses adjusted based on clinical evidence of efficacy, blood concentrations of tacrolimus and adverse events within a target whole blood trough level range of 125 to 400 ng/mL for the first 90 days post-transplant and 100 to 300 ng/mL thereafter. Participants unable to take the first dose of study drug orally or via a nasogastric tube within 48 hours following completion of the transplant procedure were discontinued from the study.

Investigational medicinal product name	Mycophenolate Mofetil
Investigational medicinal product code	
Other name	CellCept, MMF
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

The first dose of Mycophenolate Mofetil (MMF) was to be administered orally or intravenously prior to, or within 48 hours of, completion of the transplant procedure. Subsequent MMF was administered in 2 equal oral doses 12 hours apart (1 g); MMF up to 1.5 g twice daily was permitted in African American/black participants. Dose-equivalent 3 or 4 times daily was permitted at the investigator's discretion if clinically indicated. Dose changes for adverse events were permitted at the investigator's discretion if clinically indicated.

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: The baseline period includes participants included in the full analysis set (only participants that were randomized and received at least one dose of study drug).

Number of subjects in period 2[2]	Tacrolimus	Tacrolimus Modified Release (MR)	Cyclosporine
Started	212	214	212
Completed	179	183	151
Not completed	33	31	61
Graft failure	3	2	1
Converted to rapamycin	1	-	-
Adverse event, non-fatal	23	19	37
Rejection	-	1	16
Incorrect study drug dispensed	-	1	-
Poor absorption	-	1	-
Non-compliance	4	2	5
Lost to follow-up	1	-	-
Acute tubular necrosis	1	-	-
Crossover secondary to possible toxicity	-	1	-
Pancreas transplant	-	-	1
Withdrawal by subject	-	4	1

Notes:

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

Justification: The worldwide number enrolled in the trial includes all randomized participants. The baseline period includes participants included in the full analysis set (only participants that were randomized and received at least one dose of study drug).

Period 3

Period 3 title	Clinical Continuation Phase
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

This was an open label study.

Arms

Are arms mutually exclusive?	Yes
Arm title	Tacrolimus

Arm description:

Participants received a first dose of tacrolimus between 0.075 and 0.10 mg/kg twice daily, orally prior to or within 48 hours of the completion of the transplant procedure, and subsequently as twice daily oral doses adjusted based on clinical evidence of efficacy, blood concentrations of tacrolimus and adverse events. Participants also received 1.0 g mycophenolate mofetil orally twice daily throughout the study.

Arm type	Experimental
Investigational medicinal product name	Tacrolimus
Investigational medicinal product code	FK506
Other name	Prograf
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received a first dose of tacrolimus between 0.075 and 0.10 mg/kg twice daily, orally prior to or within 48 hours of the completion of the transplant procedure, and subsequently as twice daily oral doses adjusted based on clinical evidence of efficacy, blood concentrations of tacrolimus and adverse events within a target whole blood tacrolimus trough level range of 7 to 16 ng/mL for the first 90 days post-transplant and 5 to 15 ng/mL thereafter. Participants unable to take the first dose of study drug orally or via a nasogastric tube within 48 hours following completion of the transplant procedure were discontinued from the study.

Investigational medicinal product name	Mycophenolate Mofetil
Investigational medicinal product code	
Other name	CellCept, MMF
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

The first dose of Mycophenolate Mofetil (MMF) was to be administered orally or intravenously prior to, or within 48 hours of, completion of the transplant procedure. Subsequent MMF was administered in 2 equal oral doses 12 hours apart (1 g); MMF up to 1.5 g twice daily was permitted in African American/black participants. Dose-equivalent 3 or 4 times daily was permitted at the investigator's discretion if clinically indicated. Dose changes for adverse events were permitted at the investigator's discretion if clinically indicated.

Arm title	Tacrolimus Modified Release (MR)

Arm description:

Participants received a first dose of tacrolimus modified release between 0.15 and 0.20 mg/kg/day, given as a single oral dose in the morning, prior to or within 48 hours following the completion of the transplant procedure, and subsequently as once daily oral doses adjusted based on clinical evidence of efficacy, blood concentrations of tacrolimus and adverse events. Participants also received 1.0 g mycophenolate mofetil orally twice daily throughout the study.

Arm type	Active comparator
Investigational medicinal product name	Tacrolimus Modified Release (MR)
Investigational medicinal product code	FK506
Other name	Advagraf, FKMR, MR4, Astagraf XL
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received a first dose of tacrolimus modified release (MR4) between 0.15 and 0.20 mg/kg/day, given as a single oral dose in the morning, prior to or within 48 hours following the completion of the transplant procedure, and subsequently as once daily oral doses adjusted based on clinical evidence of efficacy, blood concentrations of tacrolimus and adverse events within a target whole blood tacrolimus trough level range of 7 to 16 ng/mL for the first 90 days post-transplant and 5 to 15 ng/mL thereafter. Participants unable to take the first dose of study drug orally or via a nasogastric tube within 48 hours following completion of the transplant procedure were discontinued from the study.

Investigational medicinal product name	Mycophenolate Mofetil
Investigational medicinal product code	
Other name	CellCept, MMF
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

The first dose of Mycophenolate Mofetil (MMF) was to be administered orally or intravenously prior to, or within 48 hours of, completion of the transplant procedure. Subsequent MMF was administered in 2 equal oral doses 12 hours apart (1 g); MMF up to 1.5 g twice daily was permitted in African American/black participants. Dose-equivalent 3 or 4 times daily was permitted at the investigator's discretion if clinically indicated. Dose changes for adverse events were permitted at the investigator's discretion if clinically indicated.

Arm title	Cyclosporine

Arm description:

Participants received a first dose of cyclosporine between 4 to 5 mg/kg orally prior to or within 48 hours following the completion of the transplant procedure and subsequently as twice daily oral doses adjusted based on clinical evidence of efficacy, blood concentrations of tacrolimus and adverse events. Participants also received 1.0 g mycophenolate mofetil orally twice daily throughout the study.

Arm type	Active comparator
Investigational medicinal product name	Cyclosporine
Investigational medicinal product code	
Other name	Cyclosporine, Neoral, CsA
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Participants received a first dose of cyclosporine between 4 to 5 mg/kg orally prior to or within 48 hours following the completion of the transplant procedure and subsequently as twice daily oral doses adjusted based on clinical evidence of efficacy, blood concentrations of tacrolimus and adverse events within a target whole blood trough level range of 125 to 400 ng/mL for the first 90 days post-transplant and 100 to 300 ng/mL thereafter. Participants unable to take the first dose of study drug orally or via a nasogastric tube within 48 hours following completion of the transplant procedure were discontinued from the study.

Investigational medicinal product name	Mycophenolate Mofetil
Investigational medicinal product code	
Other name	CellCept, MMF
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

The first dose of Mycophenolate Mofetil (MMF) was to be administered orally or intravenously prior to, or within 48 hours of, completion of the transplant procedure. Subsequent MMF was administered in 2 equal oral doses 12 hours apart (1 g); MMF up to 1.5 g twice daily was permitted in African American/black participants. Dose-equivalent 3 or 4 times daily was permitted at the investigator's discretion if clinically indicated. Dose changes for adverse events were permitted at the investigator's discretion if clinically indicated.

Number of subjects in period 3[3]	Tacrolimus	Tacrolimus Modified Release (MR)	Cyclosporine
Started	179	182	151
Completed	9	4	11
Not completed	170	178	140
Physician decision	1	3	-
Discharged to nursing home	-	1	-
Rejection	1	2	2
Unable to return to site for study visit	1	-	1
Incorrect study drug dispensed	-	1	-
Sponsor discontinued study	113	129	79
Patient opted out	-	-	1
Immunosuppressive treatment crossover	-	3	6
Ran out of study drug due to Hurricane	-	1	-
Withdrawal by subject	22	3	22
Graft failure	5	5	2
Adverse event, non-fatal	12	21	14
Non-compliance	8	6	7
Lost to follow-up	6	3	6
Pancreas transplant	1	-	-

Notes:

[3] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: One participant from Arm 2 (Tacrolimus Modified Release) did not enter the Clinical Continuation phase.

Baseline characteristics

Reporting groups	
Reporting group title	Tacrolimus
Reporting group description:	
Participants received a first dose of tacrolimus between 0.075 and 0.10 mg/kg twice daily, orally prior to or within 48 hours of the completion of the transplant procedure, and subsequently as twice daily oral doses adjusted based on clinical evidence of efficacy, blood concentrations of tacrolimus and adverse events. Participants also received 1.0 g mycophenolate mofetil orally twice daily throughout the study.	
Reporting group title	Tacrolimus Modified Release (MR)
Reporting group description:	
Participants received a first dose of tacrolimus modified release between 0.15 and 0.20 mg/kg/day, given as a single oral dose in the morning, prior to or within 48 hours following the completion of the transplant procedure, and subsequently as once daily oral doses adjusted based on clinical evidence of efficacy, blood concentrations of tacrolimus and adverse events. Participants also received 1.0 g mycophenolate mofetil orally twice daily throughout the study.	
Reporting group title	Cyclosporine
Reporting group description:	
Participants received a first dose of cyclosporine between 4 to 5 mg/kg orally prior to or within 48 hours following the completion of the transplant procedure and subsequently as twice daily oral doses adjusted based on clinical evidence of efficacy, blood concentrations of tacrolimus and adverse events. Participants also received 1.0 g mycophenolate mofetil orally twice daily throughout the study.	

