NOVARTIS

Clinical Trial Results Website

Sponsor

Novartis Pharmaceuticals

Generic Drug Name

everolimus

Trial Indication(s)

de novo renal transplantation

Protocol Number

CRAD001A2433

Protocol Title

A 24 month, multicenter, randomized, open-label safety and efficacy study of concentration-controlled everolimus with reduced calcineurin inhibitor vs mycophenolate with standard calcineurin inhibitor in de novo renal transplantation

Clinical Trial Phase

Phase 4

Phase of Drug Development

Phase IV

Study Start/End Dates

Study Start Date: December 2013 (Actual)
Primary Completion Date: February 2017 (Actual)
Study Completion Date: January 2018 (Actual)

Reason for Termination (If applicable)

Study Design/Methodology

This was a 2-year, randomized, multicenter, open-label, 2-arm study evaluating graft function with everolimus and reduced CNI versus MPA and standard CNI in adult de novo renal transplant recipients. Consented subjects entered the screening period and upon meeting eligibility criteria, including successful transplantation, entered the initial 12 Month treatment period and then continued in the next treatment period to Month 24

Centers

196 centers in 42 countries: South Africa(1), Netherlands(6), Italy(10), Spain(10), Switzerland(1), Belgium(4), Germany(14), Egypt(1), Slovakia (Slovak Republic)(4), Czech Republic(2), Philippines(2), France(5), United States(45), Russia(6), Austria(2), Thailand(3), Singapore(1), Greece(4), Croatia(3), Taiwan(3), Serbia(3), Argentina(7), Australia(10), India(4), Korea, Republic of(3), Japan(3), Turkey(4), Bulgaria(1), Portugal(5), Slovenia(1), Colombia(2), Lebanon(3), Saudi Arabia(3), Malaysia(2), Brazil(3), Poland(6), Israel(2), Chile(1), Norway(1), Sweden(3), Mexico(1), Kuwait(1)

Objectives:

Primary objective:

To evaluate the effect of everolimus with reduced exposure CNI versus MPA with standard exposure CNI on the binary composite of treated biopsy-proven acute rejection (tBPAR) or eGFR <50 mL/min/1.73m^2 (estimated glomerular filtration rate by MDRD4 formula) at Month 12 post-transplantation.

Secondary objectives

- The incidence of composite endpoint of tBPAR or eGFR < 50 mL/min/1.73m2 (MDRD4) at Month 24.
- To evaluate everolimus with reduced exposure CNI compared to MPA plus standard exposure CNI at 12 months post-transplantation with respect to the composite efficacy failure rate of treated biopsy proven acute rejection (tBPAR), graft loss or death.

- The incidence of composite endpoint of tBPAR, graft loss, death or eGFR < 50 mL/min/1.73m2 at Months 12 and 24.
- The incidence of composite endpoint of graft loss or death at Month 12 and 24.
- The incidence of individual endpoints of death, graft loss, tBPAR, BPAR, tAR, AR and humoral rejection at Months 12 and 24.
- The incidence of transplant recipients with eGFR < 50 mL/min/1.73m2 at Months 12 and 24.
- Renal allograft function and change in renal allograft function from Month 1 (eGFR) at Months 12 and 24.
- The evolution of renal function, as eGFR, over time by slope analysis.
- Renal function by Cystatin C-based and other alternate formulae (e.g. CKD-EPI).
- The incidence of adverse events, serious adverse events and adverse events leading to study regimen discontinuation.
- The incidence of CMV and BKV, new onset diabetes mellitus, chronic kidney disease with associated proteinuria and CNI associated adverse events.
- Urinary protein and albumin excretion by treatment estimated by urinary protein/creatinine and urinary albumin/creatinine ratios.
- The incidence of major cardiovascular events.
- The incidence of malignancies.
- To evaluate the binary composite endpoint of tBPAR or eGFR <50 mL/min/1.73m^2 (MDRD4) at Month 12 among compliant patients
- The incidence of tBPAR by severity and time to event.
- The incidence of tBPAR excluding Banff 1A grade acute rejections.
- The incidence of composite endpoint of tBPAR or eGFR < 50 mL/min/1.73m2 (MDRD4) at Month 12 by subgroup.
- The incidence of composite endpoint of tBPAR (excluding Banff grade 1A acute rejections) or eGFR < 50 mL/min/1.73m2 (MDRD4) at Month 24.
- The incidence of composite endpoint of tBPAR, graft loss, death, or loss to follow-up at Months 12 and 24.

Test Product (s), Dose(s), and Mode(s) of Administration

Investigational drug: everolimus was provided as 0.25, 0.5 and 0.75 and 1.0 mg tablets depending on locally approved dosage forms.

Duration of treatment: 24 months

Reference therapy, dose and mode of administration, batch number: MPA was provided as either mycophenolic acid (sodium) 180 or 360mg enteric-coated tablets or mycophenolate mofetil 250 or 500 mg film coated tablets or 250mg capsules, depending on locally approved dosage forms.

Cyclosporine was provided as 10, 25, 50 and 100 mg capsules, and tacrolimus as 0.5, 1.0 mg and 5.0 mg capsules.

Statistical Methods

The primary analysis was based on data at Month 12. Since many of the secondary and exploratory objectives were based on Month 12 and Month 24 data, similar analyses were made for Month 24 results.

For the primary efficacy endpoint, non-inferiority of everolimus plus reduced CNI to MPA plus standard CNI was tested in the Full analysis set (consisting of all randomized and transplanted patients) using the null hypothesis:

- H_{01}: $R_{EVR+rCNI} - R_{MPA+sCNI} \geq 0.10$ (non-inferiority margin): the difference in proportion of patients experiencing tBPAR or eGFR (MDRD4) < 50 mL/min/1.73m^2 at 12 months between the everolimus plus reduced CNI ($R_{EVR+rCNI}$) and the MPA plus standard CNI arm ($R_{MPA+sCNI}$) is at least 10%.

The alternative hypothesis was:

- H_{A1}: $R_{EVR+rCNI} - R_{MPA+sCNI} < 0.10$ (non-inferiority margin): The difference in proportion of patients experiencing tBPAR or eGFR (MDRD4) < 50 mL/min/1.73m^2 at 12 months between the everolimus plus reduced CNI ($R_{EVR+rCNI}$) and the MPA plus standard CNI arm ($R_{MPA+sCNI}$) is less than 10%.

The proportion of subjects meeting the primary endpoint of tBPAR or eGFR (MDRD4) <50 mL/min/1.73m^2 at Month 12 was compared using a confidence interval approach.

For testing superiority of everolimus plus reduced CNI to MPA plus standard CNI, the null and alternative hypothesis were:

- H_{03}: $R_{EVR+rCNI} - R_{MPA+sCNI} \geq 0$: the proportion of patients experiencing tBPAR or eGFR (MDRD4) < 50 mL/min/1.73m^2 at 12 months in the everolimus plus reduced CNI ($R_{EVR+rCNI}$) arm is greater than or equal to that in the MPA plus standard CNI arm ($R_{MPA+sCNI}$) arm, vs.

- H_{A3}: REVR+rCNI - RMPA+sCNI < 0: the proportion of patients experiencing tBPAR or eGFR (MDRD4) < 50 mL/min/1.73m^2 at 12 months in the everolimus plus reduced CNI (REVR+rCNI) arm is less than that in the MPA plus standard CNI arm (RMPA+sCNI) arm.

For the key secondary composite efficacy failure of tBPAR, graft loss or death, the following hypotheses were evaluated (α=0.025, one-sided) only if non-inferiority of EVR plus reduced CNI vs. MPA plus standard CNI was achieved for the primary endpoint (rejecting the hypothesis H_{01}).

The null hypothesis:

- H_{02}: $R_{EVR+rCNI} - R_{MPA+sCNI} \geq 0.10$ (non-inferiority margin): the difference in Kaplan-Meier event rate of the composite efficacy failure of tBPAR, graft loss or death at 12 months between the everolimus plus reduced CNI ($R_{EVR+rCNI}$) and the MPA plus standard CNI arm ($R_{MPA+sCNI}$) is at least 10%.

The alternative hypothesis:

- H_{A2}: $R_{EVR+rCNI} - R_{MPA+sCNI} < 0.10$ (non-inferiority margin): the difference in Kaplan-Meier event rate of the composite efficacy failure of tBPAR, graft loss or death at 12 months between the everolimus plus reduced CNI ($R_{EVR+rCNI}$) and the MPA plus standard CNI arm ($R_{MPA+sCNI}$) is less than 10%.

Analyses of safety parameters other than renal function parameters included AEs/infections, safety laboratory tests, vital signs, CMV and BKV events, new onset diabetes, and other safety events of interest. These analyses were performed in the Safety set consisting of all patients who received at least one dose of study drug.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:
1. Written informed consent obtained.
2. Subject randomized within 24 hr of completion of transplant surgery.
3. Recipient of a kidney with a cold ischemia time < 30 hours.
4. Recipient of a primary (or secondary, if first graft is not lost due to immunological reasons) renal transplant from a deceased heart beating, living unrelated, living related non-human leukocyte antigen identical or an expanded criteria donor.

Exclusion Criteria:
1. Subject unable to tolerate oral medication at time of randomization.
2. Use of other investigational drugs at the time of enrollment.

3. History of hypersensitivity to any of the study drugs or to drugs of similar chemical classes.
4. Multi-organ transplant recipient.
5. Recipient of ABO incompatible allograft or complement-dependent lymphocytotoxic (CDC) crossmatch positive transplant.
6. Subject at high immunological risk for rejection as determined by local practice for assessment of anti-donor reactivity e.g. high PRA, presence of pre-existing DSA.
7. Subject who is HIV-positive.
8. HBsAg and/or a HCV positive subject with evidence of elevated LFTs (ALT/AST levels ≥ 2.5 times ULN). Viral serology results obtained within 6 months prior to randomization are acceptable.
9. Recipient of a kidney from a donor who tests positive for human immunodeficiency virus (HIV), hepatitis B surface antigen (HBsAg) or anti-hepatitis C virus (HCV).
10. Subject with a BMI greater than 35.
11. Subject with severe systemic infections, current or within the two weeks prior to randomization.
12. Subject requiring systemic anticoagulation.
13. History of malignancy of any organ system.
14. Subject with severe restrictive or obstructive pulmonary disorders.
15. Subject with severe hypercholesterolemia or hypertriglyceridemia that cannot be controlled.
16. Subject with white blood cell (WBC) count ≤ 2,000 /mm3 or with platelet count ≤ 50,000 /mm3.
17. Pregnant or nursing (lactating) women.
18. Women of child-bearing potential, defined as all women physiologically capable of becoming pregnant, unless they are using effective methods of contraception during dosing of study treatment.

