



Clinical trial results:

12 month, multi-center, open-label, prospective, randomized, parallel group study investigating a standard regimen in de novo kidney transplant patients versus a Certican® based regimen either in combination with Cyclosporin A or Tacrolimus

Summary

EudraCT number	2011-005238-21
Trial protocol	DE FR
Global end of trial date	23 March 2016

Results information

Result version number	v1 (current)
This version publication date	06 April 2017
First version publication date	06 April 2017

Trial information

Trial identification

Sponsor protocol code	CRAD001ADE44
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01843348
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	23 March 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 March 2016
Global end of trial reached?	Yes
Global end of trial date	23 March 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to demonstrate non-inferiority in renal function assessed by glomerular filtration rate (Nankivell formula) in at least one of the Certican treatment regimens compared to the standard group at Month 12 post-transplantation in renal transplant patients

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 December 2012
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	Germany: 442
Country: Number of subjects enrolled	France: 170
Worldwide total number of subjects	612
EEA total number of subjects	612

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	449
From 65 to 84 years	163

85 years and over	0
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Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

In total 659 patients were screened, 655 patients were randomized and 612 patients were treated.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	TAC+MPA

Arm description:

Tacrolimus, Mycophenolic acid (MPA), corticosteroids and Simulect

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

Dosage and administration details:

0.5 mg, 1 mg or 5 mg capsules, dosing schedule: according to standard blood levels

Investigational medicinal product name	Enteric Coated Mycophenolate Sodium (EC-MPS)
Investigational medicinal product code	
Other name	Mycophenolic Acid (MPA)
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Tablets: 180 mg or 360 mg. Dosing: duration of study 360 mg bid and no less than 360 mg daily dose

Investigational medicinal product name	Mycophenolate Mofetil (MMF)
Investigational medicinal product code	
Other name	Mycophenolic Acid (MPA)
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Capsules: 250 or 500 mg. Dosing: duration of study 500 mg bid and no less than 500 mg total daily dose

Arm title	TAC+Certican
Arm description:	
Tacrolimus, Certican, corticosteroids and Simulect	
Arm type	Experimental

Investigational medicinal product name	Everolimus
Investigational medicinal product code	RAD001
Other name	Certican
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

0.25 mg, 0.5 mg 0.75 mg or 1 mg tablets,
dosing schedule: according to blood levels

Arm title	CycA+Certican
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Arm description:

Cyclosporin A, Certican, corticosteroids and Simulect

Arm type	Experimental
Investigational medicinal product name	Basiliximab
Investigational medicinal product code	
Other name	Simulect
Pharmaceutical forms	Concentrate for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Lyophilisate in vials with ampoules of sterile water for injection (5 mL), one vial containing 20 mg lyophilisate given intravenously on the day of transplantation and on day four post-transplantation.

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

Dosage and administration details:

10 mg, 25 mg, 50 mg or 100 mg capsules, dosing schedule: according to standard blood levels

Number of subjects in period 1	TAC+MPA	TAC+Certican	CycA+Certican
Started	205	208	199
Safety analysis set (SAS)	204	208	198
Full analysis set (FAS)	205	208	199
Per protocol set (PPS)	147 ^[1]	111 ^[2]	80 ^[3]
Completed	182	168	158
Not completed	23	40	41
Adverse event, serious fatal	5	3	4
Consent withdrawn by subject	4	16	18
Graft loss/retransplantation	5	8	11
Various reasons	4	9	6
Lost to follow-up	5	4	2

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Milestones were added to provide number of participants in the analysis sets.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Milestones were added to provide number of participants in the analysis sets.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Milestones were added to provide number of participants in the analysis sets.

Baseline characteristics

Reporting groups

Reporting group title	TAC+MPA
Reporting group description: Tacrolimus, Mycophenolic acid (MPA), corticosteroids and Simulect	
Reporting group title	TAC+Certican
Reporting group description: Tacrolimus, Certican, corticosteroids and Simulect	
Reporting group title	CycA+Certican
Reporting group description: Cyclosporin A, Certican, corticosteroids and Simulect	

Reporting group values	TAC+MPA	TAC+Certican	CycA+Certican
Number of subjects	205	208	199
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: years			
arithmetic mean	55.3	54.3	55.1
standard deviation	± 12.09	± 13.5	± 12.61
Gender, Male/Female Units: Subjects			
Female	65	70	66
Male	140	138	133

Reporting group values	Total		
Number of subjects	612		
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years)	0 0 0 0 0 0 0		

From 65-84 years	0		
85 years and over	0		

Age Continuous Units: years arithmetic mean standard deviation	-		
Gender, Male/Female Units: Subjects			
Female	201		
Male	411		

End points

End points reporting groups

Reporting group title	TAC+MPA
Reporting group description:	
Tacrolimus, Mycophenolic acid (MPA), corticosteroids and Simulect	
Reporting group title	TAC+Certican
Reporting group description:	
Tacrolimus, Certican, corticosteroids and Simulect	
Reporting group title	CycA+Certican
Reporting group description:	
Cyclosporin A, Certican, corticosteroids and Simulect	
Subject analysis set title	Tac+Certican - Tac+MPA - difference between groups at Month 12
Subject analysis set type	Per protocol
Subject analysis set description:	
Analysis set is composed of Tac+Certican (111) - Tac+MPA (147) for a total of 258.	
Subject analysis set title	CycA+Certican - Tac+MPA - difference between groups
Subject analysis set type	Per protocol
Subject analysis set description:	
Analysis set is composed of CycA+Certican (80) - Tac+MPA (147) for a total of 227	

Primary: Glomerular filtration rate (GFR) mL/min via Nankivell method at Month 12 - Standard Regimen vs Certican regimens

End point title	Glomerular filtration rate (GFR) mL/min via Nankivell method at Month 12 - Standard Regimen vs Certican regimens
End point description:	
To demonstrate non-inferiority in renal function assessed by glomerular filtration rate (Nankivell formula) in at least one of the Certican® treatment regimens compared to the standard regimen group at month 12 post-transplantation in renal transplant patients. Nankivell formula: $GFR = 6.7/Scr + BW/4 - S_{urea}/2 - 100/(height)^2 + C$ where Scr is the serum creatinine concentration expressed in mmol/L, BW the body weight in kg, S _{urea} the serum urea in mmol/L, height in m, and the constant C is 35 for male and 25 for female patients. The eGFR is expressed in mL/min per 1.73m ² . If a patient was on dialysis at the time of urea or creatinine assessment, the eGFR was set to 0. Analysis set = per protocol set	
End point type	Primary
End point timeframe:	
One year post transplant	