Reporting group values	Tacrolimus	Tacrolimus Modified Release (MR)	Cyclosporine
Number of subjects	212	214	212
Age categorical			
Units: Subjects			
Age continuous			
Baseline characteristics provided for the full analysis set (FAS), defined as all randomized participants who received at least one dose of study drug.			
Units: years			
arithmetic mean	48.62	47.84	47.63
standard deviation	± 12.855	± 12.995	± 12.953
Gender categorical			
Gender categorical description			
Units: Subjects			
Female	76	76	82
Male	136	138	130
Race/Ethnicity, Customized			
Units: Subjects			
White	152	160	163
Black	51	41	36
Asian	5	5	8
Other	4	8	5
Primary Diagnosis			
Units: Subjects			
Nephrosclerosis/ Hypertensive Nephropathy	54	56	43
Diabetic Nephropathy	46	38	46

Glomerulonephritis	44	43	43
Polycycstic Kidney Disease	20	26	20
Tubular/ Interstitial Disease	9	5	16
Systemic Vasculitis	9	10	7
Congenital/ Hereditary Nephropathy	7	7	13
Reflux	1	0	1
Unknown	17	24	17
Other	5	5	6
Previous Transplant Units: Subjects			
No	205	206	203
Yes	7	8	9

Reporting group values	Total		
Number of subjects	638		
Age categorical Units: Subjects			

Age continuous			
Baseline characteristics provided for the full analysis set (FAS), defined as all randomized participants who received at least one dose of study drug.			
Units: years arithmetic mean standard deviation	- -		
Gender categorical			
Gender categorical description			
Units: Subjects			
Female	234		
Male	404		
Race/Ethnicity, Customized Units: Subjects			
White	475		
Black	128		
Asian	18		
Other	17		
Primary Diagnosis Units: Subjects			
Nephrosclerosis/ Hypertensive Nephropathy	153		
Diabetic Nephropathy	130		
Glomerulonephritis	130		
Polycycstic Kidney Disease	66		
Tubular/ Interstitial Disease	30		
Systemic Vasculitis	26		
Congenital/ Hereditary Nephropathy	27		
Reflux	2		
Unknown	58		
Other	16		
Previous Transplant Units: Subjects			

No	614		
Yes	24		

End points

End points reporting groups

Reporting group title	Tacrolimus

Reporting group description:

Participants received a first dose of tacrolimus between 0.075 and 0.10 mg/kg twice daily, orally prior to or within 48 hours of the completion of the transplant procedure, and subsequently as twice daily oral doses adjusted based on clinical evidence of efficacy, blood concentrations of tacrolimus and adverse events. Participants also received 1.0 g mycophenolate mofetil orally twice daily throughout the study.

Reporting group title	Tacrolimus Modified Release (MR)

Reporting group description:

Participants received a first dose of tacrolimus modified release between 0.15 and 0.20 mg/kg/day, given as a single oral dose in the morning, prior to or within 48 hours following the completion of the transplant procedure, and subsequently as once daily oral doses adjusted based on clinical evidence of efficacy, blood concentrations of tacrolimus and adverse events. Participants also received 1.0 g mycophenolate mofetil orally twice daily throughout the study.

Reporting group title	Cyclosporine

Reporting group description:

Participants received a first dose of cyclosporine between 4 to 5 mg/kg orally prior to or within 48 hours following the completion of the transplant procedure and subsequently as twice daily oral doses adjusted based on clinical evidence of efficacy, blood concentrations of tacrolimus and adverse events. Participants also received 1.0 g mycophenolate mofetil orally twice daily throughout the study.

Reporting group title	Tacrolimus

Reporting group description:

Participants received a first dose of tacrolimus between 0.075 and 0.10 mg/kg twice daily, orally prior to or within 48 hours of the completion of the transplant procedure, and subsequently as twice daily oral doses adjusted based on clinical evidence of efficacy, blood concentrations of tacrolimus and adverse events. Participants also received 1.0 g mycophenolate mofetil orally twice daily throughout the study.

Reporting group title	Tacrolimus Modified Release (MR)

Reporting group description:

Participants received a first dose of tacrolimus modified release between 0.15 and 0.20 mg/kg/day, given as a single oral dose in the morning, prior to or within 48 hours following the completion of the transplant procedure, and subsequently as once daily oral doses adjusted based on clinical evidence of efficacy, blood concentrations of tacrolimus and adverse events. Participants also received 1.0 g mycophenolate mofetil orally twice daily throughout the study.

Reporting group title	Cyclosporine

Reporting group description:

Participants received a first dose of cyclosporine between 4 to 5 mg/kg orally prior to or within 48 hours following the completion of the transplant procedure and subsequently as twice daily oral doses adjusted based on clinical evidence of efficacy, blood concentrations of tacrolimus and adverse events. Participants also received 1.0 g mycophenolate mofetil orally twice daily throughout the study.

Reporting group title	Tacrolimus

Reporting group description:

Participants received a first dose of tacrolimus between 0.075 and 0.10 mg/kg twice daily, orally prior to or within 48 hours of the completion of the transplant procedure, and subsequently as twice daily oral doses adjusted based on clinical evidence of efficacy, blood concentrations of tacrolimus and adverse events. Participants also received 1.0 g mycophenolate mofetil orally twice daily throughout the study.

Reporting group title	Tacrolimus Modified Release (MR)

Reporting group description:

Participants received a first dose of tacrolimus modified release between 0.15 and 0.20 mg/kg/day, given as a single oral dose in the morning, prior to or within 48 hours following the completion of the transplant procedure, and subsequently as once daily oral doses adjusted based on clinical evidence of efficacy, blood concentrations of tacrolimus and adverse events. Participants also received 1.0 g mycophenolate mofetil orally twice daily throughout the study.

Reporting group title	Cyclosporine

Reporting group description:

Participants received a first dose of cyclosporine between 4 to 5 mg/kg orally prior to or within 48 hours following the completion of the transplant procedure and subsequently as twice daily oral doses adjusted based on clinical evidence of efficacy, blood concentrations of tacrolimus and adverse events.

Participants also received 1.0 g mycophenolate mofetil orally twice daily throughout the study.

Primary: Percentage of participants with Efficacy Failure

End point title	Percentage of participants with Efficacy Failure

End point description:

Efficacy failure is defined as any participant who died, experienced a graft failure (permanent return to dialysis [> 30 days] or retransplant), had a biopsy-confirmed (Banff Grade ≥ I) acute rejection (BCAR), or was lost to follow-up. Biopsies were graded according to the 1997 Banff criteria: Borderline: No intimal arteritis present but foci of mild tubulitis; Grade I: Significant interstitial infiltration and foci of moderate to severe tubulitis; Grade II: Mild to severe intimal arteritis Grade III: Transmural arteritis and/or arterial fibrinoid change and necrosis of medial smooth muscle cells with accompanying lymphocytic infiltrate in vessel. The number of participants analyzed represents the full analysis set (FAS), defined as all randomized patients who received at least one dose of study drug.

End point type	Primary

End point timeframe:

One year

End point values	Tacrolimus	Tacrolimus Modified Release (MR)	Cyclosporine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	212	214	212	
Units: percentage of participants				
number (not applicable)	15.1	14	17	

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The non-inferiority margin for the difference between treatment groups (Tacrolimus minus Cyclosporine) was pre-specified as 10%. If the lower limit of the confidence interval was greater than -10%, then Tacrolimus was considered non-inferior to Cyclosporine.

Comparison groups	Cyclosporine v Tacrolimus
Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Incidence Difference
Point estimate	-1.9
Confidence interval	
level	95.2 %
sides	2-sided
lower limit	-8.9
upper limit	5.2

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The non-inferiority margin for the difference between treatment groups (Tacrolimus MR minus Cyclosporine) was pre-specified as 10%. If the lower limit of the confidence interval was greater than -10%, then Tacrolimus MR was considered non-inferior to Cyclosporine.

Comparison groups	Cyclosporine v Tacrolimus Modified Release (MR)
Number of subjects included in analysis	426
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Incidence Difference
Point estimate	-3
Confidence interval	
level	95.2 %
sides	2-sided
lower limit	-9.9
upper limit	4

Secondary: Patient Survival at one year

End point title	Patient Survival at one year

End point description:

Patient survival is defined as any participant who is known to be alive one year after the skin closure date. Participants who died or whose outcome was unknown at one year were considered to be non-survivors. The number of participants analyzed represents the FAS.

End point type	Secondary

End point timeframe:

One year

End point values	Tacrolimus	Tacrolimus Modified Release (MR)	Cyclosporine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	212	214	212	
Units: percentage of participants				
number (not applicable)	93.9	97.2	97.2	

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The difference in survival rates was calculated as Tacrolimus minus Cyclosporine.

Comparison groups	Tacrolimus v Cyclosporine

Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Incidence Difference
Point estimate	-3.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.2
upper limit	0.6

Statistical analysis title	Statistical analysis 2
Statistical analysis description:	
The difference in survival rates was calculated as Tacrolimus MR minus Cyclosporine.	
Comparison groups	Cyclosporine v Tacrolimus Modified Release (MR)
Number of subjects included in analysis	426
Analysis specification	Pre-specified
Analysis type	other[1]
Parameter estimate	Incidence Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.1
upper limit	3.2

Notes:

[1] - The non-inferiority margin for this study was pre-specified as 10%.