Participant Flow Table

Overall Study

	EVR+rCNI	MPA+sCNI
Started	1022	1015
Completed	893	881
Not Completed	129	134
Graft Loss	35	30
Death	29	34

Subject / Gardian decision	54	51
technical problems	2	0
Pregnancy	0	2
Lost to Follow-up	9	17

Baseline Characteristics

	EVR+rCNI	MPA+sCNI	Total
Number of Participants [units: participants]	1022	1015	2037
Age Continuous (units: years) Mean ± Standard Deviation			
	48.79±14.123	48.75±14.515	48.77±14.316
Sex: Female, Male (units: participants) Count of Participants (Not Applicable)			
Female	312	308	620
Male	710	707	1417
Race/Ethnicity, Customized[1] (units: participants) Count of Participants (Not Applicable)			
Hispany or Latino	157	132	289
not Hispanic or Latino	646	661	1307
Unknown or not reported	219	222	441

Race/Ethnicity, Customized[2] (units: participants) Count of Participants (Not Applicable)			
Caucasian	743	735	1478
Asian	136	157	293
Black	43	35	78
Other	100	88	188

[1] Ethnicity
[2] Race

Summary of Efficacy

Primary Outcome Result(s)

Incidence of failure on the composite of treated biopsy-proven acute rejection (tBPAR) or estimated glomerular filtration rate (eGFR) < 50 mL/min/1.73m2.

	EVR+rCNI	MPA+sCNI
Number of Participants Analyzed [units: participants]	1022	1015
Incidence of failure on the composite of treated biopsy-proven acute rejection (tBPAR) or estimated glomerular filtration rate (eGFR) < 50 mL/min/1.73m2. (units: participants) Count of Participants (Not Applicable)		
month 12	489	456
month 24	489	443

Statistical Analysis

Groups	EVR+rCNI, MPA+sCNI	calculated at month 12
Non-Inferiority/Equivalence Test		p vale for non inferiority margin is 10 %
P Value	0.001	
Method	Other Logistic Regression Model	
Odds Ratio (OR)	3.0	
95 % Confidence Interval 2-Sided	-1.4 to 7.3	

Secondary Outcome Result(s)

Incidence of failure on the composite of (treated biopsy proven acute rejection (tBPAR), graft loss or death

	EVR+rCNI	MPA+sCNI
Number of Participants Analyzed [units: participants]	1022	1015
Incidence of failure on the composite of (treated biopsy proven acute rejection (tBPAR), graft loss or death (units: participants) Count of Participants (Not Applicable)		
month 12	146	131
month 24	169	147

Incidence of failure on the composite endpoint of tBPAR, graft loss, death or eGFR < 50 mL/min/1.73m2

	EVR+rCNI	MPA+sCNI

Number of Participants Analyzed [units: participants]	1022	1015
Incidence of failure on the composite endpoint of tBPAR, graft loss, death or eGFR < 50 mL/min/1.73m2 (units: participants) Count of Participants (Not Applicable)		
month 12	497	466
month 24	497	457

Incidence of failure on the composite endpoint of graft loss or death.

	EVR+rCNI	MPA+sCNI
Number of Participants Analyzed [units: participants]	1022	1015
Incidence of failure on the composite endpoint of graft loss or death. (units: participants) Count of Participants (Not Applicable)		
month 12	51	54
month 24	67	65

Incidence of death, graft loss, tBPAR, BPAR, tAR, AR and humoral rejection

	EVR+rCNI	MPA+sCNI
Number of Participants Analyzed [units: participants]	1022	1015
Incidence of death, graft loss, tBPAR, BPAR, tAR, AR and humoral rejection (units: participants) Count of Participants (Not Applicable)		

deaths month 12	20	28
deaths month 24	32	36
graft loss month 12	33	28
graft loss month 24	37	32
tBPAR month 12	107	91
tBPAR month 24	118	98
BPAR month 12	114	95
BPAR month 24	127	104
tAR month 12	129	117
tAR month 24	145	126
AR month 12	147	133
AR month 24	167	144
aAMR month 12	73	61
aAMR month 24	84	69
cAMR month 12	9	14
cAMR month 24	13	18

Incidence of eGFR < 50 mL/min/1.73m2

	EVR+rCNI	MPA+sCNI
Number of Participants Analyzed [units: participants]	1022	1015
Incidence of eGFR < 50 mL/min/1.73m2 (units: participants) Count of Participants (Not Applicable)		
month 12	456	424
month 24	474	423

Renal allograft function (mean estimated glomerular filtration rate, eGFR)

	EVR+rCNI	MPA+sCNI
Number of Participants Analyzed [units: participants]	1022	1015
Renal allograft function (mean estimated glomerular filtration rate, eGFR) (units: mL/min/1.73m2) Mean ± Standard Error		
baseline (week 4)	53.13 ± 0.765	52.25 ± 0.684
month 12	53.29 ± 0.698	54.49 ± 0.667
month 24	52.63 ± 0.744	54.91 ± 0.719

Evolution of renal function, as eGFR, over time by slope analysis.

	EVR+rCNI	MPA+sCNI
Number of Participants Analyzed [units: participants]	1022	1015
Evolution of renal function, as eGFR, over time by slope analysis. (units: mL/min/1.73m2) Mean ± Standard Error		
slope of eGFR	0.0001 ± 0.0008	0.0047 ± 0.0008
eGFR at month 12	55.32 ± 0.68	57.44 ± 0.67
eGFR at month 24	55.43 ± 0.60	57.28 ± 0.60

Renal function by Cystatin C-based and other alternate formulae (e.g. CKD-EPI).

	EVR+rCNI	MPA+sCNI
Number of Participants Analyzed [units: participants]	1022	1015
Renal function by Cystatin C-based and other alternate formulae (e.g. CKD-EPI). (units: micromol/L; mL/min/1.73m2) Mean ± Standard Deviation		
screening baseline (creatinine, micromol/L)	590.1 ± 262.78	601.8 ± 265.08
month 12 (creatinine, micromol/L)	129.8 ± 49.12	128.6 ± 50.80
month 24 (creatinine, micromol/L)	130.1 ± 53.54	127.6 ± 52.50
eGFR (Hoek) baseline (mL/min/1.73m2)	21.38 ± 14.296	20.10 ± 12.408
eGFR (Hoek) month 12 (mL/min/1.73m2)	50.08 ± 14.430	52.00 ± 14.533
eGFR (Hoek) month 24 (mL/min/1.73m2)	49.86 ± 14.604	52.75 ± 15.406
eGFR (MDRD4) baseline (mL/min/1.73m2)	11.79 ± 8.697	11.56 ± 8.853
eGFR (MDRD4) month 12 (mL/min/1.73m2)	57.59 ± 19.685	57.58 ± 18.768
eGFR (MDRD4) month 24 (mL/min/1.73m2)	58.07 ± 20.168	58.68 ± 19.541
eGFR-CKDEPI baseline (mL/min/1.73m2)	11.29 ± 9.094	11.05 ± 9.195
eGFR-CKDEPI month 12(mL/min/1.73m2)	58.83 ± 20.686	58.75 ± 19.757
eGFR-CKDEPI month 24 (mL/min/1.73m2)	59.39 ± 21.077	59.95 ± 20.652

Incidence of adverse events, serious adverse events and adverse events leading to study regimen discontinuation.

	EVR+rCNI	MPA+sCNI
Number of Participants Analyzed [units: participants]	1014	1012
Incidence of adverse events, serious adverse events and adverse events leading to study regimen discontinuation. (units: participants) Count of Participants (Not Applicable)		
number of participants with at least one AE/infection leading to study drug discontinuation	276	152

Incidence of cytomegalovirus and BK virus, new onset diabetes mellitus, chronic kidney disease with associated proteinuria and calcineurin inhibitor associated adverse events.

	EVR+rCNI	MPA+sCNI
Number of Participants Analyzed [units: participants]	1014	1012
Incidence of cytomegalovirus and BK virus, new onset diabetes mellitus, chronic kidney disease with associated proteinuria and calcineurin inhibitor associated adverse events. (units: participants) Count of Participants (Not Applicable)		
clinical signs of CMV infection	53	132

any BKV infection	103	154
new onset of diabetes mellitus	144	138
at least one event of interest	871	764

Urinary protein and albumin excretion by treatment estimated by urinary protein/creatinine and urinary albumin/creatinine ratios.

	EVR+rCNI	MPA+sCNI
Number of Participants Analyzed [units: participants]	1014	1012
Urinary protein and albumin excretion by treatment estimated by urinary protein/creatinine and urinary albumin/creatinine ratios. (units: mg/g) Mean ± Standard Deviation		
albumine /creatinine ratio baseline	1019.75 ± 2737.96	646.111 ± 799.234
albumine /creatinine ratio month 12	150.061 ± 482.394	111.322 ± 444.631
albumine /creatinine ratio month 24	149.049 ± 464.470	116.618 ± 433.392
protein /creatinine ratio baseline	1648.10 ± 3768.22	1142.59 ± 1003.69
protein /creatinine ratio month 12	298.557 ± 642.103	234.698 ± 583.632
protein /creatinine ratio month 24	290.242 ± 588.119	233.009 ± 524.383

Incidence of major cardiovascular events.

	EVR+rCNI	MPA+sCNI
Number of Participants Analyzed [units: participants]	1014	1012
Incidence of major cardiovascular events. (units: participants) Count of Participants (Not Applicable)		
month 24	66	86

Incidence of malignancies.

	EVR+rCNI	MPA+sCNI
Number of Participants Analyzed [units: participants]	1014	1012
Incidence of malignancies. (units: participants) Count of Participants (Not Applicable)		
	41	39

Incidence of failure on the composite of treated biopsy-proven acute rejection (tBPAR) or estimated glomerular filtration rate (eGFR) < 50 mL/min/1.73m2 among compliant subjects.