End point values	TAC+MPA	TAC+Certican	CycA+Certican	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	147	111	80	
Units: mL/min per 1.73m ²				
arithmetic mean (standard deviation)				
Month 1 - Day 1 to 60 (146,111,78)	62.62 (± 16.931)	60.54 (± 17.31)	59.47 (± 16.754)	
Month 3 - Day 61 to 136 (143,108,79)	66.36 (± 16.672)	61.21 (± 14.771)	62.22 (± 16.196)	
Month 6 - Day 137 to 228 (142,108,76)	68.05 (± 16.994)	62.76 (± 16.763)	63.17 (± 16.789)	

Month 9 - Day 229 to 319 (140,106,77)	69.47 (± 16.251)	64.68 (± 15.507)	62.89 (± 14.947)	
Month12 - Day 320 to 450 (147,111, 80)	70.41 (± 16.514)	63.34 (± 16.986)	61.51 (± 16.942)	

Statistical analyses

Statistical analysis title	CycA+Certican - TAC+MPA at Month 12
Statistical analysis description:	
The trial tests the null hypotheses that the treatment difference (investigational minus reference) in mean eGFR at re-assigned visit Month 12 is lower than the non-inferiority margin (Δ) of 7 mL/min per 1.73m ² versus the alternative that the treatment difference is equal to or greater than the non-inferiority margin	
Comparison groups	TAC+MPA v CycA+Certican
Number of subjects included in analysis	227
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	ANOVA
Parameter estimate	Least square mean
Point estimate	-9.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.82
upper limit	-4.88

Statistical analysis title	TAC+Certican - TAC + MPA at Month 12
Comparison groups	TAC+MPA v TAC+Certican
Number of subjects included in analysis	258
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0067 ^[1]
Method	ANOVA
Parameter estimate	Least squares mean
Point estimate	-5.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.56
upper limit	-1.55

Notes:

[1] - Analysis of variance (ANOVA) with tx, center, donor type factors. Raw and adjusted means were presented with one-sided p-values for un-shifted and shifted hypothesis, respectively. Significance level = 2.5% (one-sided)

Secondary: Percentage of participants with composite treatment failure endpoints - difference between groups at month 12

End point title	Percentage of participants with composite treatment failure
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End point description:

Combined endpoint included: biopsy proven acute rejection (BPAR) defined as a rejection which was acute and proven by biopsy, graft loss (GL) defined as: allograft was presumed to be lost on the day the patient starts dialysis and not able to be removed from dialysis or death. Patients who prematurely discontinued the study: if the patient did not suffer from an event before discontinuation and reason was not related to efficacy, the patient was assessed as having had no event, otherwise the patient was assessed as having had an event. Full analysis set (FAS)

End point type	Secondary
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End point timeframe:

Month 12 post transplant

End point values	TAC+MPA	TAC+Certican	CycA+Certican	Tac+Certican - Tac+MPA - difference between groups at Month 12
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	205	208	199	413
Units: Percentage of participants				
number (not applicable)				
BPAR or graft loss or death	9.8	13	24.6	3.2
BPAR, graft loss, death, or loss of follow-up	15.6	22.6	32.7	7

End point values	CycA+Certican - Tac+MPA - difference between groups			
Subject group type	Subject analysis set			
Number of subjects analysed	404			
Units: Percentage of participants				
number (not applicable)				
BPAR or graft loss or death	14.9			
BPAR, graft loss, death, or loss of follow-up	17.1			

Statistical analyses

Statistical analysis title	TAC+Certican - TAC+MPA at Month 12
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Statistical analysis description:

TAC+Certican - TAC+MPA - difference between groups

Comparison groups	TAC+MPA v TAC+Certican
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Number of subjects included in analysis	413
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Point estimate
Point estimate	0.032
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.029
upper limit	0.093

Statistical analysis title	CycA+Certican -Tac+MPA at Month 12
Statistical analysis description:	
CycA+Certican -Tac+MPA - difference between groups	
Comparison groups	TAC+MPA v CycA+Certican
Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Point estimate
Point estimate	0.149
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.076
upper limit	0.221

Secondary: Glomerular filtration rate (GFR) via Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) method at month 12 post transplant

End point title	Glomerular filtration rate (GFR) via Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) method at month 12 post transplant
End point description:	
Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) method = $GFR = 141 \times \min(Scr/\kappa, 1)^\alpha \times \max(Scr/\kappa, 1)^{1.209} \times 0.993^{Age} \times 1.018$ [if female] $\times 1.159$ [if black] where Scr is serum creatinine, κ is 0.7 for females and 0.9 for males, α is 0.329 for females and 0.411 for males, min indicates the minimum of Scr/ κ or 1, and max indicates the maximum of Scr/ κ or 1. last observation carried forward (LOCF) was used for imputation of missing values, ANCOVA model	
End point type	Secondary
End point timeframe:	
Month 12 post transplant	

End point values	TAC+MPA	TAC+Certican	CycA+Certican	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	181	166	158	
Units: mL/min per 1.73m ²				
least squares mean (confidence interval 95%)	51.62 (48.1 to 55.14)	44.42 (40.95 to 47.89)	42.44 (38.89 to 45.99)	

Statistical analyses

No statistical analyses for this end point

Secondary: Glomular filtration rate (GFR) mL/min via Cockcroft- Gault method at month 12 post transplant

End point title	Glomular filtration rate (GFR) mL/min via Cockcroft- Gault method at month 12 post transplant
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End point description:

Cockcroft-Gault formula: For men: $GFR = ((140 - \text{age}) \times \text{body weight in kg}) / (72 \times \text{serum creatinine in mg/dl})$ For women: $GFR = (0.85 \times (140 - \text{age}) \times \text{body weight in kg}) / (72 \times \text{serum creatinine in mg/dl})$, last observation carried forward (LOCF) was used for imputation of missing values, ANCOVA model

End point type	Secondary
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End point timeframe:

Month 12 post transplant

End point values	TAC+MPA	TAC+Certican	CycA+Certican	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	174	162	151	
Units: mL/min per 1.73m ²				
least squares mean (confidence interval 95%)	60.26 (55.85 to 64.68)	52.25 (47.88 to 56.61)	51.3 (46.85 to 55.74)	

Statistical analyses

No statistical analyses for this end point

Secondary: Glomular filtration rate (GFR) via Modification of Diet in Renal Disease (MDRD) method at month 12 post transplant

End point title	Glomular filtration rate (GFR) via Modification of Diet in Renal Disease (MDRD) method at month 12 post transplant
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End point description:

Modification of Diet in Renal Disease (MDRD) = For men: $GFR = 170 \times (\text{serum creatinine}^{-0.999}) \times (\text{age}^{-0.176}) \times (\text{urea nitrogen}^{-0.17}) \times (\text{albumin}^{0.318})$ For women: $GFR = 170 \times (\text{serum creatinine}^{-0.999}) \times (\text{age}^{-0.176}) \times (\text{urea nitrogen}^{-0.17}) \times \text{albumin}^{0.318} \times 0.762$ with urea nitrogen = urea / 2.144. last observation carried forward (LOCF) was used for imputation of missing values, ANCOVA model

End point type	Secondary
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End point timeframe:
Month 12 post transplant

End point values	TAC+MPA	TAC+Certican	CycA+Certican	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	172	156	140	
Units: mL/min per 1.73m ²				
least squares mean (confidence interval 95%)	53.24 (49.62 to 56.87)	45.72 (42.11 to 49.32)	43.47 (39.75 to 47.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with treatment failure endpoints at month 12

End point title	Percentage of participants with treatment failure endpoints at month 12
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End point description:

Treatment failure endpoints: biopsy proven acute rejection (BPAR) defined as a rejection which was acute and proven by biopsy, graft loss (GL) defined as: allograft was presumed to be lost on the day the patient starts dialysis and not able to be removed from dialysis or death. Patients who prematurely discontinued the study: if the patient did not suffer from an event before discontinuation and reason was not related to efficacy, the patient was assessed as having had no event, otherwise the patient was assessed as having had an event. Full analysis set (FAS)

End point type	Secondary
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End point timeframe:

Month 12 post transplant

End point values	TAC+MPA	TAC+Certican	CycA+Certican	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	205	208	199	
Units: Percentage of participants				
number (not applicable)				
Biopsy proven acute rejection (BPAR)	9.3	12	24.6	
Treated BPAR (tBPAR)	8.8	11.5	23.6	
Graft loss	5.4	6.3	9	
Death	4.9	6.3	6.5	

Statistical analyses

Statistical analysis title	TAC+Certican - TAC+MPA at Month 12
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Statistical analysis description:

BPAR - treatment differences at Month 12

Comparison groups	TAC+MPA v TAC+Certican
Number of subjects included in analysis	413
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Pearson's chi-square test
Parameter estimate	Log odds ratio
Point estimate	0.028
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.032
upper limit	0.087

Secondary: Percent of participants with delayed graft function and slow graft function

End point title	Percent of participants with delayed graft function and slow graft function
End point description: Delayed graft function (DGF) was defined as the need for dialysis within the first 7 days post-transplantation, excluding the first post-transplantation day. Slow graft function (SGF) was defined as a serum creatinine >3.0 mg/dL at Day 5 post-transplantation. Full analysis set	
End point type	Secondary
End point timeframe: Post transplant to month 12	

End point values	TAC+MPA	TAC+Certican	CycA+Certican	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	205	208	199	
Units: Percent of participants				
number (not applicable)				
Delayed graft function (197,187,172)	17.8	20.3	22.1	
Slow graft function (195,187,171)	46.2	48.7	49.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of participants with delayed graft function by day

End point title	Percent of participants with delayed graft function by day
End point description: Delayed graft function (DGF) was defined as the need for dialysis within the first 7 days post-transplantation, excluding the first post-transplantation day.	
End point type	Secondary

End point timeframe:

Post transplant up to day 7

End point values	TAC+MPA	TAC+Certican	CycA+Certican	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	38	38	
Units: Percent of participants				
number (not applicable)				
day 1 (8,7,4)	22.9	18.4	10.5	
day 2 (2,2,2)	5.7	5.3	5.3	
day 3 (5,1,2)	14.3	2.6	5.3	
day 4 (4,2,4)	11.4	5.3	10.5	
day 5 (4,5,3)	11.4	13.2	7.9	
day 6 (1,1,2)	2.9	2.6	5.3	
day 7 (2,4,0)	5.7	10.5	0	
>7 days (9,16,21)	25.7	42.1	55.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of participants with viral infections

End point title	Percent of participants with viral infections
End point description:	
Viral infections for BKV-Virus (Humane Polyomavirus 1) and Cytomegalovirus (CMV)	
End point type	Secondary
End point timeframe:	
Post transplant to month 12	

End point values	TAC+MPA	TAC+Certican	CycA+Certican	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	204	208 ^[2]	198	
Units: Percent of participants				
number (not applicable)				
Viral infections - CMV Missing	1	0	1	
Viral infections - CMV Asymptomatic	7	1	1	
Viral infections - CMV Mild	5	2	1	
Viral infections - CMV Moderate	6	1	1	
Viral infections - CMV Severe	1	0	0	
Viral infections - BKV Asymptomatic	10	8	5	
Viral infections - BKV Mild	5	7	3	
Viral infections - BKV Moderate	7	2	1	
Viral infections - BKV Severe	0	0	0	

Notes:

[2] - Number of subjects analyzed is 210: 2 pt rec'd TAC+Cert in error-analyzed w TAC+Cert

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of participants with wound healing complications during study

End point title	Percent of participants with wound healing complications during study
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End point description:

Information collected to report wound healing process which included percentage of participants with complications, fluid collections detected and occurrence of lymphoceles

End point type	Secondary
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End point timeframe:

Post transplant until individual reporting

End point values	TAC+MPA	TAC+Certican	CycA+Certican	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	204	208	198	
Units: Percent of participants				
number (not applicable)				
Wound healing complication	14.3	19.1	22.2	
Fluids detected	18.7	26.8	27.8	
Occurrence of lymphoceles	11.8	18.2	21.8	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of wound healing

End point title	Duration of wound healing
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End point description:

A wound will be considered healed if all the suture material and staples are removed and the wound is intact. Number of participants is based on all patients of the respective treatment group in the safety set, excluding patients with no answer (unknown).