Secondary: Graft Survival at one year

End point title	Graft Survival at one year
End point description:	
Graft survival defined as any participant who did not meet the criteria for graft loss, where graft loss is defined as any re-transplant, permanent return to dialysis (> 30 days), patient death, or participant whose outcome at one year was unknown. Participants were only counted once regardless of how many criteria were met. The number of participants analyzed represents the FAS.	
End point type	Secondary
End point timeframe:	
One year	

End point values	Tacrolimus	Tacrolimus Modified Release (MR)	Cyclosporine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	212	214	212	
Units: percentage of participants				
number (not applicable)	91.5	95.3	95.3	

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
The difference in survival rates was calculated as Tacrolimus minus Cyclosporine.	
Comparison groups	Cyclosporine v Tacrolimus
Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Incidence Difference
Point estimate	-3.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.5
upper limit	0.9

Statistical analysis title	Statistical analysis 2
Statistical analysis description:	
The difference in survival rates was calculated as Tacrolimus MR minus Cyclosporine.	
Comparison groups	Cyclosporine v Tacrolimus Modified Release (MR)
Number of subjects included in analysis	426
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Incidence Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4
upper limit	4.1

Secondary: Percentage of participants with biopsy confirmed acute rejection at 6 and 12 months

End point title	Percentage of participants with biopsy confirmed acute rejection at 6 and 12 months

End point description:

Rejection episodes were confirmed by biopsy by the clinical site pathologist. Biopsies were graded according to the 1997 Banff criteria: Borderline: No intimal arteritis present but foci of mild tubulitis; Grade I: Significant interstitial infiltration and foci of moderate to severe tubulitis; Grade II: Mild to severe intimal arteritis Grade III: Transmural arteritis and/or arterial fibrinoid change and necrosis of medial smooth muscle cells with accompanying lymphocytic infiltrate in vessel. Acute rejection is defined

as a grade ≥ I. The number of participants analyzed represents the FAS.

End point type	Secondary

End point timeframe:

Six months and 12 months

End point values	Tacrolimus	Tacrolimus Modified Release (MR)	Cyclosporine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	212	214	212	
Units: percentage of participants				
number (not applicable)				
At 6 Months	3.8	7.9	11.8	
At 12 Months	7.5	10.3	13.7	

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Comparison of tacrolimus with cyclosporine at 6 months. The difference in biopsy confirmed acute rejection rates was calculated as Tacrolimus minus Cyclosporine.

Comparison groups	Tacrolimus v Cyclosporine
Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Incidence Difference at 6 Months
Point estimate	-8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.1
upper limit	-3

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Comparison of Tacrolimus Modified Release with Cyclosporine at 6 months. The difference in biopsy confirmed acute rejection rates was calculated as Tacrolimus MR minus Cyclosporine.

Comparison groups	Tacrolimus Modified Release (MR) v Cyclosporine
Number of subjects included in analysis	426
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Incidence Difference at 6 Months
Point estimate	-3.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.5
upper limit	1.8

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Comparison of tacrolimus with cyclosporine at 12 months. The difference in biopsy confirmed acute rejection rates was calculated as Tacrolimus minus Cyclosporine.

Comparison groups	Tacrolimus v Cyclosporine
Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Incidence Difference at 12 Months
Point estimate	-6.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12
upper limit	-0.3

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

Comparison of Tacrolimus Modified Release with Cyclosporine at 12 months. The difference in biopsy confirmed acute rejection rates was calculated as Tacrolimus MR minus Cyclosporine.

Comparison groups	Tacrolimus Modified Release (MR) v Cyclosporine
Number of subjects included in analysis	426
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Incidence Difference at 12 months
Point estimate	-3.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.6
upper limit	2.8

Secondary: Time to first biopsy-confirmed acute rejection episode

End point title	Time to first biopsy-confirmed acute rejection episode

End point description:

Time to first biopsy-confirmed acute rejection episode defined as the number of days from skin closure (Day 0) to the date of biopsy. Rejection episodes were confirmed by biopsy by the clinical site pathologist and graded according to the 1997 Banff criteria: Borderline: No intimal arteritis present but foci of mild tubulitis; Grade I: Significant interstitial infiltration and foci of moderate to severe tubulitis;

Grade II: Mild to severe intimal arteritis Grade III: Transmural arteritis and/or arterial fibrinoid change and necrosis of medial smooth muscle cells with accompanying lymphocytic infiltrate in vessel. Acute rejection is defined as a grade ≥ I. The number of participants analyzed represents the FAS.

End point type	Secondary

End point timeframe:

One year

End point values	Tacrolimus	Tacrolimus Modified Release (MR)	Cyclosporine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	212	214	212	
Units: days				
median (full range (min-max))	156 (3 to 316)	11 (6 to 327)	52 (1 to 311)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants requiring anti-lymphocyte antibody therapy for treatment of rejection

End point title	Number of participants requiring anti-lymphocyte antibody therapy for treatment of rejection

End point description:

Rejection episodes were confirmed by biopsy by the clinical site pathologist. Participants with histologically-proven Banff Grade II or III rejection or participants with steroid-resistant rejection were treated with anti-lymphocyte antibody treatment according to institutional practice. Biopsies were graded according to the 1997 Banff criteria: Borderline: No intimal arteritis present but foci of mild tubulitis; Grade I: Significant interstitial infiltration and foci of moderate to severe tubulitis; Grade II: Mild to severe intimal arteritis; Grade III: Transmural arteritis and/or arterial fibrinoid change and necrosis of medial smooth muscle cells with accompanying lymphocytic infiltrate in vessel. The number of participants analyzed represents the FAS.

End point type	Secondary

End point timeframe:

One year

End point values	Tacrolimus	Tacrolimus Modified Release (MR)	Cyclosporine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	212	214	212	
Units: participants	6	8	18	

Statistical analyses

No statistical analyses for this end point

Secondary: Severity of acute rejection

End point title	Severity of acute rejection

End point description:

Rejection episodes were confirmed by biopsy by the clinical site pathologist. Biopsies were graded according to the 1997 Banff criteria: Borderline: No intimal arteritis present but foci of mild tubulitis; Grade IA: Significant interstitial infiltration and foci of moderate tubulitis; Grade IB: Significant interstitial infiltration and foci of severe tubulitis; Grade IIA: Mild to moderate intimal arteritis in at least 1 arterial cross section; Grade IIB: Severe intimal arteritis comprising >25% of the luminal area lost in at least 1 arterial cross section; Grade III: Transmural arteritis and/or arterial fibrinoid change and necrosis of medial smooth muscle cells with accompanying lymphocytic infiltrate in vessel. The number of participants analyzed represents the FAS with a biopsy-confirmed acute rejection episode during one year.

End point type	Secondary

End point timeframe:

One year

End point values	Tacrolimus	Tacrolimus Modified Release (MR)	Cyclosporine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	22	29	
Units: participants				
Grade I-A	8	11	14	
Grade I-B	4	3	6	
Grade II-A	3	6	6	
Grade II-B	1	1	1	
Grade III	0	1	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants experiencing multiple rejection episodes

End point title	Number of participants experiencing multiple rejection episodes

End point description:

This analysis includes rejection episodes that were either confirmed by biopsy by the clinical site pathologist or were clinically treated. The number of participants analyzed represents the FAS.

End point type	Secondary

End point timeframe:

One year

End point values	Tacrolimus	Tacrolimus Modified Release (MR)	Cyclosporine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	212	214	212	
Units: participants	2	4	8	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with clinically treated acute rejection episodes

End point title	Number of participants with clinically treated acute rejection episodes

End point description:

A clinically treated acute rejection episode was any biopsy-confirmed or suspected rejection episode that was treated with immunosuppressive therapy. The number of participants analyzed represents the FAS.

End point type	Secondary

End point timeframe:

One year

End point values	Tacrolimus	Tacrolimus Modified Release (MR)	Cyclosporine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	212	214	212	
Units: participants	25	39	45	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Treatment failure

End point title	Number of participants with Treatment failure

End point description:

Treatment failure was defined as the discontinuation of randomized study drug for any reason. Participants who met the definition of treatment failure were to be followed throughout the 12-month treatment period. The number of participants analyzed represents the FAS.

End point type	Secondary

End point timeframe:

One year

End point values	Tacrolimus	Tacrolimus Modified Release (MR)	Cyclosporine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	212	214	212	
Units: participants	33	31	61	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who crossed over due to treatment failure

End point title	Number of participants who crossed over due to treatment failure

End point description:

Participants were allowed to cross over to an alternative primary immunosuppressive regimen (either to the tacrolimus or cyclosporine treatment arms) to address an adverse event which led to randomized study drug discontinuation or in the case of severe or refractory rejection. Crossover to the modified release tacrolimus treatment arm was not permitted. The number of participants analyzed represents the FAS.

End point type	Secondary

End point timeframe:

One year

End point values	Tacrolimus	Tacrolimus Modified Release (MR)	Cyclosporine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	212	214	212	
Units: participants	6	10	39	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Month 1 in Serum Creatinine at Month 6 and Month 12

End point title	Change from Month 1 in Serum Creatinine at Month 6 and Month 12

End point description:

Renal function was assessed by the change from Month 1 in serum creatinine six months and 12 months after transplant. The number (N) of participants analyzed represents the FAS with available data at Month 1 and at each time point.