	EVR+rCNI	MPA+sCNI
Number of Participants Analyzed [units: participants]	187	277
Incidence of failure on the composite of treated biopsy-proven acute rejection (tBPAR) or estimated glomerular		

filtration rate (eGFR) < 50 mL/min/1.73m2 among compliant subjects. (units: participants) Count of Participants (Not Applicable)		
month 12	60	106
month 24	62	102

Incidence tBPAR by severity and time to event

	EVR+rCNI	**MPA+sCNI**
Number of Participants Analyzed [units: participants]	1022	1015
Incidence tBPAR by severity and time to event (units: participants) Count of Participants (Not Applicable)		
Patient's maximum tBPAR grade : no grade (missing)	25	18
Patient's maximum tBPAR grade : grade IA	34	36
Patient's maximum tBPAR grade : grade IB	23	17
Patient's maximum tBPAR grade : grade IIA	21	24
Patient's maximum tBPAR grade : grade IIB	9	3
Patient's maximum tBPAR grade : grade III	6	0
overall number of tBPAR regardless of grade	146	116
number of tBPAR regardless of grade days 1-90	72	63

number of tBPAR regardless of grade days 91-180	24	14
number of tBPAR regardless of grade days 181-360	25	20
number of tBPAR regardless of grade days 361-540	12	15
number of tBPAR regardless of grade days 541-720	11	2
number of tBPAR regardless of grade days 721-810	2	2

Incidence of tBPAR excluding grade IA rejections

	EVR+rCNI	MPA+sCNI
Number of Participants Analyzed [units: participants]	1022	1015
Incidence of tBPAR excluding grade IA rejections (units: participants) Count of Participants (Not Applicable)		
month 12	66	53
month 24	74	55

Incidence of composite of tBPAR or eGRF<50 mL/min/1.73m2 by subgroup

	EVR+rCNI	MPA+sCNI

Number of Participants Analyzed [units: participants]	1022	1015
Incidence of composite of tBPAR or eGRF<50 mL/min/1.73m2 by subgroup (units: participants) Count of Participants (Not Applicable)		
month 12	489	456
month 24	489	443

Incidence of tBPAR (excluding grade IA rejections) or GFR<50 mL/min/1.73m2

	EVR+rCNI	MPA+sCNI
Number of Participants Analyzed [units: participants]	1022	1015
Incidence of tBPAR (excluding grade IA rejections) or GFR<50 mL/min/1.73m2 (units: participants) Count of Participants (Not Applicable)		
month 12	475	441
month 24	475	426

Incidence of failure on the composite of (treated biopsy proven acute rejection (tBPAR), graft loss or death or loss to follow-up

	EVR+rCNI	MPA+sCNI
Number of Participants Analyzed [units: participants]	1022	1015
Incidence of failure on the composite of (treated biopsy proven acute rejection (tBPAR), graft loss or death or loss to follow-up		

(units: participants) Count of Participants (Not Applicable)		
month 12	181	170
month 24	218	201

Summary of Safety

Safety Results

All-Cause Mortality

	Everolimus plus@reduced CNI N = 1014	MPA plus standard@CNI N = 1012
Total participants affected	20 (1.97%)	29 (2.87%)

Serious Adverse Events by System Organ Class

Time Frame	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 up to approximately 4 years.
Additional Description	treatment emergent AE / SAE . Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events fields "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.
Source Vocabulary for Table Default	MedDRA (20.1)

Assessment Type for Table Default	Systematic Assessment

	Everolimus plus@reduced CNI N = 1014	MPA plus standard@CNI N = 1012
Total participants affected	593 (58.48%)	613 (60.57%)
Blood and lymphatic system disorders		
Agranulocytosis	2 (0.20%)	0 (0.00%)
Anaemia	14 (1.38%)	6 (0.59%)
Atypical haemolytic uraemic syndrome	1 (0.10%)	0 (0.00%)
Bone marrow failure	0 (0.00%)	1 (0.10%)
Febrile neutropenia	0 (0.00%)	5 (0.49%)
Granulocytopenia	0 (0.00%)	1 (0.10%)
Haemolysis	2 (0.20%)	0 (0.00%)
Haemolytic uraemic syndrome	1 (0.10%)	2 (0.20%)
Iron deficiency anaemia	0 (0.00%)	1 (0.10%)
Leukocytosis	1 (0.10%)	0 (0.00%)
Leukopenia	4 (0.39%)	12 (1.19%)
Lymphadenopathy	1 (0.10%)	0 (0.00%)
Lymphatic obstruction	1 (0.10%)	0 (0.00%)
Lymphopenia	0 (0.00%)	1 (0.10%)
Nephrogenic anaemia	0 (0.00%)	1 (0.10%)
Neutropenia	1 (0.10%)	6 (0.59%)

Pancytopenia	2 (0.20%)	1 (0.10%)
Polycythaemia	0 (0.00%)	2 (0.20%)
Sickle cell anaemia with crisis	1 (0.10%)	0 (0.00%)
Splenomegaly	0 (0.00%)	1 (0.10%)
Thrombocytopenia	3 (0.30%)	1 (0.10%)
Thrombotic microangiopathy	8 (0.79%)	3 (0.30%)
Cardiac disorders		
Acute coronary syndrome	4 (0.39%)	2 (0.20%)
Acute myocardial infarction	6 (0.59%)	6 (0.59%)
Angina pectoris	6 (0.59%)	5 (0.49%)
Angina unstable	1 (0.10%)	1 (0.10%)
Aortic valve stenosis	0 (0.00%)	1 (0.10%)
Arrhythmia	0 (0.00%)	1 (0.10%)
Arrhythmia supraventricular	1 (0.10%)	0 (0.00%)
Arteriosclerosis coronary artery	0 (0.00%)	2 (0.20%)
Atrial fibrillation	12 (1.18%)	12 (1.19%)
Atrial flutter	4 (0.39%)	1 (0.10%)
Bradycardia	3 (0.30%)	1 (0.10%)
Cardiac arrest	4 (0.39%)	4 (0.40%)
Cardiac asthma	0 (0.00%)	1 (0.10%)
Cardiac dysfunction	1 (0.10%)	0 (0.00%)
Cardiac failure	9 (0.89%)	7 (0.69%)

Cardiac failure acute	2 (0.20%)	0 (0.00%)
Cardiac failure chronic	2 (0.20%)	1 (0.10%)
Cardiac failure congestive	6 (0.59%)	3 (0.30%)
Cardiorenal syndrome	1 (0.10%)	0 (0.00%)
Cardio-respiratory arrest	1 (0.10%)	0 (0.00%)
Coronary artery disease	2 (0.20%)	6 (0.59%)
Coronary artery insufficiency	0 (0.00%)	1 (0.10%)
Coronary artery stenosis	2 (0.20%)	1 (0.10%)
Hypertensive heart disease	1 (0.10%)	0 (0.00%)
Ischaemic cardiomyopathy	0 (0.00%)	1 (0.10%)
Left ventricular failure	1 (0.10%)	0 (0.00%)
Left ventricular hypertrophy	0 (0.00%)	1 (0.10%)
Myocardial infarction	5 (0.49%)	6 (0.59%)
Myocardial ischaemia	0 (0.00%)	1 (0.10%)
Pericarditis	1 (0.10%)	0 (0.00%)
Pericarditis constrictive	0 (0.00%)	1 (0.10%)
Pulseless electrical activity	0 (0.00%)	1 (0.10%)
Tachycardia	0 (0.00%)	2 (0.20%)
Ventricular extrasystoles	0 (0.00%)	1 (0.10%)
Ventricular tachyarrhythmia	1 (0.10%)	0 (0.00%)
Ventricular tachycardia	1 (0.10%)	0 (0.00%)

Congenital, familial and genetic disorders		
Arteriovenous malformation	0 (0.00%)	1 (0.10%)
Congenital cystic kidney disease	0 (0.00%)	1 (0.10%)
Congenital megaureter	1 (0.10%)	0 (0.00%)
Hydrocele	1 (0.10%)	2 (0.20%)
Tracheo-oesophageal fistula	0 (0.00%)	1 (0.10%)
Ear and labyrinth disorders		
Mastoid effusion	1 (0.10%)	0 (0.00%)
Sudden hearing loss	1 (0.10%)	0 (0.00%)
Tinnitus	0 (0.00%)	1 (0.10%)
Vertigo	1 (0.10%)	0 (0.00%)
Endocrine disorders		
Goitre	1 (0.10%)	0 (0.00%)
Hyperparathyroidism	1 (0.10%)	0 (0.00%)
Hyperparathyroidism tertiary	0 (0.00%)	1 (0.10%)
Eye disorders		
Cataract	1 (0.10%)	3 (0.30%)
Glaucoma	0 (0.00%)	1 (0.10%)
Optic ischaemic neuropathy	0 (0.00%)	1 (0.10%)
Retinal detachment	0 (0.00%)	1 (0.10%)
Vision blurred	0 (0.00%)	1 (0.10%)

Visual acuity reduced	0 (0.00%)	1 (0.10%)
Gastrointestinal disorders		
Abdominal hernia	4 (0.39%)	2 (0.20%)
Abdominal pain	9 (0.89%)	14 (1.38%)
Abdominal pain lower	1 (0.10%)	1 (0.10%)
Abdominal pain upper	4 (0.39%)	3 (0.30%)
Abdominal wall haematoma	1 (0.10%)	1 (0.10%)
Acute abdomen	1 (0.10%)	0 (0.00%)
Anal polyp	1 (0.10%)	0 (0.00%)
Anogenital dysplasia	0 (0.00%)	1 (0.10%)
Barrett's oesophagus	1 (0.10%)	0 (0.00%)
Chronic gastritis	1 (0.10%)	0 (0.00%)
Colitis	1 (0.10%)	1 (0.10%)
Colitis ischaemic	1 (0.10%)	0 (0.00%)
Colitis ulcerative	0 (0.00%)	1 (0.10%)
Constipation	1 (0.10%)	3 (0.30%)
Crohn's disease	1 (0.10%)	1 (0.10%)
Diabetic gastroparesis	0 (0.00%)	1 (0.10%)
Diarrhoea	27 (2.66%)	55 (5.43%)
Diverticulum	1 (0.10%)	0 (0.00%)
Diverticulum intestinal	1 (0.10%)	0 (0.00%)
Diverticulum intestinal haemorrhagic	0 (0.00%)	2 (0.20%)
Duodenal perforation	0 (0.00%)	1 (0.10%)
Duodenal ulcer	0 (0.00%)	1 (0.10%)