End point type	Secondary
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End point timeframe:

Post transplant until individual reporting

End point values	TAC+MPA	TAC+Certican	CycA+Certican	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	28	34	38	
Units: days				
arithmetic mean (standard deviation)	42.4 (± 41.13)	54.1 (± 61.97)	85.3 (± 62.7)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

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

Adverse event reporting additional description:

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

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Tac+MPA
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Reporting group description:

Tac+MPA

Reporting group title	CycA+Certican
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Reporting group description:

CycA+Certican

Reporting group title	Tac+Certican
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Reporting group description:

Tac+Certican

Serious adverse events	Tac+MPA	CycA+Certican	Tac+Certican
Total subjects affected by serious adverse events			
subjects affected / exposed	135 / 204 (66.18%)	144 / 198 (72.73%)	161 / 210 (76.67%)
number of deaths (all causes)	4	2	2
number of deaths resulting from adverse events	0	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-cell unclassifiable lymphoma high grade			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal cell carcinoma			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Bowen's disease			

subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Cardiac myxoma			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac valve fibroelastoma			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Clear cell renal cell carcinoma			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Colon cancer			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Fibroma			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Lung neoplasm malignant			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Malignant melanoma			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Marrow hyperplasia			

subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Mucinous adenocarcinoma of appendix			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Neuroendocrine tumour			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parathyroid tumour benign			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	1 / 204 (0.49%)	1 / 198 (0.51%)	0 / 210 (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
Rectal neoplasm			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal cancer			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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 cell carcinoma			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seminoma			

subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Arteriosclerosis			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriovenous fistula			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	2 / 204 (0.98%)	3 / 198 (1.52%)	0 / 210 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma			
subjects affected / exposed	5 / 204 (2.45%)	3 / 198 (1.52%)	9 / 210 (4.29%)
occurrences causally related to treatment / all	0 / 5	1 / 3	2 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	3 / 210 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	2 / 210 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive crisis			
subjects affected / exposed	3 / 204 (1.47%)	1 / 198 (0.51%)	0 / 210 (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
Hypotension			

subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Lymphocele			
subjects affected / exposed	12 / 204 (5.88%)	24 / 198 (12.12%)	19 / 210 (9.05%)
occurrences causally related to treatment / all	0 / 12	17 / 28	14 / 21
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphoedema			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Lymphorrhoea			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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	0 / 204 (0.00%)	1 / 198 (0.51%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic venous thrombosis			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral artery aneurysm			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral artery stenosis			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Phlebitis deep			

subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shock haemorrhagic			
subjects affected / exposed	0 / 204 (0.00%)	3 / 198 (1.52%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subclavian vein thrombosis			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Thrombosis			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vena cava thrombosis			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Venous thrombosis			
subjects affected / exposed	1 / 204 (0.49%)	1 / 198 (0.51%)	0 / 210 (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
Surgical and medical procedures			
Renal transplant			
subjects affected / exposed	4 / 204 (1.96%)	5 / 198 (2.53%)	5 / 210 (2.38%)
occurrences causally related to treatment / all	0 / 4	3 / 5	1 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Steroid therapy			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transurethral prostatectomy			

subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular anastomosis			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug intolerance			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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 physical health deterioration			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperthermia			
subjects affected / exposed	1 / 204 (0.49%)	1 / 198 (0.51%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impaired healing			
subjects affected / exposed	2 / 204 (0.98%)	4 / 198 (2.02%)	5 / 210 (2.38%)
occurrences causally related to treatment / all	0 / 2	4 / 4	5 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incarcerated hernia			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Inflammation			

subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Malaise			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 204 (0.00%)	3 / 198 (1.52%)	0 / 210 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Oedema			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Oedema peripheral			
subjects affected / exposed	0 / 204 (0.00%)	2 / 198 (1.01%)	4 / 210 (1.90%)
occurrences causally related to treatment / all	0 / 0	0 / 2	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
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 swelling			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Immune system disorders			
Anaphylactic reaction			

subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic allograft nephropathy			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Hypersensitivity			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kidney transplant rejection			
subjects affected / exposed	8 / 204 (3.92%)	22 / 198 (11.11%)	19 / 210 (9.05%)
occurrences causally related to treatment / all	0 / 8	5 / 27	3 / 22
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal transplant failure			
subjects affected / exposed	8 / 204 (3.92%)	11 / 198 (5.56%)	9 / 210 (4.29%)
occurrences causally related to treatment / all	0 / 9	1 / 12	1 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transplant rejection			
subjects affected / exposed	8 / 204 (3.92%)	17 / 198 (8.59%)	5 / 210 (2.38%)
occurrences causally related to treatment / all	0 / 10	5 / 20	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	3 / 204 (1.47%)	3 / 198 (1.52%)	2 / 210 (0.95%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometriosis			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Ovarian cyst			

subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Pelvic haematoma			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostatitis			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	1 / 204 (0.49%)	1 / 198 (0.51%)	0 / 210 (0.00%)
occurrences causally related to treatment / all	0 / 3	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	2 / 210 (0.95%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea exertional			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Haemoptysis			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemothorax			

subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial lung disease			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal cyst			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung disorder			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Pleural effusion			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Pulmonary congestion			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Pulmonary embolism			
subjects affected / exposed	4 / 204 (1.96%)	5 / 198 (2.53%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 4	0 / 6	1 / 1
deaths causally related to treatment / all	0 / 3	0 / 0	0 / 0
Pulmonary mass			

subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	3 / 210 (1.43%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 204 (0.00%)	3 / 198 (1.52%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Affective disorder			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Depression			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depressive symptom			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Disorientation			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Mental disorder			

subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device leakage			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Device occlusion			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	2 / 204 (0.98%)	0 / 198 (0.00%)	0 / 210 (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
Hydrocholecystis			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Portal vein thrombosis			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Anticoagulation drug level below therapeutic			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatine increased			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	2 / 210 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Blood creatinine decreased subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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 creatinine increased subjects affected / exposed	11 / 204 (5.39%)	19 / 198 (9.60%)	20 / 210 (9.52%)
occurrences causally related to treatment / all	0 / 11	5 / 22	6 / 22
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
C-reactive protein increased subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac monitoring subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Creatinine renal clearance decreased subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Epstein-Barr virus antigen positive subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
General physical condition abnormal subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Haemoglobin decreased subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic enzyme increased			

subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	2 / 210 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight decreased			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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			
Abdominal wound dehiscence			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Anastomotic complication			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Ankle fracture			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
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 injury			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Arteriovenous fistula site complication			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriovenous fistula thrombosis			
subjects affected / exposed	1 / 204 (0.49%)	1 / 198 (0.51%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Complications of transplanted kidney			

subjects affected / exposed	18 / 204 (8.82%)	18 / 198 (9.09%)	22 / 210 (10.48%)
occurrences causally related to treatment / all	0 / 18	3 / 18	4 / 23
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Femoral neck fracture			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Graft complication			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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 haemorrhage			
subjects affected / exposed	0 / 204 (0.00%)	4 / 198 (2.02%)	2 / 210 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Graft thrombosis			
subjects affected / exposed	1 / 204 (0.49%)	2 / 198 (1.01%)	2 / 210 (0.95%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hand fracture			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Incisional hernia			