End point type	Secondary

End point timeframe:

Month 1, Month 6, and Month 12

End point values	Tacrolimus	Tacrolimus Modified Release (MR)	Cyclosporine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	212	214	212	
Units: mg/dL				
arithmetic mean (standard deviation)				
At 6 months [N=184, 184, 169]	-0.09 (± 0.63)	-0.08 (± 0.56)	-0.01 (± 0.53)	
At 12 months [N=173, 182, 147]	-0.08 (± 0.76)	-0.14 (± 0.62)	-0.04 (± 0.53)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Month 1 in Creatinine Clearance at Month 6 and Month 12

End point title	Change from Month 1 in Creatinine Clearance at Month 6 and Month 12

End point description:

Renal function was assessed by creatinine clearance, calculated using the Cockcroft-Gault formula. The number (N) of participants analyzed represents the FAS with available data at Month 1 and at each time point.

End point type	Secondary

End point timeframe:

Month 1, Month 6, and Month 12

End point values	Tacrolimus	Tacrolimus Modified Release (MR)	Cyclosporine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	212	214	212	
Units: mL/min				
arithmetic mean (standard deviation)				
At 6 months [N=184, 184, 167]	0.83 (± 13.77)	0.47 (± 12.9)	-1.79 (± 14.09)	
At 12 months [N=173, 182, 145]	1.5 (± 16.07)	2.62 (± 14.32)	-0.25 (± 14.54)	

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Estimate of Patient Survival at the end of the study

End point title	Kaplan-Meier Estimate of Patient Survival at the end of the

	study

End point description:

Patient survival was defined as any participant who was alive at the end of the study. Patient survival was censored at the time of last follow-up contact. The number of participants analyzed represents the FAS.

End point type	Secondary

End point timeframe:

End of study (maximum time on study was 1,941 days)

End point values	Tacrolimus	Tacrolimus Modified Release (MR)	Cyclosporine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	212	214	212	
Units: percentage of participants				
number (confidence interval 95%)	91.2 (86.8 to 95.7)	93.2 (89.7 to 96.8)	91.7 (87.7 to 95.8)	

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Tacrolimus v Cyclosporine
Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.5
upper limit	5.5

Statistical analysis title	Statistical analysis 2
Comparison groups	Tacrolimus Modified Release (MR) v Cyclosporine
Number of subjects included in analysis	426
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.9
upper limit	6.9

Secondary: Kaplan-Meier Estimate of Graft Survival at the end of the study

End point title	Kaplan-Meier Estimate of Graft Survival at the end of the study

End point description:

Graft survival was defined as any participant who did not meet the definition of graft loss, where graft loss was any retransplant or the permanent return to dialysis (more than 30 days) or patient death. Graft survival was censored at the time of last follow-up contact. The number of participants analyzed represents the FAS.

End point type	Secondary

End point timeframe:

End of study (maximum time on study was 1,941 days)

End point values	Tacrolimus	Tacrolimus Modified Release (MR)	Cyclosporine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	212	214	212	
Units: percentage of participants				
number (confidence interval 95%)	82.7 (76.9 to 88.4)	84.7 (79 to 90.4)	83.9 (78.6 to 89.3)	

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Cyclosporine v Tacrolimus
Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.1
upper limit	6.6

Statistical analysis title	Statistical analysis 2
Comparison groups	Tacrolimus Modified Release (MR) v Cyclosporine

Number of subjects included in analysis	426
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.1
upper limit	8.6

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 1941 days

Adverse event reporting additional description:

An adverse event (AE) was defined as any reaction, side effect, or other untoward medical occurrence, regardless of the relationship to study drug, which occurred during the conduct of the study. Clinically significant adverse changes in clinical status, ECGs, routine labs, x-rays, physical examinations, etc., were considered adverse events.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	6.1

Reporting groups

Reporting group title	Tacrolimus

Reporting group description:

Participants received a first dose of tacrolimus between 0.075 and 0.10 mg/kg twice daily, orally prior to or within 48 hours of the completion of the transplant procedure, and subsequently as twice daily oral doses adjusted based on clinical evidence of efficacy, blood concentrations of tacrolimus and adverse events. Participants also received 1.0 g mycophenolate mofetil orally twice daily throughout the study.

Reporting group title	Cyclosporine

Reporting group description:

Participants received a first dose of cyclosporine between 4 to 5 mg/kg orally prior to or within 48 hours following the completion of the transplant procedure and subsequently as twice daily oral doses adjusted based on clinical evidence of efficacy, blood concentrations of tacrolimus and adverse events. Participants also received 1.0 g mycophenolate mofetil orally twice daily throughout the study.

Reporting group title	Tacrolimus Modified Release

Reporting group description:

Participants received a first dose of tacrolimus modified release between 0.15 and 0.20 mg/kg/day, given as a single oral dose in the morning, prior to or within 48 hours following the completion of the transplant procedure, and subsequently as once daily oral doses adjusted based on clinical evidence of efficacy, blood concentrations of tacrolimus and adverse events. Participants also received 1.0 g mycophenolate mofetil orally twice daily throughout the study.

Serious adverse events	Tacrolimus	Cyclosporine	Tacrolimus Modified Release
Total subjects affected by serious adverse events			
subjects affected / exposed	148 / 212 (69.81%)	139 / 212 (65.57%)	141 / 214 (65.89%)
number of deaths (all causes)	13	9	9
number of deaths resulting from adverse events	5	1	3
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenoma benign			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
B-cell lymphoma			

subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal cell carcinoma			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	0 / 0	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder cancer			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carcinoid tumour of the appendix			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carcinoid tumour of the pancreas			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carcinoid tumour of the stomach			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervix carcinoma			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kaposi's sarcoma			

subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal cancer			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm malignant			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphoroliferative disorder			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastatic renal cell carcinoma			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Ovarian cancer			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	3 / 212 (1.42%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal cell carcinoma stage unspecified			
subjects affected / exposed	1 / 212 (0.47%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma			

subjects affected / exposed	4 / 212 (1.89%)	2 / 212 (0.94%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	6 / 6	2 / 2	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	3 / 214 (1.40%)
occurrences causally related to treatment / all	1 / 1	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine cancer			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arterial stenosis limb			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arterial thrombosis limb			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriovenous fistula, acquired			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atherosclerosis			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			

subjects affected / exposed	7 / 212 (3.30%)	4 / 212 (1.89%)	4 / 214 (1.87%)
occurrences causally related to treatment / all	1 / 8	0 / 5	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral arterial stenosis			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral artery occlusion			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gangrene			
subjects affected / exposed	1 / 212 (0.47%)	2 / 212 (0.94%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	0 / 1	0 / 4	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma			
subjects affected / exposed	2 / 212 (0.94%)	2 / 212 (0.94%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	1 / 2	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 212 (0.00%)	3 / 212 (1.42%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive crisis			
subjects affected / exposed	0 / 212 (0.00%)	2 / 212 (0.94%)	3 / 214 (1.40%)
occurrences causally related to treatment / all	0 / 0	1 / 2	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	2 / 212 (0.94%)	2 / 212 (0.94%)	5 / 214 (2.34%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iliac artery stenosis			

subjects affected / exposed	0 / 212 (0.00%)	2 / 212 (0.94%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intermittent Claudication			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jugular vein thrombosis			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphocele			
subjects affected / exposed	2 / 212 (0.94%)	4 / 212 (1.89%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 3	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphorrhoea			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orthostatic hypotension			
subjects affected / exposed	1 / 212 (0.47%)	1 / 212 (0.47%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral artery aneurysm			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral artery dissection			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral ischaemia			

subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral occlusive disease			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral vascular disorder			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 0	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Phlebitis			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renovascular Hypertension			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shock haemorrhagic			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular Insufficiency			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Venous stenosis			

subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Abdominal hernia repair			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal panniculectomy			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominoplasty			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystectomy			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colostomy closure			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary arterial stent insertion			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip arthroplasty			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hospitalisation			

subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia repair			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Knee arthroplasty			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrectomy			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreas transplant			
subjects affected / exposed	1 / 212 (0.47%)	1 / 212 (0.47%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parathyroidectomy			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal resection			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Umbilical hernia repair			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Pregnancy			

subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Adhesion			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anasarca			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			
subjects affected / exposed	1 / 212 (0.47%)	1 / 212 (0.47%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Catheter site haemorrhage			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	2 / 212 (0.94%)	0 / 212 (0.00%)	4 / 214 (1.87%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impaired healing			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			

subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	2 / 212 (0.94%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	5 / 212 (2.36%)	8 / 212 (3.77%)	5 / 214 (2.34%)
occurrences causally related to treatment / all	0 / 5	1 / 9	3 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rigors			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Swelling			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic inflammatory response syndrome			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ulcer haemorrhage			

subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Graft loss			
subjects affected / exposed	1 / 212 (0.47%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kidney transplant rejection			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Social circumstances			
Murder			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Treatment noncompliance			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometriosis			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Epididymitis			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erectile dysfunction			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gynaecomastia			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Menorrhagia			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cyst			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cyst torsion			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic muscles inadequate			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Priapism			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostatitis			

subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	3 / 214 (1.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Scrotal oedema			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Testicular infarction			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterovaginal prolapse			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vaginal haemorrhage			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute Respiratory failure			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic Obstructive airways Disease			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic Obstructive airways Disease exacerbated			

subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	2 / 212 (0.94%)	2 / 212 (0.94%)	3 / 214 (1.40%)
occurrences causally related to treatment / all	0 / 4	1 / 2	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea exacerbated			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea exertional			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal oedema			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung disorder			

subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Maxillary sinusitis			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleurisy			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleuritic pain			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	6 / 212 (2.83%)	3 / 212 (1.42%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 6	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Pulmonary hypertension			

subjects affected / exposed	2 / 212 (0.94%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	2 / 212 (0.94%)	0 / 212 (0.00%)	3 / 214 (1.40%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Restrictive pulmonary disease			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Completed Suicide			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Confusional state			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	3 / 212 (1.42%)	0 / 212 (0.00%)	3 / 214 (1.40%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hallucination			

subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Major depression			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status changes			
subjects affected / exposed	2 / 212 (0.94%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychotic disorder			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	2 / 212 (0.94%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary colic			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary dilatation			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			

subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	3 / 214 (1.40%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	1 / 212 (0.47%)	1 / 212 (0.47%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	1 / 212 (0.47%)	2 / 212 (0.94%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	0 / 1	0 / 2	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic lesion			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood creatine increased			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	18 / 212 (8.49%)	15 / 212 (7.08%)	11 / 214 (5.14%)
occurrences causally related to treatment / all	15 / 26	8 / 16	4 / 12
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood glucose increased			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood in stool			

subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood urea increased			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac stress test abnormal			
subjects affected / exposed	1 / 212 (0.47%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus test positive			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematocrit decreased			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoglobin decreased			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic enzyme increased			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
International normalised ratio increased			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urine output decreased			

subjects affected / exposed	0 / 212 (0.00%)	3 / 212 (1.42%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	1 / 3	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Volume blood decreased			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight decreased			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Acetabulum fracture			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle fracture			
subjects affected / exposed	2 / 212 (0.94%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriovenous graft site complication			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriovenous graft thrombosis			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Burns third degree			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac pacemaker malfunction			

subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Complications of transplant surgery			
subjects affected / exposed	5 / 212 (2.36%)	2 / 212 (0.94%)	3 / 214 (1.40%)
occurrences causally related to treatment / all	2 / 6	1 / 2	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug toxicity			
subjects affected / exposed	1 / 212 (0.47%)	2 / 212 (0.94%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	1 / 1	2 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	2 / 212 (0.94%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	1 / 212 (0.47%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fibula fracture			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot Fracture			
subjects affected / exposed	2 / 212 (0.94%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Graft complication			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Graft dysfunction			

subjects affected / exposed	5 / 212 (2.36%)	2 / 212 (0.94%)	3 / 214 (1.40%)
occurrences causally related to treatment / all	3 / 5	2 / 3	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria traumatic			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	1 / 212 (0.47%)	1 / 212 (0.47%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incision site complication			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incision site haemorrhage			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incisional hernia			
subjects affected / exposed	2 / 212 (0.94%)	1 / 212 (0.47%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Medical device complication			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meniscus lesion			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic fracture			

subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perinephric collection			
subjects affected / exposed	1 / 212 (0.47%)	2 / 212 (0.94%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perirenal haematoma			
subjects affected / exposed	1 / 212 (0.47%)	1 / 212 (0.47%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural discharge			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural pain			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural urine leak			
subjects affected / exposed	1 / 212 (0.47%)	1 / 212 (0.47%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative haematoma			
subjects affected / exposed	1 / 212 (0.47%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative ileus			

subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural complication			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pubic rami fracture			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal haematoma			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal injury			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 212 (0.00%)	2 / 212 (0.94%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin laceration			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			

subjects affected / exposed	2 / 212 (0.94%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Therapeutic agent toxicity			
subjects affected / exposed	5 / 212 (2.36%)	1 / 212 (0.47%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	5 / 5	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thoracic vertebral fracture			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	3 / 214 (1.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic haematoma			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ulna fracture			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound dehiscence			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound secretion			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wrist fracture			

subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Anomalous pulmonary venous connection			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital cystic kidney disease			
subjects affected / exposed	1 / 212 (0.47%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Angina pectoris			
subjects affected / exposed	3 / 212 (1.42%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic valve disease			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Aortic valve incompetence			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic valve stenosis			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	2 / 212 (0.94%)	3 / 212 (1.42%)	3 / 214 (1.40%)
occurrences causally related to treatment / all	0 / 4	0 / 3	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Atrial flutter			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block complete			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block second degree			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	3 / 212 (1.42%)	2 / 212 (0.94%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	1 / 3	0 / 2	0 / 1
deaths causally related to treatment / all	1 / 3	0 / 2	0 / 1
Cardiac failure			

subjects affected / exposed	2 / 212 (0.94%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure acute			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	3 / 212 (1.42%)	1 / 212 (0.47%)	6 / 214 (2.80%)
occurrences causally related to treatment / all	0 / 9	0 / 1	0 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardio-respiratory arrest			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Cardiogenic shock			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Congestive cardiomyopathy			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	4 / 212 (1.89%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery insufficiency			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			

subjects affected / exposed	5 / 212 (2.36%)	4 / 212 (1.89%)	4 / 214 (1.87%)
occurrences causally related to treatment / all	0 / 5	0 / 4	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 3	0 / 0
Myocardial ischaemia			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Palpitations			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Right ventricular failure			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular bigeminy			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular tachycardia			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebellar haemorrhage			

subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cerebral haemorrhage			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 212 (0.00%)	2 / 212 (0.94%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Convulsion			
subjects affected / exposed	3 / 212 (1.42%)	1 / 212 (0.47%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	2 / 4	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depressed level of consciousness			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic hyperosmolar coma			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	2 / 212 (0.94%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysaesthesia			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis			

subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Guillain Barre syndrome			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	2 / 212 (0.94%)	0 / 212 (0.00%)	3 / 214 (1.40%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic encephalopathy			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar radiculopathy			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Migraine			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple sclerosis			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuropathy			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuropathy peripheral			

subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Normal pressure hydrocephalus			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parkinson's disease			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sleep apnoea syndrome			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sleep paralysis			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 212 (0.00%)	2 / 212 (0.94%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viith nerve paralysis			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	6 / 212 (2.83%)	5 / 212 (2.36%)	4 / 214 (1.87%)
occurrences causally related to treatment / all	3 / 6	2 / 6	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coagulopathy			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	1 / 212 (0.47%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemolysis			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukocytosis			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	1 / 212 (0.47%)	3 / 212 (1.42%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenopathy			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 212 (0.00%)	2 / 212 (0.94%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Normochromic normocytic anaemia			

subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	2 / 212 (0.94%)	0 / 212 (0.00%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombotic microangiopathy			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vertigo			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Retinitis			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal adhesions			
subjects affected / exposed	1 / 212 (0.47%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Abdominal haematoma			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal hernia			
subjects affected / exposed	2 / 212 (0.94%)	0 / 212 (0.00%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	5 / 212 (2.36%)	5 / 212 (2.36%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	2 / 5	0 / 5	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal strangulated hernia			
subjects affected / exposed	0 / 212 (0.00%)	3 / 212 (1.42%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal wall cyst			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal wall disorder			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute abdomen			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis perforated			

subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ischaemic			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	1 / 212 (0.47%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	12 / 212 (5.66%)	3 / 212 (1.42%)	10 / 214 (4.67%)
occurrences causally related to treatment / all	3 / 14	1 / 3	3 / 13
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea haemorrhagic			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	2 / 212 (0.94%)	1 / 212 (0.47%)	3 / 214 (1.40%)
occurrences causally related to treatment / all	2 / 2	0 / 1	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer			

subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspepsia			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocutaneous fistula			
subjects affected / exposed	2 / 212 (0.94%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Faecaloma			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Food poisoning			
subjects affected / exposed	0 / 212 (0.00%)	2 / 212 (0.94%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer			
subjects affected / exposed	0 / 212 (0.00%)	2 / 212 (0.94%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer haemorrhage			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer perforation			

subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis erosive			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	5 / 212 (2.36%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	1 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gingival hyperplasia			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impaired gastric emptying			
subjects affected / exposed	0 / 212 (0.00%)	2 / 212 (0.94%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	0 / 0	2 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			

subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal ischaemia			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	1 / 212 (0.47%)	2 / 212 (0.94%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	7 / 212 (3.30%)	3 / 212 (1.42%)	6 / 214 (2.80%)
occurrences causally related to treatment / all	1 / 8	0 / 3	1 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal erosion			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophagitis			
subjects affected / exposed	1 / 212 (0.47%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			

subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis due to biliary obstruction			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis haemorrhagic			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritoneal haematoma			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proctalgia			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal polyp			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal ulcer			

subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retroperitoneal haematoma			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salivary gland enlargement			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	2 / 212 (0.94%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subileus			
subjects affected / exposed	1 / 212 (0.47%)	1 / 212 (0.47%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Umbilical hernia			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Umbilical hernia, obstructive			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			

subjects affected / exposed	8 / 212 (3.77%)	5 / 212 (2.36%)	8 / 214 (3.74%)
occurrences causally related to treatment / all	1 / 9	0 / 5	2 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute prerenal failure			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Azotaemia			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder disorder			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder neck obstruction			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysuria			
subjects affected / exposed	2 / 212 (0.94%)	2 / 212 (0.94%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	2 / 212 (0.94%)	4 / 212 (1.89%)	4 / 214 (1.87%)
occurrences causally related to treatment / all	1 / 2	2 / 4	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage urinary tract			

subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydronephrosis			
subjects affected / exposed	3 / 212 (1.42%)	4 / 212 (1.89%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	0 / 3	1 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydroureter			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephropathy			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephropathy Toxic			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrotic Syndrome			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstructive uropathy			
subjects affected / exposed	2 / 212 (0.94%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvi-ureteric obstruction			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proteinuria			

subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal Impairment			
subjects affected / exposed	4 / 212 (1.89%)	3 / 212 (1.42%)	3 / 214 (1.40%)
occurrences causally related to treatment / all	3 / 4	2 / 3	3 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal artery stenosis			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal artery thrombosis			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure acute			
subjects affected / exposed	9 / 212 (4.25%)	7 / 212 (3.30%)	4 / 214 (1.87%)
occurrences causally related to treatment / all	3 / 11	2 / 7	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure chronic			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal insufficiency			
subjects affected / exposed	2 / 212 (0.94%)	0 / 212 (0.00%)	5 / 214 (2.34%)
occurrences causally related to treatment / all	0 / 2	0 / 0	3 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal vein thrombosis			
subjects affected / exposed	1 / 212 (0.47%)	1 / 212 (0.47%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stress incontinence			

subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureteric obstruction			
subjects affected / exposed	1 / 212 (0.47%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureteric stenosis			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urethral meatus stenosis			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urethral obstruction			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary incontinence			
subjects affected / exposed	2 / 212 (0.94%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			
subjects affected / exposed	1 / 212 (0.47%)	2 / 212 (0.94%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract obstruction			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinoma			

subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Goitre			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperparathyroidism			
subjects affected / exposed	1 / 212 (0.47%)	1 / 212 (0.47%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperparathyroidism tertiary			
subjects affected / exposed	3 / 212 (1.42%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 212 (0.47%)	1 / 212 (0.47%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	1 / 2	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	1 / 212 (0.47%)	2 / 212 (0.94%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone Spur			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Compartment syndrome			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Fistula			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Flank pain			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fracture malunion			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gouty arthritis			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc space narrowing			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint swelling			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Localised osteoarthritis			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Monoarthritis			

subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	2 / 212 (0.94%)	0 / 212 (0.00%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Plantar fasciitis			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator cuff syndrome			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spondylosis			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic lupus erythematosus			

subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess limb			
subjects affected / exposed	1 / 212 (0.47%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	2 / 212 (0.94%)	2 / 212 (0.94%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	0 / 2	0 / 2	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial pyelonephritis			
subjects affected / exposed	2 / 212 (0.94%)	0 / 212 (0.00%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	3 / 212 (1.42%)	1 / 212 (0.47%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	1 / 4	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis acute			

subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopulmonary aspergillosis			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Catheter related infection			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Catheter sepsis			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	4 / 212 (1.89%)	4 / 212 (1.89%)	5 / 214 (2.34%)
occurrences causally related to treatment / all	3 / 7	2 / 4	3 / 5
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cellulitis gangrenous			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Choriomeningitis lymphocytic			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Clostridial infection			

subjects affected / exposed	1 / 212 (0.47%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium colitis			
subjects affected / exposed	1 / 212 (0.47%)	1 / 212 (0.47%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	0 / 1	1 / 1	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Condyloma acuminatum			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus colitis			
subjects affected / exposed	2 / 212 (0.94%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus gastritis			
subjects affected / exposed	0 / 212 (0.00%)	2 / 212 (0.94%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	2 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus infection			
subjects affected / exposed	15 / 212 (7.08%)	11 / 212 (5.19%)	11 / 214 (5.14%)
occurrences causally related to treatment / all	14 / 17	6 / 14	6 / 12
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Cytomegalovirus oesophagitis			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus viraemia			
subjects affected / exposed	2 / 212 (0.94%)	0 / 212 (0.00%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	1 / 2	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic foot infection			

subjects affected / exposed	1 / 212 (0.47%)	2 / 212 (0.94%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea infectious			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocarditis			
subjects affected / exposed	2 / 212 (0.94%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocarditis bacterial			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia bacteraemia			
subjects affected / exposed	1 / 212 (0.47%)	1 / 212 (0.47%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia urinary tract infection			
subjects affected / exposed	3 / 212 (1.42%)	5 / 212 (2.36%)	6 / 214 (2.80%)
occurrences causally related to treatment / all	0 / 4	2 / 5	2 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Furuncle			
subjects affected / exposed	1 / 212 (0.47%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis fungal			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			

subjects affected / exposed	4 / 212 (1.89%)	3 / 212 (1.42%)	14 / 214 (6.54%)
occurrences causally related to treatment / all	2 / 4	0 / 4	6 / 15
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	5 / 212 (2.36%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	3 / 5	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Groin infection			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Helicobacter gastritis			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes virus infection			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	3 / 212 (1.42%)	1 / 212 (0.47%)	3 / 214 (1.40%)
occurrences causally related to treatment / all	2 / 4	1 / 1	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpetic gingivostomatitis			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Human polyomavirus infection			
subjects affected / exposed	9 / 212 (4.25%)	1 / 212 (0.47%)	5 / 214 (2.34%)
occurrences causally related to treatment / all	9 / 10	0 / 1	1 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infected cyst			

subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infected skin ulcer			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	3 / 214 (1.40%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	4 / 214 (1.87%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Klebsiella bacteraemia			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lobar pneumonia			
subjects affected / exposed	1 / 212 (0.47%)	1 / 212 (0.47%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Localised infection			
subjects affected / exposed	1 / 212 (0.47%)	1 / 212 (0.47%)	3 / 214 (1.40%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection pseudomonal			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mastoiditis			

subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis aseptic			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis cryptococcal			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mycobacterium avium complex infection			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal candidiasis			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orchitis			
subjects affected / exposed	1 / 212 (0.47%)	1 / 212 (0.47%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	2 / 212 (0.94%)	1 / 212 (0.47%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	0 / 2	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Papilloma viral infection			

subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parvovirus infection			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perinephric abscess			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngotonsillitis			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Phlebitis infective			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	4 / 212 (1.89%)	7 / 212 (3.30%)	10 / 214 (4.67%)
occurrences causally related to treatment / all	2 / 4	3 / 11	4 / 11
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 2
Pneumonia fungal			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia haemophilus			

subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia klebsiella			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia staphylococcal			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative abscess			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative infection			
subjects affected / exposed	0 / 212 (0.00%)	2 / 212 (0.94%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	4 / 212 (1.89%)	3 / 212 (1.42%)	5 / 214 (2.34%)
occurrences causally related to treatment / all	2 / 4	0 / 3	3 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	1 / 212 (0.47%)	2 / 212 (0.94%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			

subjects affected / exposed	6 / 212 (2.83%)	4 / 212 (1.89%)	8 / 214 (3.74%)
occurrences causally related to treatment / all	5 / 6	2 / 4	3 / 8
deaths causally related to treatment / all	3 / 4	0 / 0	0 / 2
Septic shock			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin bacterial infection			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 212 (0.47%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal infection			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Streptococcal bacteraemia			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Streptococcal infection			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Streptococcal sepsis			

subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Strongyloidiasis			
subjects affected / exposed	3 / 212 (1.42%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	2 / 212 (0.94%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheobronchitis			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tuberculosis			
subjects affected / exposed	1 / 212 (0.47%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	15 / 212 (7.08%)	15 / 212 (7.08%)	11 / 214 (5.14%)
occurrences causally related to treatment / all	3 / 18	4 / 17	3 / 12
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection bacterial			
subjects affected / exposed	3 / 212 (1.42%)	4 / 212 (1.89%)	3 / 214 (1.40%)
occurrences causally related to treatment / all	2 / 3	1 / 4	3 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection enterococcal			

subjects affected / exposed	2 / 212 (0.94%)	1 / 212 (0.47%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection fungal			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection pseudomonal			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection staphylococcal			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	5 / 212 (2.36%)	5 / 212 (2.36%)	5 / 214 (2.34%)
occurrences causally related to treatment / all	5 / 8	0 / 5	5 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Vaginitis			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vancomycin-resistant enterococcal infection			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Varicella			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			

subjects affected / exposed	1 / 212 (0.47%)	1 / 212 (0.47%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 212 (0.00%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vulval abscess			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	1 / 212 (0.47%)	1 / 212 (0.47%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	9 / 212 (4.25%)	6 / 212 (2.83%)	10 / 214 (4.67%)
occurrences causally related to treatment / all	1 / 10	0 / 6	1 / 13
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			
subjects affected / exposed	2 / 212 (0.94%)	4 / 212 (1.89%)	6 / 214 (2.80%)
occurrences causally related to treatment / all	2 / 2	2 / 4	7 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus inadequate control			
subjects affected / exposed	4 / 212 (1.89%)	2 / 212 (0.94%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	3 / 4	1 / 2	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes with hyperosmolarity			

subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic foot			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic ketoacidosis			
subjects affected / exposed	1 / 212 (0.47%)	1 / 212 (0.47%)	4 / 214 (1.87%)
occurrences causally related to treatment / all	0 / 1	0 / 2	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fluid overload			
subjects affected / exposed	2 / 212 (0.94%)	1 / 212 (0.47%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gout			
subjects affected / exposed	1 / 212 (0.47%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	1 / 212 (0.47%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	5 / 212 (2.36%)	3 / 212 (1.42%)	5 / 214 (2.34%)
occurrences causally related to treatment / all	2 / 6	0 / 3	3 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	5 / 212 (2.36%)	1 / 212 (0.47%)	5 / 214 (2.34%)
occurrences causally related to treatment / all	3 / 6	0 / 1	2 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypocalcaemia			