Encapsulating peritoneal sclerosis	1 (0.10%)	0 (0.00%)
Enteritis	1 (0.10%)	0 (0.00%)
Enterocolitis	2 (0.20%)	1 (0.10%)
Food poisoning	0 (0.00%)	1 (0.10%)
Gastric haemorrhage	1 (0.10%)	0 (0.00%)
Gastric ulcer	0 (0.00%)	1 (0.10%)
Gastritis	1 (0.10%)	0 (0.00%)
Gastritis erosive	0 (0.00%)	1 (0.10%)
Gastritis haemorrhagic	0 (0.00%)	1 (0.10%)
Gastrointestinal fistula	1 (0.10%)	0 (0.00%)
Gastrointestinal haemorrhage	2 (0.20%)	4 (0.40%)
Gastrooesophageal reflux disease	0 (0.00%)	1 (0.10%)
Haematochezia	1 (0.10%)	0 (0.00%)
Haemorrhoidal haemorrhage	1 (0.10%)	0 (0.00%)
Haemorrhoids	0 (0.00%)	1 (0.10%)
Hernial eventration	1 (0.10%)	0 (0.00%)
Hiatus hernia	0 (0.00%)	1 (0.10%)
Ileus	5 (0.49%)	2 (0.20%)
Impaired gastric emptying	1 (0.10%)	1 (0.10%)
Inguinal hernia	2 (0.20%)	5 (0.49%)
Intestinal obstruction	2 (0.20%)	2 (0.20%)
Intestinal perforation	2 (0.20%)	1 (0.10%)

Intra-abdominal fluid collection	5 (0.49%)	1 (0.10%)
Intra-abdominal haematoma	2 (0.20%)	1 (0.10%)
Intra-abdominal haemorrhage	1 (0.10%)	0 (0.00%)
Large intestine perforation	1 (0.10%)	0 (0.00%)
Large intestine polyp	1 (0.10%)	0 (0.00%)
Lumbar hernia	0 (0.00%)	1 (0.10%)
Mallory-Weiss syndrome	1 (0.10%)	0 (0.00%)
Melaena	0 (0.00%)	1 (0.10%)
Mouth ulceration	1 (0.10%)	2 (0.20%)
Nausea	3 (0.30%)	9 (0.89%)
Oesophageal achalasia	1 (0.10%)	0 (0.00%)
Oesophageal spasm	0 (0.00%)	1 (0.10%)
Oesophagitis	0 (0.00%)	1 (0.10%)
Pancreatitis	1 (0.10%)	2 (0.20%)
Pancreatitis acute	0 (0.00%)	2 (0.20%)
Pancreatitis chronic	0 (0.00%)	1 (0.10%)
Rectal haemorrhage	0 (0.00%)	2 (0.20%)
Retching	0 (0.00%)	1 (0.10%)
Retroperitoneal haematoma	2 (0.20%)	5 (0.49%)
Retroperitoneal haemorrhage	0 (0.00%)	1 (0.10%)
Salivary gland enlargement	1 (0.10%)	0 (0.00%)

Small intestinal obstruction	2 (0.20%)	4 (0.40%)
Stomatitis	0 (0.00%)	2 (0.20%)
Umbilical hernia	3 (0.30%)	0 (0.00%)
Volvulus	1 (0.10%)	0 (0.00%)
Volvulus of small bowel	1 (0.10%)	0 (0.00%)
Vomiting	6 (0.59%)	13 (1.28%)
General disorders and administration site conditions		
Asthenia	0 (0.00%)	1 (0.10%)
Catheter site haemorrhage	1 (0.10%)	0 (0.00%)
Chest discomfort	1 (0.10%)	0 (0.00%)
Chest pain	1 (0.10%)	2 (0.20%)
Chills	1 (0.10%)	2 (0.20%)
Death	0 (0.00%)	2 (0.20%)
Fatigue	2 (0.20%)	2 (0.20%)
Gait inability	0 (0.00%)	1 (0.10%)
General physical health deterioration	0 (0.00%)	1 (0.10%)
Generalised oedema	1 (0.10%)	0 (0.00%)
Hyperthermia	1 (0.10%)	0 (0.00%)
Hypothermia	0 (0.00%)	1 (0.10%)
Ill-defined disorder	0 (0.00%)	1 (0.10%)
Impaired healing	10 (0.99%)	1 (0.10%)
Malaise	2 (0.20%)	1 (0.10%)

Medical device site discomfort	1 (0.10%)	0 (0.00%)
Medical device site inflammation	1 (0.10%)	0 (0.00%)
Microlithiasis	0 (0.00%)	1 (0.10%)
Multiple organ dysfunction syndrome	1 (0.10%)	0 (0.00%)
Non-cardiac chest pain	1 (0.10%)	2 (0.20%)
Oedema peripheral	7 (0.69%)	4 (0.40%)
Pain	0 (0.00%)	1 (0.10%)
Peripheral swelling	0 (0.00%)	2 (0.20%)
Pyrexia	35 (3.45%)	36 (3.56%)
Sudden death	1 (0.10%)	0 (0.00%)
Suprapubic pain	0 (0.00%)	1 (0.10%)
Swelling	0 (0.00%)	1 (0.10%)
Systemic inflammatory response syndrome	1 (0.10%)	2 (0.20%)
Hepatobiliary disorders		
Bile duct stone	1 (0.10%)	0 (0.00%)
Biliary colic	0 (0.00%)	1 (0.10%)
Biliary dilatation	0 (0.00%)	1 (0.10%)
Cholangitis	1 (0.10%)	0 (0.00%)
Cholecystitis	2 (0.20%)	3 (0.30%)
Cholecystitis acute	0 (0.00%)	1 (0.10%)
Cholelithiasis	0 (0.00%)	2 (0.20%)
Cholestasis	1 (0.10%)	0 (0.00%)
Hepatocellular injury	0 (0.00%)	1 (0.10%)

Perforation bile duct	0 (0.00%)	1 (0.10%)
Immune system disorders		
Anaphylactic reaction	0 (0.00%)	1 (0.10%)
Chronic allograft nephropathy	0 (0.00%)	1 (0.10%)
Hypersensitivity	0 (0.00%)	1 (0.10%)
Immunosuppression	1 (0.10%)	0 (0.00%)
Kidney transplant rejection	18 (1.78%)	17 (1.68%)
Renal transplant failure	4 (0.39%)	5 (0.49%)
Transplant rejection	45 (4.44%)	25 (2.47%)
Infections and infestations		
Abdominal abscess	1 (0.10%)	1 (0.10%)
Abdominal infection	1 (0.10%)	0 (0.00%)
Actinomycosis	1 (0.10%)	0 (0.00%)
Adenoviral haemorrhagic cystitis	0 (0.00%)	1 (0.10%)
Adenovirus infection	2 (0.20%)	1 (0.10%)
Anal abscess	1 (0.10%)	1 (0.10%)
Appendicitis	0 (0.00%)	3 (0.30%)
Arteriovenous fistula site infection	0 (0.00%)	1 (0.10%)
Arthritis bacterial	0 (0.00%)	1 (0.10%)
Arthritis infective	1 (0.10%)	0 (0.00%)
Asymptomatic bacteriuria	1 (0.10%)	0 (0.00%)
Atypical pneumonia	2 (0.20%)	0 (0.00%)

Bacteraemia	3 (0.30%)	0 (0.00%)
Bacterial diarrhoea	0 (0.00%)	1 (0.10%)
Bacterial infection	0 (0.00%)	1 (0.10%)
Bacterial prostatitis	1 (0.10%)	1 (0.10%)
Bacterial pyelonephritis	2 (0.20%)	1 (0.10%)
Bacterial sepsis	1 (0.10%)	1 (0.10%)
Bacteriuria	0 (0.00%)	2 (0.20%)
BK virus infection	3 (0.30%)	5 (0.49%)
Blister infected	0 (0.00%)	1 (0.10%)
Bronchitis	2 (0.20%)	3 (0.30%)
Bronchopulmonary aspergillosis	1 (0.10%)	2 (0.20%)
Campylobacter gastroenteritis	1 (0.10%)	0 (0.00%)
Candida infection	2 (0.20%)	0 (0.00%)
Candiduria	0 (0.00%)	1 (0.10%)
Cellulitis	5 (0.49%)	6 (0.59%)
Chest wall abscess	0 (0.00%)	1 (0.10%)
Chronic sinusitis	1 (0.10%)	0 (0.00%)
Chronic tonsillitis	1 (0.10%)	1 (0.10%)
Clostridium difficile colitis	4 (0.39%)	3 (0.30%)
Clostridium difficile infection	1 (0.10%)	0 (0.00%)
Corona virus infection	1 (0.10%)	0 (0.00%)
Cryptococcosis	0 (0.00%)	3 (0.30%)
Cystitis viral	1 (0.10%)	0 (0.00%)
Cytomegalovirus colitis	0 (0.00%)	9 (0.89%)

Cytomegalovirus enteritis	0 (0.00%)	1 (0.10%)
Cytomegalovirus gastroenteritis	0 (0.00%)	3 (0.30%)
Cytomegalovirus gastrointestinal infection	0 (0.00%)	1 (0.10%)
Cytomegalovirus hepatitis	0 (0.00%)	2 (0.20%)
Cytomegalovirus infection	6 (0.59%)	48 (4.74%)
Dengue fever	1 (0.10%)	0 (0.00%)
Dermatophytosis	1 (0.10%)	0 (0.00%)
Device related infection	1 (0.10%)	3 (0.30%)
Device related sepsis	1 (0.10%)	0 (0.00%)
Diabetic foot infection	1 (0.10%)	2 (0.20%)
Diarrhoea infectious	1 (0.10%)	0 (0.00%)
Disseminated tuberculosis	1 (0.10%)	0 (0.00%)
Diverticulitis	3 (0.30%)	3 (0.30%)
Ear infection	1 (0.10%)	0 (0.00%)
Encephalitis	1 (0.10%)	0 (0.00%)
Endocarditis	1 (0.10%)	1 (0.10%)
Enteritis infectious	1 (0.10%)	0 (0.00%)
Enterococcal infection	1 (0.10%)	1 (0.10%)
Enterococcal sepsis	1 (0.10%)	0 (0.00%)
Enterocolitis viral	1 (0.10%)	0 (0.00%)
Epididymitis	0 (0.00%)	1 (0.10%)
Erysipelas	3 (0.30%)	0 (0.00%)