subjects affected / exposed	0 / 204 (0.00%)	3 / 198 (1.52%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	1 / 3	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kidney rupture			
subjects affected / exposed	0 / 204 (0.00%)	2 / 198 (1.01%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perinephric collection			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Perirenal haematoma			
subjects affected / exposed	2 / 204 (0.98%)	0 / 198 (0.00%)	0 / 210 (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
Post procedural haematoma			
subjects affected / exposed	1 / 204 (0.49%)	3 / 198 (1.52%)	0 / 210 (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
Post procedural haematuria			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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 / 204 (0.00%)	4 / 198 (2.02%)	2 / 210 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural urine leak			

subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Radius fracture			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Seroma			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shunt aneurysm			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Shunt blood flow excessive			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Shunt occlusion			
subjects affected / exposed	2 / 204 (0.98%)	0 / 198 (0.00%)	0 / 210 (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
Shunt thrombosis			
subjects affected / exposed	3 / 204 (1.47%)	0 / 198 (0.00%)	3 / 210 (1.43%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxicity to various agents			

subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transplant dysfunction			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Traumatic haematoma			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic haemothorax			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Ureteric anastomosis complication			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	2 / 210 (0.95%)
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 graft stenosis			
subjects affected / exposed	2 / 204 (0.98%)	0 / 198 (0.00%)	0 / 210 (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
Wound dehiscence			
subjects affected / exposed	3 / 204 (1.47%)	4 / 198 (2.02%)	3 / 210 (1.43%)
occurrences causally related to treatment / all	0 / 4	3 / 4	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound necrosis			
subjects affected / exposed	1 / 204 (0.49%)	1 / 198 (0.51%)	0 / 210 (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
Congenital, familial and genetic disorders			
Abdominal wall anomaly			

subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Congenital cystic kidney disease			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Hydrocele			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
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 disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 204 (0.00%)	2 / 198 (1.01%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	2 / 204 (0.98%)	3 / 198 (1.52%)	2 / 210 (0.95%)
occurrences causally related to treatment / all	0 / 2	1 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	4 / 204 (1.96%)	1 / 198 (0.51%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block second degree			

subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradyarrhythmia			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Bradycardia			
subjects affected / exposed	1 / 204 (0.49%)	1 / 198 (0.51%)	0 / 210 (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 failure			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac flutter			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Cardiogenic shock			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	2 / 210 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardiomyopathy			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiovascular disorder			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Coronary artery disease			

subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracardiac thrombus			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Long QT syndrome			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mitral valve disease			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Myocardial infarction			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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			
Balance disorder			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Cerebral ischaemia			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Monoparesis			

subjects affected / exposed	0 / 204 (0.00%)	2 / 198 (1.01%)	0 / 210 (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
Neuralgia			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Polyneuropathy			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post herpetic neuralgia			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sensory loss			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 204 (0.49%)	4 / 198 (2.02%)	3 / 210 (1.43%)
occurrences causally related to treatment / all	0 / 1	0 / 4	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Haemolytic uraemic syndrome			

subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Histiocytosis haematophagic			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Leukopenia			
subjects affected / exposed	5 / 204 (2.45%)	2 / 198 (1.01%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 5	2 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenopathy			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphatic disorder			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Nephrogenic anaemia			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Neutropenia			
subjects affected / exposed	2 / 204 (0.98%)	0 / 198 (0.00%)	0 / 210 (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
Pancytopenia			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Splenic lesion			

subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Thrombocytopenia			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Sudden hearing loss			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Vertigo			
subjects affected / exposed	1 / 204 (0.49%)	1 / 198 (0.51%)	0 / 210 (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
Eye disorders			
Eyelid oedema			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal detachment			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
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 disorders			
Abdominal distension			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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 hernia			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	1 / 210 (0.48%)
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 pain			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	1 / 210 (0.48%)
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 pain upper			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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 wall haematoma			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal sphincter atony			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis microscopic			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticular perforation			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			

subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 204 (0.49%)	1 / 198 (0.51%)	0 / 210 (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
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Haemorrhoids			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hernial eventration			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Hiatus hernia			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal ischaemia			

subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intra-abdominal haematoma			
subjects affected / exposed	1 / 204 (0.49%)	1 / 198 (0.51%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Localised intraabdominal fluid collection			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower gastrointestinal haemorrhage			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Nausea			
subjects affected / exposed	2 / 204 (0.98%)	0 / 198 (0.00%)	0 / 210 (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
Oesophageal ulcer			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
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	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritoneal haemorrhage			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Pneumoperitoneum			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
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	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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 / 204 (0.00%)	0 / 198 (0.00%)	2 / 210 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retroperitoneal haemorrhage			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	0 / 204 (0.00%)	2 / 198 (1.01%)	0 / 210 (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
Volvulus			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
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 and subcutaneous tissue disorders			
Actinic keratosis			

subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Angioedema			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	2 / 210 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin lesion			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin ulcer			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stasis dermatitis			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
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 and urinary disorders			
Acute kidney injury			
subjects affected / exposed	9 / 204 (4.41%)	7 / 198 (3.54%)	12 / 210 (5.71%)
occurrences causally related to treatment / all	0 / 10	2 / 9	3 / 13
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder pain			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder tamponade			

subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Dysuria			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Focal segmental glomerulosclerosis			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glomerulonephritis			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Hydronephrosis			
subjects affected / exposed	2 / 204 (0.98%)	0 / 198 (0.00%)	4 / 210 (1.90%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Micturition disorder			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Nephrocalcinosis			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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	0 / 204 (0.00%)	3 / 198 (1.52%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postrenal failure			

subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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 / 204 (0.00%)	1 / 198 (0.51%)	5 / 210 (2.38%)
occurrences causally related to treatment / all	0 / 0	1 / 1	3 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal artery dissection			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
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 artery stenosis			
subjects affected / exposed	4 / 204 (1.96%)	2 / 198 (1.01%)	2 / 210 (0.95%)
occurrences causally related to treatment / all	0 / 4	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal cyst			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
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 cyst haemorrhage			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
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 failure			
subjects affected / exposed	1 / 204 (0.49%)	1 / 198 (0.51%)	0 / 210 (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
Renal haematoma			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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 haemorrhage			

subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
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 impairment			
subjects affected / exposed	2 / 204 (0.98%)	4 / 198 (2.02%)	8 / 210 (3.81%)
occurrences causally related to treatment / all	0 / 2	0 / 4	1 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal infarct			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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 tubular disorder			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	2 / 210 (0.95%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal tubular necrosis			
subjects affected / exposed	0 / 204 (0.00%)	2 / 198 (1.01%)	0 / 210 (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
Ureteral necrosis			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	2 / 210 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureteric stenosis			
subjects affected / exposed	1 / 204 (0.49%)	1 / 198 (0.51%)	2 / 210 (0.95%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urethral stenosis			
subjects affected / exposed	2 / 204 (0.98%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary fistula			

subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			
subjects affected / exposed	3 / 204 (1.47%)	1 / 198 (0.51%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract obstruction			
subjects affected / exposed	1 / 204 (0.49%)	2 / 198 (1.01%)	5 / 210 (2.38%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinoma			
subjects affected / exposed	1 / 204 (0.49%)	2 / 198 (1.01%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 1	1 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vesicoureteric reflux			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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			
Hyperparathyroidism			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parathyroid gland enlargement			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Hypercreatinaemia			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Muscle haemorrhage			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myalgia			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal osteoarthritis			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Aspergillus infection			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atypical pneumonia			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BK virus infection			

subjects affected / exposed	3 / 204 (1.47%)	1 / 198 (0.51%)	3 / 210 (1.43%)
occurrences causally related to treatment / all	0 / 3	0 / 1	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	2 / 210 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial pyelonephritis			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	2 / 204 (0.98%)	2 / 198 (1.01%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Corona virus infection			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cryptosporidiosis infection			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Cytomegalovirus colitis			

subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Cytomegalovirus infection			
subjects affected / exposed	11 / 204 (5.39%)	2 / 198 (1.01%)	2 / 210 (0.95%)
occurrences causally related to treatment / all	0 / 13	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea infectious			
subjects affected / exposed	4 / 204 (1.96%)	6 / 198 (3.03%)	6 / 210 (2.86%)
occurrences causally related to treatment / all	0 / 4	1 / 6	4 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Enterococcal infection			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Enterocolitis viral			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Epididymitis			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Epstein-Barr virus infection			

subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	1 / 204 (0.49%)	1 / 198 (0.51%)	0 / 210 (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
Escherichia infection			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia sepsis			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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 infection			
subjects affected / exposed	2 / 204 (0.98%)	2 / 198 (1.01%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 2	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	2 / 204 (0.98%)	3 / 198 (1.52%)	5 / 210 (2.38%)
occurrences causally related to treatment / all	0 / 2	1 / 3	4 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis norovirus			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Graft infection			
subjects affected / exposed	1 / 204 (0.49%)	1 / 198 (0.51%)	4 / 210 (1.90%)
occurrences causally related to treatment / all	0 / 1	2 / 2	3 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemophilus infection			

subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Herpes simplex			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
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 zoster			
subjects affected / exposed	2 / 204 (0.98%)	0 / 198 (0.00%)	0 / 210 (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
Infected lymphocele			
subjects affected / exposed	1 / 204 (0.49%)	3 / 198 (1.52%)	2 / 210 (0.95%)
occurrences causally related to treatment / all	0 / 1	3 / 3	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	2 / 204 (0.98%)	5 / 198 (2.53%)	5 / 210 (2.38%)
occurrences causally related to treatment / all	0 / 2	2 / 5	3 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	3 / 210 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kidney infection			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Klebsiella infection			
subjects affected / exposed	0 / 204 (0.00%)	2 / 198 (1.01%)	0 / 210 (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
Localised infection			

subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Lung infection			
subjects affected / exposed	2 / 204 (0.98%)	1 / 198 (0.51%)	3 / 210 (1.43%)
occurrences causally related to treatment / all	0 / 2	1 / 1	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mastitis			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Myocarditis infectious			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orchitis			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	1 / 204 (0.49%)	1 / 198 (0.51%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	4 / 204 (1.96%)	8 / 198 (4.04%)	10 / 210 (4.76%)
occurrences causally related to treatment / all	0 / 4	6 / 8	6 / 11
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
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 fungal			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia legionella			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Polyomavirus-associated nephropathy			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Pulmonary sepsis			
subjects affected / exposed	0 / 204 (0.00%)	2 / 198 (1.01%)	0 / 210 (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
Pyelonephritis			
subjects affected / exposed	10 / 204 (4.90%)	8 / 198 (4.04%)	9 / 210 (4.29%)
occurrences causally related to treatment / all	0 / 12	7 / 12	6 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	5 / 210 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 1	2 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal abscess			

subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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 cyst infection			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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 tract infection			
subjects affected / exposed	1 / 204 (0.49%)	1 / 198 (0.51%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotavirus infection			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	5 / 210 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 1	4 / 5
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Septic shock			
subjects affected / exposed	2 / 204 (0.98%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Shunt infection			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	2 / 210 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection			

subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureteritis			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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 tract infection			
subjects affected / exposed	21 / 204 (10.29%)	16 / 198 (8.08%)	27 / 210 (12.86%)
occurrences causally related to treatment / all	0 / 27	9 / 24	16 / 38
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	9 / 204 (4.41%)	7 / 198 (3.54%)	6 / 210 (2.86%)
occurrences causally related to treatment / all	0 / 10	4 / 7	2 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicella zoster virus infection			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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 infection			
subjects affected / exposed	2 / 204 (0.98%)	0 / 198 (0.00%)	0 / 210 (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
Metabolism and nutrition disorders			
Acidosis			

subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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
Decreased appetite			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Dehydration			
subjects affected / exposed	2 / 204 (0.98%)	3 / 198 (1.52%)	3 / 210 (1.43%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			
subjects affected / exposed	3 / 204 (1.47%)	4 / 198 (2.02%)	5 / 210 (2.38%)
occurrences causally related to treatment / all	0 / 3	0 / 4	2 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 204 (0.00%)	1 / 198 (0.51%)	0 / 210 (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 ketoacidosis			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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
Hypercalcaemia			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			

subjects affected / exposed	5 / 204 (2.45%)	1 / 198 (0.51%)	3 / 210 (1.43%)
occurrences causally related to treatment / all	0 / 5	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypocalcaemia			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	2 / 210 (0.95%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	0 / 210 (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	0 / 204 (0.00%)	0 / 198 (0.00%)	3 / 210 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophosphataemia			
subjects affected / exposed	1 / 204 (0.49%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 204 (0.00%)	0 / 198 (0.00%)	1 / 210 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
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	Tac+MPA	CycA+Certican	Tac+Certican
Total subjects affected by non-serious adverse events			
subjects affected / exposed	200 / 204 (98.04%)	196 / 198 (98.99%)	205 / 210 (97.62%)
Vascular disorders			
Haematoma			
subjects affected / exposed	10 / 204 (4.90%)	17 / 198 (8.59%)	16 / 210 (7.62%)
occurrences (all)	10	19	17
Hypertension			