subjects affected / exposed	2 / 212 (0.94%)	0 / 212 (0.00%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	1 / 212 (0.47%)	2 / 212 (0.94%)	1 / 214 (0.47%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	1 / 212 (0.47%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophosphataemia			
subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypovolaemia			
subjects affected / exposed	2 / 212 (0.94%)	0 / 212 (0.00%)	2 / 214 (0.93%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malnutrition			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic acidosis			
subjects affected / exposed	1 / 212 (0.47%)	0 / 212 (0.00%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obesity			

subjects affected / exposed	0 / 212 (0.00%)	1 / 212 (0.47%)	0 / 214 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Tacrolimus	Cyclosporine	Tacrolimus Modified Release
Total subjects affected by non-serious adverse events			
subjects affected / exposed	209 / 212 (98.58%)	209 / 212 (98.58%)	213 / 214 (99.53%)
Vascular disorders			
Hypertension			
subjects affected / exposed	63 / 212 (29.72%)	69 / 212 (32.55%)	59 / 214 (27.57%)
occurrences (all)	100	101	92
Hypotension			
subjects affected / exposed	17 / 212 (8.02%)	17 / 212 (8.02%)	19 / 214 (8.88%)
occurrences (all)	23	20	24
Orthostatic Hypotension			
subjects affected / exposed	9 / 212 (4.25%)	5 / 212 (2.36%)	15 / 214 (7.01%)
occurrences (all)	9	5	15
General disorders and administration site conditions			
Anasarca			
subjects affected / exposed	8 / 212 (3.77%)	4 / 212 (1.89%)	12 / 214 (5.61%)
occurrences (all)	8	5	13
Asthenia			
subjects affected / exposed	22 / 212 (10.38%)	22 / 212 (10.38%)	16 / 214 (7.48%)
occurrences (all)	24	24	20
Chest pain			
subjects affected / exposed	16 / 212 (7.55%)	12 / 212 (5.66%)	19 / 214 (8.88%)
occurrences (all)	20	16	19
Fatigue			
subjects affected / exposed	22 / 212 (10.38%)	26 / 212 (12.26%)	32 / 214 (14.95%)
occurrences (all)	27	27	37
Oedema			
subjects affected / exposed	27 / 212 (12.74%)	25 / 212 (11.79%)	17 / 214 (7.94%)
occurrences (all)	35	29	24

Oedema peripheral			
subjects affected / exposed	72 / 212 (33.96%)	97 / 212 (45.75%)	75 / 214 (35.05%)
occurrences (all)	110	143	120
Pain			
subjects affected / exposed	8 / 212 (3.77%)	14 / 212 (6.60%)	11 / 214 (5.14%)
occurrences (all)	11	18	17
Pyrexia			
subjects affected / exposed	20 / 212 (9.43%)	28 / 212 (13.21%)	21 / 214 (9.81%)
occurrences (all)	35	36	27
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	26 / 212 (12.26%)	21 / 212 (9.91%)	15 / 214 (7.01%)
occurrences (all)	30	24	22
Dyspnoea			
subjects affected / exposed	22 / 212 (10.38%)	26 / 212 (12.26%)	27 / 214 (12.62%)
occurrences (all)	24	30	34
Dyspnoea exertional			
subjects affected / exposed	12 / 212 (5.66%)	8 / 212 (3.77%)	10 / 214 (4.67%)
occurrences (all)	13	9	12
Pharyngolaryngeal Pain			
subjects affected / exposed	15 / 212 (7.08%)	11 / 212 (5.19%)	16 / 214 (7.48%)
occurrences (all)	16	13	19
Psychiatric disorders			
Anxiety			
subjects affected / exposed	23 / 212 (10.85%)	21 / 212 (9.91%)	27 / 214 (12.62%)
occurrences (all)	25	25	30
Depression			
subjects affected / exposed	13 / 212 (6.13%)	11 / 212 (5.19%)	11 / 214 (5.14%)
occurrences (all)	15	13	12
Insomnia			
subjects affected / exposed	60 / 212 (28.30%)	45 / 212 (21.23%)	52 / 214 (24.30%)
occurrences (all)	68	57	68
Investigations			
Blood creatinine increased			
subjects affected / exposed	41 / 212 (19.34%)	36 / 212 (16.98%)	32 / 214 (14.95%)
occurrences (all)	68	51	48

Blood magnesium decreased			
subjects affected / exposed	19 / 212 (8.96%)	12 / 212 (5.66%)	15 / 214 (7.01%)
occurrences (all)	22	18	25
Blood phosphorus decreased			
subjects affected / exposed	10 / 212 (4.72%)	6 / 212 (2.83%)	11 / 214 (5.14%)
occurrences (all)	11	6	11
Cardiac Murmur			
subjects affected / exposed	11 / 212 (5.19%)	5 / 212 (2.36%)	7 / 214 (3.27%)
occurrences (all)	12	5	8
Hepatic enzyme increased			
subjects affected / exposed	6 / 212 (2.83%)	11 / 212 (5.19%)	9 / 214 (4.21%)
occurrences (all)	8	11	9
Liver function test abnormal			
subjects affected / exposed	6 / 212 (2.83%)	8 / 212 (3.77%)	11 / 214 (5.14%)
occurrences (all)	6	8	13
Urine output decreased			
subjects affected / exposed	8 / 212 (3.77%)	10 / 212 (4.72%)	12 / 214 (5.61%)
occurrences (all)	8	11	15
Weight increased			
subjects affected / exposed	18 / 212 (8.49%)	22 / 212 (10.38%)	14 / 214 (6.54%)
occurrences (all)	21	28	14
Injury, poisoning and procedural complications			
Complications of transplant surgery			
subjects affected / exposed	11 / 212 (5.19%)	10 / 212 (4.72%)	5 / 214 (2.34%)
occurrences (all)	15	14	9
Graft dysfunction			
subjects affected / exposed	41 / 212 (19.34%)	31 / 212 (14.62%)	27 / 214 (12.62%)
occurrences (all)	48	36	41
Incision site complication			
subjects affected / exposed	46 / 212 (21.70%)	42 / 212 (19.81%)	31 / 214 (14.49%)
occurrences (all)	69	71	56
Post procedural discharge			
subjects affected / exposed	6 / 212 (2.83%)	12 / 212 (5.66%)	10 / 214 (4.67%)
occurrences (all)	7	13	11
Post procedural pain			

subjects affected / exposed	42 / 212 (19.81%)	37 / 212 (17.45%)	27 / 214 (12.62%)
occurrences (all)	77	67	73
Therapeutic agent toxicity			
subjects affected / exposed	14 / 212 (6.60%)	13 / 212 (6.13%)	13 / 214 (6.07%)
occurrences (all)	17	18	14
Cardiac disorders			
Tachycardia			
subjects affected / exposed	11 / 212 (5.19%)	10 / 212 (4.72%)	9 / 214 (4.21%)
occurrences (all)	13	10	12
Nervous system disorders			
Dizziness			
subjects affected / exposed	27 / 212 (12.74%)	23 / 212 (10.85%)	21 / 214 (9.81%)
occurrences (all)	33	32	27
Headache			
subjects affected / exposed	50 / 212 (23.58%)	52 / 212 (24.53%)	45 / 214 (21.03%)
occurrences (all)	71	75	66
Hypoaesthesia			
subjects affected / exposed	5 / 212 (2.36%)	11 / 212 (5.19%)	8 / 214 (3.74%)
occurrences (all)	6	12	14
Paraesthesia			
subjects affected / exposed	3 / 212 (1.42%)	13 / 212 (6.13%)	12 / 214 (5.61%)
occurrences (all)	3	13	17
Tremor			
subjects affected / exposed	73 / 212 (34.43%)	42 / 212 (19.81%)	75 / 214 (35.05%)
occurrences (all)	86	47	93
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	59 / 212 (27.83%)	55 / 212 (25.94%)	68 / 214 (31.78%)
occurrences (all)	75	67	92
Leukocytosis			
subjects affected / exposed	4 / 212 (1.89%)	9 / 212 (4.25%)	11 / 214 (5.14%)
occurrences (all)	4	11	11
Leukopenia			
subjects affected / exposed	33 / 212 (15.57%)	25 / 212 (11.79%)	35 / 214 (16.36%)
occurrences (all)	42	31	44
Neutropenia			

subjects affected / exposed	9 / 212 (4.25%)	5 / 212 (2.36%)	11 / 214 (5.14%)
occurrences (all)	9	6	13
Polycythaemia			
subjects affected / exposed	13 / 212 (6.13%)	9 / 212 (4.25%)	12 / 214 (5.61%)
occurrences (all)	16	10	15
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	15 / 212 (7.08%)	18 / 212 (8.49%)	11 / 214 (5.14%)
occurrences (all)	17	19	17
Abdominal pain			
subjects affected / exposed	22 / 212 (10.38%)	35 / 212 (16.51%)	26 / 214 (12.15%)
occurrences (all)	24	46	40
Abdominal pain upper			
subjects affected / exposed	21 / 212 (9.91%)	18 / 212 (8.49%)	16 / 214 (7.48%)
occurrences (all)	25	24	19
Constipation			
subjects affected / exposed	68 / 212 (32.08%)	82 / 212 (38.68%)	85 / 214 (39.72%)
occurrences (all)	86	107	112
Diarrhoea			
subjects affected / exposed	91 / 212 (42.92%)	53 / 212 (25.00%)	94 / 214 (43.93%)
occurrences (all)	146	74	140
Dyspepsia			
subjects affected / exposed	36 / 212 (16.98%)	32 / 212 (15.09%)	32 / 214 (14.95%)
occurrences (all)	42	41	39
Flatulence			
subjects affected / exposed	22 / 212 (10.38%)	14 / 212 (6.60%)	15 / 214 (7.01%)
occurrences (all)	24	17	16
Gastrooesophageal reflux disease			
subjects affected / exposed	5 / 212 (2.36%)	12 / 212 (5.66%)	9 / 214 (4.21%)
occurrences (all)	6	15	11
Gingival hyperplasia			
subjects affected / exposed	0 / 212 (0.00%)	15 / 212 (7.08%)	1 / 214 (0.47%)
occurrences (all)	0	18	1
Haemorrhoids			
subjects affected / exposed	5 / 212 (2.36%)	6 / 212 (2.83%)	12 / 214 (5.61%)
occurrences (all)	5	6	14

Loose stools			
subjects affected / exposed	14 / 212 (6.60%)	4 / 212 (1.89%)	11 / 214 (5.14%)
occurrences (all)	17	4	12
Nausea			
subjects affected / exposed	71 / 212 (33.49%)	90 / 212 (42.45%)	74 / 214 (34.58%)
occurrences (all)	114	128	129
Vomiting			
subjects affected / exposed	49 / 212 (23.11%)	46 / 212 (21.70%)	51 / 214 (23.83%)
occurrences (all)	69	69	83
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	13 / 212 (6.13%)	22 / 212 (10.38%)	18 / 214 (8.41%)
occurrences (all)	13	25	19
Alopecia			
subjects affected / exposed	15 / 212 (7.08%)	4 / 212 (1.89%)	14 / 214 (6.54%)
occurrences (all)	15	6	14
Pruritus			
subjects affected / exposed	20 / 212 (9.43%)	15 / 212 (7.08%)	24 / 214 (11.21%)
occurrences (all)	24	18	30
Rash			
subjects affected / exposed	10 / 212 (4.72%)	5 / 212 (2.36%)	11 / 214 (5.14%)
occurrences (all)	13	5	15
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	23 / 212 (10.85%)	20 / 212 (9.43%)	15 / 214 (7.01%)
occurrences (all)	30	27	17
Haematuria			
subjects affected / exposed	18 / 212 (8.49%)	20 / 212 (9.43%)	15 / 214 (7.01%)
occurrences (all)	20	29	20
Proteinuria			
subjects affected / exposed	5 / 212 (2.36%)	10 / 212 (4.72%)	13 / 214 (6.07%)
occurrences (all)	7	12	15
Endocrine disorders			
Hirsutism			
subjects affected / exposed	0 / 212 (0.00%)	18 / 212 (8.49%)	0 / 214 (0.00%)
occurrences (all)	0	20	0
Musculoskeletal and connective tissue			

disorders			
Arthralgia			
subjects affected / exposed	26 / 212 (12.26%)	28 / 212 (13.21%)	27 / 214 (12.62%)
occurrences (all)	31	34	29
Back pain			
subjects affected / exposed	27 / 212 (12.74%)	29 / 212 (13.68%)	32 / 214 (14.95%)
occurrences (all)	30	37	35
Muscle Cramp			
subjects affected / exposed	17 / 212 (8.02%)	22 / 212 (10.38%)	20 / 214 (9.35%)
occurrences (all)	19	25	24
Osteopenia			
subjects affected / exposed	12 / 212 (5.66%)	13 / 212 (6.13%)	13 / 214 (6.07%)
occurrences (all)	12	13	13
Osteoporosis			
subjects affected / exposed	4 / 212 (1.89%)	5 / 212 (2.36%)	11 / 214 (5.14%)
occurrences (all)	4	5	11
Pain in Extremity			
subjects affected / exposed	27 / 212 (12.74%)	26 / 212 (12.26%)	27 / 214 (12.62%)
occurrences (all)	28	33	30
Infections and infestations			
Bronchitis			
subjects affected / exposed	11 / 212 (5.19%)	9 / 212 (4.25%)	10 / 214 (4.67%)
occurrences (all)	12	12	11
Escherichia urinary tract infection			
subjects affected / exposed	11 / 212 (5.19%)	18 / 212 (8.49%)	14 / 214 (6.54%)
occurrences (all)	21	29	19
Herpes simplex			
subjects affected / exposed	8 / 212 (3.77%)	9 / 212 (4.25%)	11 / 214 (5.14%)
occurrences (all)	9	11	12
Herpes zoster			
subjects affected / exposed	9 / 212 (4.25%)	16 / 212 (7.55%)	10 / 214 (4.67%)
occurrences (all)	9	17	12
Human polyomavirus infection			
subjects affected / exposed	10 / 212 (4.72%)	5 / 212 (2.36%)	12 / 214 (5.61%)
occurrences (all)	11	6	14
Nasopharyngitis			

subjects affected / exposed	12 / 212 (5.66%)	14 / 212 (6.60%)	12 / 214 (5.61%)
occurrences (all)	18	14	12
Oral Candidiasis			
subjects affected / exposed	9 / 212 (4.25%)	13 / 212 (6.13%)	15 / 214 (7.01%)
occurrences (all)	11	19	22
Sinusitis			
subjects affected / exposed	7 / 212 (3.30%)	5 / 212 (2.36%)	15 / 214 (7.01%)
occurrences (all)	18	17	30
Upper respiratory tract infection			
subjects affected / exposed	24 / 212 (11.32%)	29 / 212 (13.68%)	27 / 214 (12.62%)
occurrences (all)	58	52	62
Urinary tract infection bacterial			
subjects affected / exposed	11 / 212 (5.19%)	9 / 212 (4.25%)	9 / 214 (4.21%)
occurrences (all)	19	12	11
Urinary tract infection			
subjects affected / exposed	49 / 212 (23.11%)	42 / 212 (19.81%)	30 / 214 (14.02%)
occurrences (all)	89	88	60
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	16 / 212 (7.55%)	4 / 212 (1.89%)	10 / 214 (4.67%)
occurrences (all)	20	5	16
Diabetes mellitus			
subjects affected / exposed	20 / 212 (9.43%)	9 / 212 (4.25%)	25 / 214 (11.68%)
occurrences (all)	36	16	39
Dyslipidaemia			
subjects affected / exposed	4 / 212 (1.89%)	6 / 212 (2.83%)	12 / 214 (5.61%)
occurrences (all)	8	11	25
Fluid overload			
subjects affected / exposed	14 / 212 (6.60%)	9 / 212 (4.25%)	9 / 214 (4.21%)
occurrences (all)	17	13	14
Hypercholesterolaemia			
subjects affected / exposed	10 / 212 (4.72%)	16 / 212 (7.55%)	8 / 214 (3.74%)
occurrences (all)	12	18	14
Hyperglycaemia			
subjects affected / exposed	37 / 212 (17.45%)	28 / 212 (13.21%)	30 / 214 (14.02%)
occurrences (all)	54	37	47

Hyperkalaemia			
subjects affected / exposed	48 / 212 (22.64%)	38 / 212 (17.92%)	40 / 214 (18.69%)
occurrences (all)	70	51	62
Hyperlipidaemia			
subjects affected / exposed	35 / 212 (16.51%)	52 / 212 (24.53%)	35 / 214 (16.36%)
occurrences (all)	57	65	52
Hypocalcaemia			
subjects affected / exposed	15 / 212 (7.08%)	25 / 212 (11.79%)	13 / 214 (6.07%)
occurrences (all)	24	31	20
Hypokalaemia			
subjects affected / exposed	31 / 212 (14.62%)	33 / 212 (15.57%)	31 / 214 (14.49%)
occurrences (all)	37	47	39
Hypomagnesaemia			
subjects affected / exposed	57 / 212 (26.89%)	44 / 212 (20.75%)	52 / 214 (24.30%)
occurrences (all)	79	57	71
Hypophosphataemia			
subjects affected / exposed	59 / 212 (27.83%)	45 / 212 (21.23%)	50 / 214 (23.36%)
occurrences (all)	65	52	56
Metabolic acidosis			
subjects affected / exposed	12 / 212 (5.66%)	11 / 212 (5.19%)	15 / 214 (7.01%)
occurrences (all)	15	13	19

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 May 2003	Amendment 1 (May 8, 2003) involved the following changes to the original protocol: · Dosing amounts, schedules, and routes of administration were modified. · Inclusion and exclusion criteria were modified. · The study visit schedule for the initial treatment period was modified. · Hepatic profile sample collection times were modified. · Tests performed at central laboratories were clarified. · Sponsor personnel contact information was updated. · Typographical errors were corrected and minor clerical changes were incorporated.
13 November 2003	Amendment 2 (November 13, 2003) involved the following changes: · The primary and secondary efficacy assessments were modified. · A section describing interim analyses was added. · The inclusion criteria were clarified. · Descriptions of statistical analyses were modified. · The follow-up duration for adverse events was clarified. · Typographical errors were corrected and minor clerical changes were incorporated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

The clinical continuation phase was terminated by the Sponsor.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/17217442