Escherichia bacteraemia	0 (0.00%)	2 (0.20%)
Escherichia infection	1 (0.10%)	1 (0.10%)
Escherichia pyelonephritis	1 (0.10%)	1 (0.10%)
Escherichia sepsis	5 (0.49%)	1 (0.10%)
Escherichia urinary tract infection	1 (0.10%)	7 (0.69%)
Febrile infection	1 (0.10%)	1 (0.10%)
Fungal infection	1 (0.10%)	1 (0.10%)
Fungal sepsis	0 (0.00%)	2 (0.20%)
Gangrene	1 (0.10%)	2 (0.20%)
Gastroenteritis	18 (1.78%)	23 (2.27%)
Gastroenteritis clostridial	0 (0.00%)	1 (0.10%)
Gastroenteritis cryptosporidial	0 (0.00%)	1 (0.10%)
Gastroenteritis norovirus	0 (0.00%)	6 (0.59%)
Gastroenteritis viral	1 (0.10%)	3 (0.30%)
Gastrointestinal infection	2 (0.20%)	1 (0.10%)
Groin abscess	3 (0.30%)	2 (0.20%)
Haematoma infection	2 (0.20%)	0 (0.00%)
Hepatic cyst infection	1 (0.10%)	0 (0.00%)
Hepatitis C	0 (0.00%)	1 (0.10%)
Hepatitis E	0 (0.00%)	1 (0.10%)
Hepatitis viral	0 (0.00%)	1 (0.10%)
Herpes simplex	1 (0.10%)	1 (0.10%)
Herpes simplex pneumonia	1 (0.10%)	0 (0.00%)
Herpes zoster	5 (0.49%)	4 (0.40%)

Herpes zoster disseminated	0 (0.00%)	1 (0.10%)
HIV infection	0 (0.00%)	1 (0.10%)
Ileal gangrene	0 (0.00%)	1 (0.10%)
Infected lymphocele	4 (0.39%)	1 (0.10%)
Infected seroma	1 (0.10%)	1 (0.10%)
Infected skin ulcer	3 (0.30%)	2 (0.20%)
Infection	2 (0.20%)	1 (0.10%)
Infectious colitis	0 (0.00%)	1 (0.10%)
Infectious pleural effusion	1 (0.10%)	0 (0.00%)
Influenza	6 (0.59%)	5 (0.49%)
Intervertebral discitis	0 (0.00%)	2 (0.20%)
Intestinal sepsis	1 (0.10%)	0 (0.00%)
Kidney infection	1 (0.10%)	2 (0.20%)
Klebsiella bacteraemia	0 (0.00%)	1 (0.10%)
Klebsiella sepsis	2 (0.20%)	0 (0.00%)
Lower respiratory tract infection	1 (0.10%)	3 (0.30%)
Lung infection	1 (0.10%)	2 (0.20%)
Medical device site cellulitis	1 (0.10%)	0 (0.00%)
Medical device site infection	0 (0.00%)	1 (0.10%)
Meningitis bacterial	1 (0.10%)	0 (0.00%)
Meningitis cryptococcal	1 (0.10%)	0 (0.00%)
Nasopharyngitis	1 (0.10%)	1 (0.10%)
Neutropenic sepsis	0 (0.00%)	1 (0.10%)

Nocardiosis	0 (0.00%)	1 (0.10%)
Oral candidiasis	0 (0.00%)	2 (0.20%)
Oral herpes	1 (0.10%)	1 (0.10%)
Orchitis	1 (0.10%)	3 (0.30%)
Osteomyelitis	5 (0.49%)	2 (0.20%)
Osteomyelitis chronic	2 (0.20%)	0 (0.00%)
Parvovirus B19 infection	1 (0.10%)	0 (0.00%)
Perinephric abscess	2 (0.20%)	0 (0.00%)
Peritonitis	1 (0.10%)	0 (0.00%)
Peritonsillar abscess	1 (0.10%)	1 (0.10%)
Pharyngotonsillitis	0 (0.00%)	1 (0.10%)
Pneumococcal sepsis	1 (0.10%)	0 (0.00%)
Pneumocystis jirovecii pneumonia	6 (0.59%)	3 (0.30%)
Pneumonia	55 (5.42%)	36 (3.56%)
Pneumonia bacterial	1 (0.10%)	1 (0.10%)
Pneumonia cryptococcal	0 (0.00%)	2 (0.20%)
Pneumonia cytomegaloviral	1 (0.10%)	4 (0.40%)
Pneumonia fungal	0 (0.00%)	1 (0.10%)
Pneumonia haemophilus	0 (0.00%)	1 (0.10%)
Pneumonia influenzal	1 (0.10%)	0 (0.00%)
Pneumonia legionella	1 (0.10%)	1 (0.10%)
Polyomavirus-associated nephropathy	4 (0.39%)	10 (0.99%)
Postoperative abscess	0 (0.00%)	1 (0.10%)
Postoperative wound infection	3 (0.30%)	3 (0.30%)

Pseudomembranous colitis	0 (0.00%)	1 (0.10%)
Pseudomonal bacteraemia	0 (0.00%)	1 (0.10%)
Pseudomonal sepsis	0 (0.00%)	1 (0.10%)
Pulmonary tuberculosis	2 (0.20%)	1 (0.10%)
Pyelonephritis	24 (2.37%)	33 (3.26%)
Pyelonephritis acute	6 (0.59%)	13 (1.28%)
Pyelonephritis chronic	1 (0.10%)	1 (0.10%)
Pyuria	0 (0.00%)	1 (0.10%)
Renal cyst infection	1 (0.10%)	3 (0.30%)
Renal graft infection	2 (0.20%)	0 (0.00%)
Respiratory tract infection	5 (0.49%)	5 (0.49%)
Respiratory tract infection fungal	0 (0.00%)	1 (0.10%)
Respiratory tract infection viral	0 (0.00%)	1 (0.10%)
Rhinitis	1 (0.10%)	0 (0.00%)
Rhinovirus infection	0 (0.00%)	1 (0.10%)
Salmonellosis	0 (0.00%)	1 (0.10%)
Sepsis	20 (1.97%)	7 (0.69%)
Septic shock	6 (0.59%)	8 (0.79%)
Sinusitis	1 (0.10%)	1 (0.10%)
Sinusitis fungal	0 (0.00%)	1 (0.10%)
Staphylococcal bacteraemia	1 (0.10%)	1 (0.10%)
Streptococcal sepsis	1 (0.10%)	0 (0.00%)

Subcutaneous abscess	2 (0.20%)	0 (0.00%)
Systemic candida	0 (0.00%)	1 (0.10%)
Tonsillitis bacterial	1 (0.10%)	0 (0.00%)
Tooth abscess	0 (0.00%)	1 (0.10%)
Tracheobronchitis	1 (0.10%)	1 (0.10%)
Transplant abscess	1 (0.10%)	0 (0.00%)
Tuberculosis	1 (0.10%)	0 (0.00%)
Tuberculosis gastrointestinal	0 (0.00%)	1 (0.10%)
Upper respiratory tract infection	5 (0.49%)	4 (0.40%)
Urinary tract infection	78 (7.69%)	93 (9.19%)
Urinary tract infection bacterial	4 (0.39%)	1 (0.10%)
Urinary tract infection enterococcal	1 (0.10%)	0 (0.00%)
Urinary tract infection fungal	0 (0.00%)	1 (0.10%)
Urosepsis	23 (2.27%)	23 (2.27%)
Varicella	0 (0.00%)	1 (0.10%)
Viral diarrhoea	1 (0.10%)	1 (0.10%)
Viral infection	2 (0.20%)	2 (0.20%)
Viral myocarditis	0 (0.00%)	1 (0.10%)
Viral upper respiratory tract infection	1 (0.10%)	1 (0.10%)
Vulvovaginal mycotic infection	0 (0.00%)	1 (0.10%)
Wound abscess	1 (0.10%)	0 (0.00%)
Wound infection	5 (0.49%)	4 (0.40%)

Injury, poisoning and procedural complications		
Accidental overdose	1 (0.10%)	0 (0.00%)
Anaemia postoperative	1 (0.10%)	0 (0.00%)
Anaesthetic complication	1 (0.10%)	0 (0.00%)
Anastomotic haemorrhage	1 (0.10%)	0 (0.00%)
Ankle fracture	1 (0.10%)	0 (0.00%)
Aponeurosis contusion	0 (0.00%)	3 (0.30%)
Arterial injury	1 (0.10%)	0 (0.00%)
Arteriovenous fistula aneurysm	1 (0.10%)	3 (0.30%)
Arteriovenous fistula site complication	1 (0.10%)	4 (0.40%)
Arteriovenous fistula thrombosis	2 (0.20%)	1 (0.10%)
Avulsion fracture	1 (0.10%)	0 (0.00%)
Complications of transplant surgery	1 (0.10%)	1 (0.10%)
Complications of transplanted kidney	34 (3.35%)	28 (2.77%)
Contusion	0 (0.00%)	1 (0.10%)
Coronary bypass stenosis	0 (0.00%)	1 (0.10%)
Delayed graft function	7 (0.69%)	2 (0.20%)
Fall	1 (0.10%)	1 (0.10%)
Femoral neck fracture	2 (0.20%)	1 (0.10%)
Femur fracture	2 (0.20%)	0 (0.00%)

Forearm fracture	0 (0.00%)	1 (0.10%)
Graft complication	2 (0.20%)	3 (0.30%)
Graft haemorrhage	1 (0.10%)	1 (0.10%)
Graft loss	16 (1.58%)	12 (1.19%)
Graft thrombosis	2 (0.20%)	0 (0.00%)
Humerus fracture	1 (0.10%)	1 (0.10%)
Incision site complication	0 (0.00%)	1 (0.10%)
Incisional hernia	8 (0.79%)	1 (0.10%)
Injury	1 (0.10%)	0 (0.00%)
Joint dislocation	1 (0.10%)	0 (0.00%)
Laceration	1 (0.10%)	0 (0.00%)
Limb injury	0 (0.00%)	1 (0.10%)
Lower limb fracture	1 (0.10%)	0 (0.00%)
Lumbar vertebral fracture	0 (0.00%)	1 (0.10%)
Muscle strain	0 (0.00%)	1 (0.10%)
Musculoskeletal injury	0 (0.00%)	1 (0.10%)
Overdose	0 (0.00%)	3 (0.30%)
Pelvic fracture	1 (0.10%)	0 (0.00%)
Peripheral arterial reocclusion	0 (0.00%)	1 (0.10%)
Perirenal haematoma	1 (0.10%)	1 (0.10%)
Post procedural complication	3 (0.30%)	1 (0.10%)
Post procedural discharge	0 (0.00%)	1 (0.10%)

Post procedural haematoma	3 (0.30%)	1 (0.10%)
Post procedural haematuria	2 (0.20%)	1 (0.10%)
Post procedural haemorrhage	4 (0.39%)	4 (0.40%)
Post procedural persistent drain fluid	1 (0.10%)	1 (0.10%)
Post procedural urine leak	0 (0.00%)	1 (0.10%)
Postoperative fever	1 (0.10%)	0 (0.00%)
Postoperative hernia	2 (0.20%)	1 (0.10%)
Procedural haemorrhage	1 (0.10%)	1 (0.10%)
Radius fracture	1 (0.10%)	2 (0.20%)
Renal lymphocele	3 (0.30%)	1 (0.10%)
Renal transplant torsion	1 (0.10%)	0 (0.00%)
Rib fracture	1 (0.10%)	1 (0.10%)
Scar	1 (0.10%)	0 (0.00%)
Scrotal haematoma	0 (0.00%)	2 (0.20%)
Seroma	5 (0.49%)	2 (0.20%)
Shunt aneurysm	2 (0.20%)	1 (0.10%)
Shunt stenosis	2 (0.20%)	0 (0.00%)
Spinal fracture	1 (0.10%)	0 (0.00%)
Stress fracture	1 (0.10%)	0 (0.00%)
Subarachnoid haemorrhage	2 (0.20%)	1 (0.10%)
Subcutaneous haematoma	1 (0.10%)	0 (0.00%)

Tendon rupture	2 (0.20%)	3 (0.30%)
Tibia fracture	0 (0.00%)	2 (0.20%)
Toxicity to various agents	5 (0.49%)	4 (0.40%)
Transplant dysfunction	7 (0.69%)	7 (0.69%)
Transplant failure	1 (0.10%)	1 (0.10%)
Transplantation complication	5 (0.49%)	1 (0.10%)
Traumatic fracture	1 (0.10%)	0 (0.00%)
Ulna fracture	1 (0.10%)	0 (0.00%)
Upper limb fracture	0 (0.00%)	1 (0.10%)
Ureteric anastomosis complication	1 (0.10%)	1 (0.10%)
Urinary anastomotic leak	1 (0.10%)	1 (0.10%)
Vaccination complication	1 (0.10%)	0 (0.00%)
Vascular graft complication	1 (0.10%)	1 (0.10%)
Vascular graft stenosis	0 (0.00%)	1 (0.10%)
Vascular graft thrombosis	1 (0.10%)	0 (0.00%)
Vascular pseudoaneurysm	1 (0.10%)	0 (0.00%)
Wound decomposition	1 (0.10%)	0 (0.00%)
Wound dehiscence	10 (0.99%)	3 (0.30%)
Wound secretion	1 (0.10%)	0 (0.00%)
Wrist fracture	0 (0.00%)	1 (0.10%)

Investigations

Alanine aminotransferase increased	0 (0.00%)	1 (0.10%)
Anticoagulation drug level above therapeutic	1 (0.10%)	0 (0.00%)
Aspartate aminotransferase increased	0 (0.00%)	1 (0.10%)
Biopsy kidney	1 (0.10%)	0 (0.00%)
Blood creatine increased	2 (0.20%)	3 (0.30%)
Blood creatinine abnormal	1 (0.10%)	2 (0.20%)
Blood creatinine increased	50 (4.93%)	36 (3.56%)
Blood glucose increased	1 (0.10%)	0 (0.00%)
Blood phosphorus decreased	0 (0.00%)	1 (0.10%)
Blood urea increased	1 (0.10%)	0 (0.00%)
Catheterisation cardiac	1 (0.10%)	0 (0.00%)
C-reactive protein increased	2 (0.20%)	0 (0.00%)
Ejection fraction abnormal	0 (0.00%)	1 (0.10%)
Electrocardiogram T wave inversion	0 (0.00%)	1 (0.10%)
Haemoglobin decreased	0 (0.00%)	1 (0.10%)
Haptoglobin decreased	1 (0.10%)	0 (0.00%)
Immunosuppressant drug level increased	1 (0.10%)	0 (0.00%)
Inflammatory marker increased	1 (0.10%)	2 (0.20%)

Liver function test increased	1 (0.10%)	0 (0.00%)
Norovirus test positive	1 (0.10%)	0 (0.00%)
Occult blood positive	1 (0.10%)	0 (0.00%)
Polyomavirus test positive	0 (0.00%)	1 (0.10%)
Transaminases increased	0 (0.00%)	1 (0.10%)
Troponin increased	0 (0.00%)	1 (0.10%)
Urine output decreased	3 (0.30%)	0 (0.00%)
Weight decreased	0 (0.00%)	1 (0.10%)
Metabolism and nutrition disorders		
Cachexia	0 (0.00%)	2 (0.20%)
Calciphylaxis	1 (0.10%)	0 (0.00%)
Decreased appetite	2 (0.20%)	2 (0.20%)
Dehydration	6 (0.59%)	11 (1.09%)
Diabetes mellitus	9 (0.89%)	10 (0.99%)
Diabetes mellitus inadequate control	1 (0.10%)	2 (0.20%)
Diabetic ketoacidosis	3 (0.30%)	2 (0.20%)
Electrolyte imbalance	1 (0.10%)	0 (0.00%)
Fluid overload	5 (0.49%)	3 (0.30%)
Fluid retention	1 (0.10%)	0 (0.00%)
Gout	1 (0.10%)	1 (0.10%)
Hypercalcaemia	0 (0.00%)	1 (0.10%)
Hyperglycaemia	5 (0.49%)	6 (0.59%)
Hyperkalaemia	11 (1.08%)	10 (0.99%)

Hyperlipidaemia	1 (0.10%)	0 (0.00%)
Hypertriglyceridaemia	1 (0.10%)	0 (0.00%)
Hypervolaemia	0 (0.00%)	1 (0.10%)
Hypocalcaemia	2 (0.20%)	1 (0.10%)
Hypoglycaemia	0 (0.00%)	5 (0.49%)
Hypokalaemia	3 (0.30%)	0 (0.00%)
Hypomagnesaemia	0 (0.00%)	1 (0.10%)
Hyponatraemia	1 (0.10%)	5 (0.49%)
Hypophosphataemia	0 (0.00%)	1 (0.10%)
Hypovolaemia	0 (0.00%)	1 (0.10%)
Iron deficiency	0 (0.00%)	1 (0.10%)
Malnutrition	0 (0.00%)	1 (0.10%)
Metabolic acidosis	0 (0.00%)	4 (0.40%)
Type 1 diabetes mellitus	0 (0.00%)	1 (0.10%)
Musculoskeletal and connective tissue disorders		
Arthralgia	2 (0.20%)	2 (0.20%)
Back pain	3 (0.30%)	1 (0.10%)
Flank pain	0 (0.00%)	1 (0.10%)
Gouty arthritis	0 (0.00%)	2 (0.20%)
Groin pain	0 (0.00%)	1 (0.10%)
Intervertebral disc protrusion	2 (0.20%)	1 (0.10%)
Intervertebral disc space narrowing	0 (0.00%)	1 (0.10%)
Lumbar spinal stenosis	0 (0.00%)	1 (0.10%)
Muscular weakness	2 (0.20%)	2 (0.20%)

Musculoskeletal pain	1 (0.10%)	1 (0.10%)
Myalgia intercostal	1 (0.10%)	0 (0.00%)
Osteitis	0 (0.00%)	2 (0.20%)
Osteoarthritis	4 (0.39%)	2 (0.20%)
Osteonecrosis	9 (0.89%)	1 (0.10%)
Pain in extremity	0 (0.00%)	1 (0.10%)
Pubic pain	1 (0.10%)	0 (0.00%)
Sacroiliitis	1 (0.10%)	0 (0.00%)
Spinal column stenosis	0 (0.00%)	1 (0.10%)
Spinal osteoarthritis	0 (0.00%)	1 (0.10%)
Synovial cyst	1 (0.10%)	0 (0.00%)
Tendonitis	0 (0.00%)	1 (0.10%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Adenocarcinoma gastric	1 (0.10%)	0 (0.00%)
Adenocarcinoma pancreas	0 (0.00%)	1 (0.10%)
Basal cell carcinoma	10 (0.99%)	4 (0.40%)
Benign gastrointestinal neoplasm	0 (0.00%)	1 (0.10%)
Benign neoplasm of thyroid gland	1 (0.10%)	0 (0.00%)
Benign pancreatic neoplasm	0 (0.00%)	1 (0.10%)
Bladder cancer	0 (0.00%)	1 (0.10%)
Bowen's disease	1 (0.10%)	0 (0.00%)
Brain neoplasm	0 (0.00%)	1 (0.10%)

Breast cancer	0 (0.00%)	3 (0.30%)
Bronchioloalveolar carcinoma	0 (0.00%)	1 (0.10%)
Cerebral haemangioma	0 (0.00%)	1 (0.10%)
Clear cell renal cell carcinoma	1 (0.10%)	0 (0.00%)
Epstein-Barr virus associated lymphoma	0 (0.00%)	1 (0.10%)
Gastric cancer	1 (0.10%)	0 (0.00%)
Leydig cell tumour of the testis	0 (0.00%)	1 (0.10%)
Lipoma	0 (0.00%)	1 (0.10%)
Lung adenocarcinoma	0 (0.00%)	1 (0.10%)
Lymphoproliferative disorder	0 (0.00%)	1 (0.10%)
Malignant melanoma	4 (0.39%)	1 (0.10%)
Malignant neoplasm of pleura metastatic	1 (0.10%)	0 (0.00%)
Metastases to bone	1 (0.10%)	0 (0.00%)
Metastases to lymph nodes	1 (0.10%)	0 (0.00%)
Metastases to peritoneum	1 (0.10%)	0 (0.00%)
Metastases to spine	0 (0.00%)	1 (0.10%)
Metastatic squamous cell carcinoma	1 (0.10%)	0 (0.00%)
Monoclonal gammopathy	1 (0.10%)	0 (0.00%)
Neoplasm malignant	0 (0.00%)	1 (0.10%)