subjects affected / exposed occurrences (all)	52 / 204 (25.49%) 61	57 / 198 (28.79%) 65	62 / 210 (29.52%) 78
Hypotension subjects affected / exposed occurrences (all)	13 / 204 (6.37%) 14	16 / 198 (8.08%) 16	11 / 210 (5.24%) 13
Lymphocele subjects affected / exposed occurrences (all)	20 / 204 (9.80%) 20	31 / 198 (15.66%) 31	22 / 210 (10.48%) 23
Surgical and medical procedures Renal transplant subjects affected / exposed occurrences (all)	8 / 204 (3.92%) 8	17 / 198 (8.59%) 19	9 / 210 (4.29%) 12
General disorders and administration site conditions Impaired healing subjects affected / exposed occurrences (all)	5 / 204 (2.45%) 5	15 / 198 (7.58%) 15	13 / 210 (6.19%) 13
Oedema subjects affected / exposed occurrences (all)	11 / 204 (5.39%) 12	8 / 198 (4.04%) 9	9 / 210 (4.29%) 11
Oedema peripheral subjects affected / exposed occurrences (all)	62 / 204 (30.39%) 77	99 / 198 (50.00%) 117	82 / 210 (39.05%) 103
Immune system disorders Kidney transplant rejection subjects affected / exposed occurrences (all)	8 / 204 (3.92%) 8	14 / 198 (7.07%) 18	9 / 210 (4.29%) 9
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	11 / 204 (5.39%) 13	14 / 198 (7.07%) 14	15 / 210 (7.14%) 17
Dyspnoea subjects affected / exposed occurrences (all)	21 / 204 (10.29%) 23	19 / 198 (9.60%) 24	22 / 210 (10.48%) 24
Psychiatric disorders Anxiety			

subjects affected / exposed occurrences (all)	8 / 204 (3.92%) 8	9 / 198 (4.55%) 10	15 / 210 (7.14%) 16
Insomnia subjects affected / exposed occurrences (all)	41 / 204 (20.10%) 44	24 / 198 (12.12%) 25	39 / 210 (18.57%) 40
Sleep disorder subjects affected / exposed occurrences (all)	22 / 204 (10.78%) 26	22 / 198 (11.11%) 31	21 / 210 (10.00%) 23
Investigations Blood creatinine increased subjects affected / exposed occurrences (all)	25 / 204 (12.25%) 28	26 / 198 (13.13%) 31	27 / 210 (12.86%) 29
Blood glucose increased subjects affected / exposed occurrences (all)	6 / 204 (2.94%) 6	8 / 198 (4.04%) 8	15 / 210 (7.14%) 16
C-reactive protein increased subjects affected / exposed occurrences (all)	9 / 204 (4.41%) 9	13 / 198 (6.57%) 14	15 / 210 (7.14%) 19
Haemoglobin decreased subjects affected / exposed occurrences (all)	9 / 204 (4.41%) 9	9 / 198 (4.55%) 11	11 / 210 (5.24%) 12
Injury, poisoning and procedural complications Complications of transplanted kidney subjects affected / exposed occurrences (all)	28 / 204 (13.73%) 28	43 / 198 (21.72%) 47	36 / 210 (17.14%) 37
Procedural pain subjects affected / exposed occurrences (all)	26 / 204 (12.75%) 30	21 / 198 (10.61%) 21	25 / 210 (11.90%) 26
Wound complication subjects affected / exposed occurrences (all)	68 / 204 (33.33%) 76	56 / 198 (28.28%) 63	64 / 210 (30.48%) 75
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all)	14 / 204 (6.86%) 14	10 / 198 (5.05%) 13	10 / 210 (4.76%) 10
Nervous system disorders			

Headache			
subjects affected / exposed	15 / 204 (7.35%)	15 / 198 (7.58%)	25 / 210 (11.90%)
occurrences (all)	15	18	30
Tremor			
subjects affected / exposed	30 / 204 (14.71%)	9 / 198 (4.55%)	22 / 210 (10.48%)
occurrences (all)	30	9	22
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	44 / 204 (21.57%)	58 / 198 (29.29%)	53 / 210 (25.24%)
occurrences (all)	48	66	58
Leukopenia			
subjects affected / exposed	34 / 204 (16.67%)	11 / 198 (5.56%)	17 / 210 (8.10%)
occurrences (all)	35	11	20
Thrombocytopenia			
subjects affected / exposed	8 / 204 (3.92%)	20 / 198 (10.10%)	20 / 210 (9.52%)
occurrences (all)	8	20	22
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	16 / 204 (7.84%)	18 / 198 (9.09%)	18 / 210 (8.57%)
occurrences (all)	17	19	20
Abdominal pain upper			
subjects affected / exposed	14 / 204 (6.86%)	12 / 198 (6.06%)	19 / 210 (9.05%)
occurrences (all)	16	14	22
Constipation			
subjects affected / exposed	71 / 204 (34.80%)	81 / 198 (40.91%)	69 / 210 (32.86%)
occurrences (all)	76	88	82
Diarrhoea			
subjects affected / exposed	19 / 204 (9.31%)	6 / 198 (3.03%)	17 / 210 (8.10%)
occurrences (all)	20	8	20
Dyspepsia			
subjects affected / exposed	14 / 204 (6.86%)	9 / 198 (4.55%)	17 / 210 (8.10%)
occurrences (all)	15	9	18
Flatulence			
subjects affected / exposed	24 / 204 (11.76%)	25 / 198 (12.63%)	35 / 210 (16.67%)
occurrences (all)	30	26	36
Nausea			

subjects affected / exposed occurrences (all)	46 / 204 (22.55%) 55	42 / 198 (21.21%) 49	44 / 210 (20.95%) 49
Vomiting subjects affected / exposed occurrences (all)	27 / 204 (13.24%) 31	22 / 198 (11.11%) 23	22 / 210 (10.48%) 23
Skin and subcutaneous tissue disorders Acne subjects affected / exposed occurrences (all)	3 / 204 (1.47%) 3	4 / 198 (2.02%) 4	11 / 210 (5.24%) 12
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all)	14 / 204 (6.86%) 15	14 / 198 (7.07%) 14	14 / 210 (6.67%) 15
Haematuria subjects affected / exposed occurrences (all)	14 / 204 (6.86%) 15	13 / 198 (6.57%) 13	19 / 210 (9.05%) 19
Leukocyturia subjects affected / exposed occurrences (all)	14 / 204 (6.86%) 19	8 / 198 (4.04%) 9	13 / 210 (6.19%) 15
Nocturia subjects affected / exposed occurrences (all)	12 / 204 (5.88%) 12	14 / 198 (7.07%) 14	11 / 210 (5.24%) 12
Pollakiuria subjects affected / exposed occurrences (all)	9 / 204 (4.41%) 9	9 / 198 (4.55%) 9	11 / 210 (5.24%) 11
Proteinuria subjects affected / exposed occurrences (all)	24 / 204 (11.76%) 24	30 / 198 (15.15%) 31	26 / 210 (12.38%) 26
Renal impairment subjects affected / exposed occurrences (all)	15 / 204 (7.35%) 15	8 / 198 (4.04%) 12	13 / 210 (6.19%) 13
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	4 / 204 (1.96%) 4	11 / 198 (5.56%) 12	7 / 210 (3.33%) 9
Back pain			