Non-small cell lung cancer	0 (0.00%)	1 (0.10%)
Oesophageal adenocarcinoma	0 (0.00%)	1 (0.10%)
Papillary tumour of renal pelvis	0 (0.00%)	1 (0.10%)
Plasmacytoma	0 (0.00%)	1 (0.10%)
Polycythaemia vera	1 (0.10%)	0 (0.00%)
Post transplant lymphoproliferative disorder	0 (0.00%)	2 (0.20%)
Prostate cancer	3 (0.30%)	0 (0.00%)
Renal cancer	2 (0.20%)	1 (0.10%)
Renal cell carcinoma	1 (0.10%)	1 (0.10%)
Salivary gland cancer	0 (0.00%)	1 (0.10%)
Skin cancer	0 (0.00%)	1 (0.10%)
Squamous cell carcinoma	8 (0.79%)	4 (0.40%)
Squamous cell carcinoma of skin	0 (0.00%)	5 (0.49%)
Testicular neoplasm	1 (0.10%)	0 (0.00%)
Tumour of ampulla of Vater	0 (0.00%)	1 (0.10%)
Uterine leiomyoma	1 (0.10%)	0 (0.00%)
Nervous system disorders		
Ataxia	0 (0.00%)	1 (0.10%)
Autoimmune encephalopathy	0 (0.00%)	1 (0.10%)
Brain injury	1 (0.10%)	0 (0.00%)

Brain stem infarction	0 (0.00%)	1 (0.10%)
Central nervous system lesion	0 (0.00%)	1 (0.10%)
Cerebellar stroke	0 (0.00%)	1 (0.10%)
Cerebral haemorrhage	1 (0.10%)	1 (0.10%)
Cerebral infarction	1 (0.10%)	0 (0.00%)
Cerebral ischaemia	1 (0.10%)	0 (0.00%)
Cerebrovascular accident	0 (0.00%)	2 (0.20%)
Coma	1 (0.10%)	0 (0.00%)
Dizziness	2 (0.20%)	3 (0.30%)
Encephalopathy	0 (0.00%)	1 (0.10%)
Headache	3 (0.30%)	7 (0.69%)
Hyponatraemic seizure	1 (0.10%)	0 (0.00%)
Hypotonia	1 (0.10%)	0 (0.00%)
Hypoxic-ischaemic encephalopathy	0 (0.00%)	1 (0.10%)
Ischaemic stroke	0 (0.00%)	1 (0.10%)
Metabolic encephalopathy	1 (0.10%)	0 (0.00%)
Migraine	0 (0.00%)	1 (0.10%)
Myelitis transverse	0 (0.00%)	1 (0.10%)
Neuropathy peripheral	0 (0.00%)	1 (0.10%)
Neurotoxicity	1 (0.10%)	2 (0.20%)
Presyncope	1 (0.10%)	0 (0.00%)
Sciatica	1 (0.10%)	0 (0.00%)
Seizure	1 (0.10%)	0 (0.00%)
Spinal cord compression	0 (0.00%)	1 (0.10%)

Syncope	1 (0.10%)	3 (0.30%)
Transient ischaemic attack	0 (0.00%)	1 (0.10%)
Transverse sinus thrombosis	0 (0.00%)	1 (0.10%)
Tremor	2 (0.20%)	1 (0.10%)
Visual field defect	1 (0.10%)	0 (0.00%)
Pregnancy, puerperium and perinatal conditions		
Cephalhaematoma	0 (0.00%)	1 (0.10%)
Product issues		
Device dislocation	2 (0.20%)	1 (0.10%)
Device leakage	0 (0.00%)	1 (0.10%)
Device malfunction	0 (0.00%)	1 (0.10%)
Psychiatric disorders		
Acute psychosis	1 (0.10%)	0 (0.00%)
Aggression	0 (0.00%)	1 (0.10%)
Anxiety	1 (0.10%)	0 (0.00%)
Depression	0 (0.00%)	1 (0.10%)
Hallucination, visual	0 (0.00%)	1 (0.10%)
Mental disorder	0 (0.00%)	1 (0.10%)
Mental status changes	1 (0.10%)	2 (0.20%)
Post-traumatic stress disorder	0 (0.00%)	1 (0.10%)
Psychotic disorder	0 (0.00%)	1 (0.10%)
Suicide attempt	0 (0.00%)	1 (0.10%)

Renal and urinary disorders		
Acute kidney injury	46 (4.54%)	37 (3.66%)
Anuria	1 (0.10%)	1 (0.10%)
Bladder neck obstruction	1 (0.10%)	0 (0.00%)
Bladder obstruction	1 (0.10%)	0 (0.00%)
Bladder perforation	0 (0.00%)	1 (0.10%)
Calculus urinary	0 (0.00%)	2 (0.20%)
Chronic kidney disease	1 (0.10%)	0 (0.00%)
Cystitis haemorrhagic	1 (0.10%)	0 (0.00%)
Diabetic nephropathy	0 (0.00%)	1 (0.10%)
Dysuria	1 (0.10%)	5 (0.49%)
End stage renal disease	1 (0.10%)	0 (0.00%)
Focal segmental glomerulosclerosis	1 (0.10%)	3 (0.30%)
Glomerulonephritis	1 (0.10%)	2 (0.20%)
Glomerulonephritis chronic	1 (0.10%)	0 (0.00%)
Glomerulonephritis membranoproliferative	1 (0.10%)	1 (0.10%)
Glomerulonephritis membranous	1 (0.10%)	1 (0.10%)
Glycosuria	0 (0.00%)	1 (0.10%)
Haematuria	9 (0.89%)	14 (1.38%)
Haemorrhage urinary tract	0 (0.00%)	1 (0.10%)
Hydronephrosis	9 (0.89%)	6 (0.59%)
Hydroureter	1 (0.10%)	0 (0.00%)

Hypertonic bladder	0 (0.00%)	1 (0.10%)
IgM nephropathy	1 (0.10%)	0 (0.00%)
Ischaemic nephropathy	0 (0.00%)	1 (0.10%)
Leukocyturia	0 (0.00%)	1 (0.10%)
Mesangioproliferative glomerulonephritis	1 (0.10%)	0 (0.00%)
Nephritis	1 (0.10%)	0 (0.00%)
Nephrolithiasis	0 (0.00%)	1 (0.10%)
Nephropathy	0 (0.00%)	1 (0.10%)
Nephropathy toxic	1 (0.10%)	0 (0.00%)
Nephrotic syndrome	0 (0.00%)	1 (0.10%)
Obstructive nephropathy	1 (0.10%)	1 (0.10%)
Oliguria	2 (0.20%)	0 (0.00%)
Pelvi-ureteric obstruction	1 (0.10%)	0 (0.00%)
Perinephric collection	2 (0.20%)	5 (0.49%)
Pollakiuria	2 (0.20%)	0 (0.00%)
Prerenal failure	0 (0.00%)	1 (0.10%)
Proteinuria	15 (1.48%)	3 (0.30%)
Pyelocaliectasis	2 (0.20%)	1 (0.10%)
Renal artery dissection	1 (0.10%)	0 (0.00%)
Renal artery occlusion	0 (0.00%)	1 (0.10%)
Renal artery stenosis	4 (0.39%)	7 (0.69%)
Renal artery thrombosis	1 (0.10%)	2 (0.20%)
Renal cortical necrosis	1 (0.10%)	0 (0.00%)
Renal cyst	0 (0.00%)	1 (0.10%)
Renal cyst haemorrhage	2 (0.20%)	1 (0.10%)

Renal cyst ruptured	0 (0.00%)	1 (0.10%)
Renal failure	1 (0.10%)	3 (0.30%)
Renal haematoma	1 (0.10%)	1 (0.10%)
Renal impairment	23 (2.27%)	25 (2.47%)
Renal ischaemia	0 (0.00%)	1 (0.10%)
Renal necrosis	0 (0.00%)	1 (0.10%)
Renal tubular atrophy	1 (0.10%)	1 (0.10%)
Renal tubular necrosis	3 (0.30%)	5 (0.49%)
Renal vein thrombosis	2 (0.20%)	1 (0.10%)
Tubulointerstitial nephritis	0 (0.00%)	1 (0.10%)
Ureteric dilatation	1 (0.10%)	1 (0.10%)
Ureteric obstruction	3 (0.30%)	1 (0.10%)
Ureteric stenosis	3 (0.30%)	6 (0.59%)
Urethral obstruction	1 (0.10%)	1 (0.10%)
Urethral stenosis	2 (0.20%)	1 (0.10%)
Urge incontinence	0 (0.00%)	1 (0.10%)
Urinary bladder haemorrhage	1 (0.10%)	0 (0.00%)
Urinary bladder polyp	0 (0.00%)	1 (0.10%)
Urinary fistula	3 (0.30%)	2 (0.20%)
Urinary incontinence	9 (0.89%)	1 (0.10%)
Urinary retention	1 (0.10%)	8 (0.79%)
Urinary tract obstruction	2 (0.20%)	4 (0.40%)
Urinoma	1 (0.10%)	0 (0.00%)
Vesicoureteric reflux	1 (0.10%)	0 (0.00%)

Reproductive system and breast disorders		
Acquired hydrocele	0 (0.00%)	1 (0.10%)
Benign prostatic hyperplasia	2 (0.20%)	3 (0.30%)
Cervical dysplasia	1 (0.10%)	0 (0.00%)
Endometriosis	1 (0.10%)	0 (0.00%)
Erectile dysfunction	1 (0.10%)	0 (0.00%)
Menorrhagia	1 (0.10%)	0 (0.00%)
Ovarian cyst ruptured	1 (0.10%)	0 (0.00%)
Prostatitis	3 (0.30%)	4 (0.40%)
Scrotal oedema	1 (0.10%)	0 (0.00%)
Testicular oedema	1 (0.10%)	0 (0.00%)
Respiratory, thoracic and mediastinal disorders		
Acute pulmonary oedema	2 (0.20%)	2 (0.20%)
Acute respiratory failure	2 (0.20%)	4 (0.40%)
Asthma	1 (0.10%)	1 (0.10%)
Asthmatic crisis	0 (0.00%)	1 (0.10%)
Bronchospasm	0 (0.00%)	1 (0.10%)
Cough	0 (0.00%)	2 (0.20%)
Dyspnoea	8 (0.79%)	7 (0.69%)
Dyspnoea exertional	1 (0.10%)	1 (0.10%)
Epistaxis	1 (0.10%)	0 (0.00%)
Haemoptysis	2 (0.20%)	2 (0.20%)
Hyperventilation	1 (0.10%)	0 (0.00%)

Hypoxia	1 (0.10%)	2 (0.20%)
Interstitial lung disease	1 (0.10%)	0 (0.00%)
Lung disorder	2 (0.20%)	0 (0.00%)
Lung infiltration	0 (0.00%)	1 (0.10%)
Pleural effusion	1 (0.10%)	0 (0.00%)
Pleurisy	1 (0.10%)	0 (0.00%)
Pleuritic pain	1 (0.10%)	2 (0.20%)
Pneumonia aspiration	1 (0.10%)	0 (0.00%)
Pneumonitis	4 (0.39%)	0 (0.00%)
Productive cough	0 (0.00%)	1 (0.10%)
Pulmonary artery thrombosis	1 (0.10%)	0 (0.00%)
Pulmonary congestion	1 (0.10%)	0 (0.00%)
Pulmonary embolism	17 (1.68%)	6 (0.59%)
Pulmonary hypertension	1 (0.10%)	2 (0.20%)
Pulmonary mass	0 (0.00%)	1 (0.10%)
Pulmonary oedema	3 (0.30%)	2 (0.20%)
Respiratory failure	3 (0.30%)	4 (0.40%)
Skin and subcutaneous tissue disorders		
Blister	0 (0.00%)	1 (0.10%)
Capillaritis	0 (0.00%)	1 (0.10%)
Dermatitis allergic	0 (0.00%)	1 (0.10%)
Diabetic foot	0 (0.00%)	1 (0.10%)
Erythema	0 (0.00%)	1 (0.10%)
Hyperhidrosis	0 (0.00%)	1 (0.10%)
Neuropathic ulcer	0 (0.00%)	1 (0.10%)

Peau d'orange	1 (0.10%)	0 (0.00%)
Skin necrosis	1 (0.10%)	0 (0.00%)
Skin oedema	1 (0.10%)	0 (0.00%)
Skin ulcer	1 (0.10%)	1 (0.10%)
Urticaria	1 (0.10%)	1 (0.10%)
Social circumstances		
Loss of personal independence in daily activities	1 (0.10%)	0 (0.00%)
Walking disability	1 (0.10%)	0 (0.00%)
Surgical and medical procedures		
Arteriovenous fistula operation	0 (0.00%)	1 (0.10%)
Orchidectomy	1 (0.10%)	0 (0.00%)
Vascular disorders		
Accelerated hypertension	1 (0.10%)	0 (0.00%)
Aortic aneurysm	1 (0.10%)	0 (0.00%)
Aortic perforation	0 (0.00%)	1 (0.10%)
Arterial stenosis	1 (0.10%)	0 (0.00%)
Arterial thrombosis	1 (0.10%)	0 (0.00%)
Arteriovenous fistula	1 (0.10%)	1 (0.10%)
Artery dissection	1 (0.10%)	0 (0.00%)
Deep vein thrombosis	20 (1.97%)	12 (1.19%)
Embolism venous	1 (0.10%)	0 (0.00%)
Haematoma	1 (0.10%)	3 (0.30%)

Hypertension	2 (0.20%)	6 (0.59%)
Hypertensive crisis	3 (0.30%)	5 (0.49%)
Hypertensive emergency	1 (0.10%)	0 (0.00%)
Hypotension	3 (0.30%)	8 (0.79%)
Intermittent claudication	0 (0.00%)	1 (0.10%)
Lymphocele	34 (3.35%)	21 (2.08%)
Lymphorrhoea	3 (0.30%)	0 (0.00%)
Malignant hypertension	1 (0.10%)	0 (0.00%)
Orthostatic hypotension	0 (0.00%)	1 (0.10%)
Pelvic venous thrombosis	0 (0.00%)	1 (0.10%)
Peripheral arterial occlusive disease	1 (0.10%)	1 (0.10%)
Peripheral artery stenosis	0 (0.00%)	2 (0.20%)
Peripheral artery thrombosis	2 (0.20%)	1 (0.10%)
Peripheral ischaemia	2 (0.20%)	1 (0.10%)
Phlebitis	1 (0.10%)	0 (0.00%)
Shock haemorrhagic	1 (0.10%)	2 (0.20%)
Thrombophlebitis superficial	0 (0.00%)	1 (0.10%)
Thrombosis	2 (0.20%)	0 (0.00%)
Varicose ulceration	1 (0.10%)	0 (0.00%)
Venous stenosis	0 (0.00%)	1 (0.10%)
Venous thrombosis	1 (0.10%)	3 (0.30%)
Venous thrombosis limb	0 (0.00%)	1 (0.10%)

Other Adverse Events by System Organ Class

Time Frame	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 up to approximately 4 years.
Additional Description	treatment emergent AE / SAE . Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events fields "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.
Source Vocabulary for Table Default	MedDRA (20.1)
Assessment Type for Table Default	Systematic Assessment
Frequent Event Reporting Threshold	5%

	Everolimus plus@reduced CNI N = 1014	**MPA plus standard@CNI N = 1012**
Total participants affected	951 (93.79%)	942 (93.08%)
Blood and lymphatic system disorders		
Anaemia	227 (22.39%)	238 (23.52%)
Leukocytosis	24 (2.37%)	58 (5.73%)
Leukopenia	94 (9.27%)	194 (19.17%)
Polycythaemia	52 (5.13%)	42 (4.15%)
Thrombocytopenia	74 (7.30%)	41 (4.05%)
Cardiac disorders		
Tachycardia	53 (5.23%)	52 (5.14%)

Gastrointestinal disorders		
Abdominal pain	94 (9.27%)	104 (10.28%)
Abdominal pain upper	39 (3.85%)	62 (6.13%)
Constipation	245 (24.16%)	242 (23.91%)
Diarrhoea	242 (23.87%)	318 (31.42%)
Nausea	191 (18.84%)	225 (22.23%)
Vomiting	120 (11.83%)	140 (13.83%)
General disorders and administration site conditions		
Fatigue	59 (5.82%)	64 (6.32%)
Oedema peripheral	347 (34.22%)	244 (24.11%)
Pyrexia	112 (11.05%)	132 (13.04%)
Infections and infestations		
BK virus infection	56 (5.52%)	101 (9.98%)
Cytomegalovirus infection	24 (2.37%)	93 (9.19%)
Nasopharyngitis	110 (10.85%)	117 (11.56%)
Upper respiratory tract infection	81 (7.99%)	102 (10.08%)
Urinary tract infection	219 (21.60%)	249 (24.60%)
Injury, poisoning and procedural complications		
Complications of transplanted kidney	63 (6.21%)	54 (5.34%)
Incision site pain	51 (5.03%)	61 (6.03%)
Procedural pain	90 (8.88%)	99 (9.78%)

Investigations		
Blood creatinine increased	141 (13.91%)	133 (13.14%)
Weight increased	38 (3.75%)	66 (6.52%)
Metabolism and nutrition disorders		
Diabetes mellitus	133 (13.12%)	120 (11.86%)
Dyslipidaemia	98 (9.66%)	57 (5.63%)
Hypercalcaemia	39 (3.85%)	67 (6.62%)
Hypercholesterolaemia	103 (10.16%)	61 (6.03%)
Hyperglycaemia	140 (13.81%)	144 (14.23%)
Hyperkalaemia	164 (16.17%)	184 (18.18%)
Hyperlipidaemia	135 (13.31%)	75 (7.41%)
Hypertriglyceridaemia	58 (5.72%)	24 (2.37%)
Hyperuricaemia	49 (4.83%)	64 (6.32%)
Hypocalcaemia	109 (10.75%)	98 (9.68%)
Hypokalaemia	148 (14.60%)	87 (8.60%)
Hypomagnesaemia	134 (13.21%)	168 (16.60%)
Hypophosphataemia	190 (18.74%)	167 (16.50%)
Metabolic acidosis	77 (7.59%)	98 (9.68%)
Vitamin D deficiency	53 (5.23%)	57 (5.63%)
Musculoskeletal and connective tissue disorders		
Arthralgia	63 (6.21%)	65 (6.42%)
Back pain	93 (9.17%)	98 (9.68%)
Pain in extremity	66 (6.51%)	61 (6.03%)

Nervous system disorders		
Dizziness	51 (5.03%)	54 (5.34%)
Headache	133 (13.12%)	113 (11.17%)
Tremor	100 (9.86%)	145 (14.33%)
Psychiatric disorders		
Anxiety	51 (5.03%)	59 (5.83%)
Insomnia	100 (9.86%)	138 (13.64%)
Renal and urinary disorders		
Dysuria	60 (5.92%)	74 (7.31%)
Haematuria	102 (10.06%)	101 (9.98%)
Proteinuria	131 (12.92%)	69 (6.82%)
Respiratory, thoracic and mediastinal disorders		
Cough	86 (8.48%)	102 (10.08%)
Dyspnoea	73 (7.20%)	70 (6.92%)
Skin and subcutaneous tissue disorders		
Acne	56 (5.52%)	37 (3.66%)
Alopecia	27 (2.66%)	59 (5.83%)
Vascular disorders		
Hypertension	240 (23.67%)	230 (22.73%)
Hypotension	62 (6.11%)	78 (7.71%)

Other Relevant Findings

Definition: *Important finding not meeting the criteria for efficacy/safety results (ie, notable change in laboratory or drug trough values that posed no safety issue, but is of medical interest).*

Example: *Mean (SD) parameters of company product*

Conclusion:

The results of this study suggest that a treatment regimen combining everolimus and a reduced dose of a calcineurin inhibitor (either tacrolimus or cyclosporine) is a valid alternative to mycophenolic acid plus tacrolimus (the current standard of care regimen) or cyclosporine, allowing good efficacy provided dosing recommendations are complied with, as well as good and stable renal function and a safety profile comparable to what is already known. Consistent with earlier findings in the everolimus development program, viral infections, in particular cytomegalovirus and BK virus infections, were less frequently reported in patients in an everolimus treatment regimen compared to those treated with mycophenolic acid.

Date of Clinical Trial Report

23-Jul-2018