subjects affected / exposed occurrences (all)	17 / 204 (8.33%) 17	10 / 198 (5.05%) 13	16 / 210 (7.62%) 17
Muscle spasms subjects affected / exposed occurrences (all)	9 / 204 (4.41%) 9	7 / 198 (3.54%) 7	11 / 210 (5.24%) 12
Infections and infestations			
BK virus infection subjects affected / exposed occurrences (all)	45 / 204 (22.06%) 53	18 / 198 (9.09%) 18	36 / 210 (17.14%) 41
Bronchitis subjects affected / exposed occurrences (all)	13 / 204 (6.37%) 18	4 / 198 (2.02%) 4	5 / 210 (2.38%) 5
Cytomegalovirus infection subjects affected / exposed occurrences (all)	33 / 204 (16.18%) 40	3 / 198 (1.52%) 3	11 / 210 (5.24%) 11
Diarrhoea infectious subjects affected / exposed occurrences (all)	56 / 204 (27.45%) 69	29 / 198 (14.65%) 35	40 / 210 (19.05%) 47
Nasopharyngitis subjects affected / exposed occurrences (all)	29 / 204 (14.22%) 34	21 / 198 (10.61%) 24	31 / 210 (14.76%) 39
Urinary tract infection subjects affected / exposed occurrences (all)	81 / 204 (39.71%) 135	72 / 198 (36.36%) 119	74 / 210 (35.24%) 140
Metabolism and nutrition disorders			
Diabetes mellitus subjects affected / exposed occurrences (all)	24 / 204 (11.76%) 25	24 / 198 (12.12%) 24	33 / 210 (15.71%) 34
Dyslipidaemia subjects affected / exposed occurrences (all)	2 / 204 (0.98%) 2	7 / 198 (3.54%) 7	11 / 210 (5.24%) 12
Fluid overload subjects affected / exposed occurrences (all)	7 / 204 (3.43%) 11	13 / 198 (6.57%) 13	7 / 210 (3.33%) 7
Hypercalcaemia			

subjects affected / exposed	16 / 204 (7.84%)	13 / 198 (6.57%)	16 / 210 (7.62%)
occurrences (all)	16	13	16
Hypercholesterolaemia			
subjects affected / exposed	5 / 204 (2.45%)	17 / 198 (8.59%)	16 / 210 (7.62%)
occurrences (all)	5	17	16
Hyperglycaemia			
subjects affected / exposed	12 / 204 (5.88%)	25 / 198 (12.63%)	20 / 210 (9.52%)
occurrences (all)	14	26	20
Hyperkalaemia			
subjects affected / exposed	65 / 204 (31.86%)	58 / 198 (29.29%)	53 / 210 (25.24%)
occurrences (all)	79	71	57
Hyperlipidaemia			
subjects affected / exposed	8 / 204 (3.92%)	23 / 198 (11.62%)	13 / 210 (6.19%)
occurrences (all)	8	23	13
Hyperphosphataemia			
subjects affected / exposed	5 / 204 (2.45%)	12 / 198 (6.06%)	7 / 210 (3.33%)
occurrences (all)	6	12	7
Hypertriglyceridaemia			
subjects affected / exposed	3 / 204 (1.47%)	10 / 198 (5.05%)	13 / 210 (6.19%)
occurrences (all)	3	11	13
Hyperuricaemia			
subjects affected / exposed	20 / 204 (9.80%)	14 / 198 (7.07%)	10 / 210 (4.76%)
occurrences (all)	20	14	10
Hypocalcaemia			
subjects affected / exposed	20 / 204 (9.80%)	17 / 198 (8.59%)	27 / 210 (12.86%)
occurrences (all)	21	17	29
Hypokalaemia			
subjects affected / exposed	33 / 204 (16.18%)	41 / 198 (20.71%)	37 / 210 (17.62%)
occurrences (all)	37	47	42
Hypophosphataemia			
subjects affected / exposed	23 / 204 (11.27%)	30 / 198 (15.15%)	36 / 210 (17.14%)
occurrences (all)	25	30	37
Iron deficiency			
subjects affected / exposed	6 / 204 (2.94%)	10 / 198 (5.05%)	8 / 210 (3.81%)
occurrences (all)	6	10	9
Metabolic acidosis			

subjects affected / exposed	24 / 204 (11.76%)	21 / 198 (10.61%)	25 / 210 (11.90%)
occurrences (all)	25	22	27
Vitamin D deficiency			
subjects affected / exposed	21 / 204 (10.29%)	14 / 198 (7.07%)	20 / 210 (9.52%)
occurrences (all)	21	14	20

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 April 2013	Amendment was to optimize patient safety and to enhance study performance and feasibility. Patient safety was optimized by limiting the risk of overexposure to Certican by change of starting dose. The Starting Dose was changed to 1.5 mg/day (2x 0.75mg).
13 August 2013	Amendment addresses exclusion criteria and visit assessments to be performed, enhances feasibility and patient safety. Exclusion criteria were changed in accordance to the informed consent and to add the term "total abstinence" to highly effective contraception methods. Further changes of the protocol comprised prevention of second blood drawings at baseline (not necessary), therefore enhanced safety for the patients
14 July 2014	Amendment was issued to update the investigator's brochure. According to the investigator's brochure contraception of 8 weeks after end of treatment was necessary as there was no data available that support a shorter time period. Informed consent was adapted according to these changes. In addition a higher recommended starting dose was recommended for patients receiving a combination of tacrolimus and Certican, due to different pharmacokinetics and to reach target everolimus trough level accurately timed
02 February 2015	Amendment was issued in response to German Health Authority's request. The protocol was modified to implement most recent notifications for use of MPA based on the dear health care professional letter (DHCPL) that was sent out for CellCept by Roche 12-Dec-2014. In detail the study medication stopping rules were adopted to clearly follow the recommendations given in the DHCPL.
12 January 2016	Amendment 5 (12-Jan-2016) was issued in response to German Health Authority's request, the protocol was modified to implement most recent notifications for use of MPA based on the dear health care professional letter (DHCPL) that was sent out for CellCept by Roche 10-Nov-2015

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported