



Clinical trial results:

A multicenter, randomized, open-labeled study to steer immunosuppressive and antiviral therapy by measurement of virus- (CMV, ADV, HSV) specific T cells in addition to determination of trough levels of immunosuppressants in pediatric kidney allograft recipients. An explorative study.

Summary

EudraCT number	2009-012436-32
Trial protocol	DE
Global end of trial date	26 March 2019

Results information

Result version number	v1 (current)
This version publication date	11 November 2023
First version publication date	11 November 2023

Trial information

Trial identification

Sponsor protocol code	IVIST01
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Hannover Medical School
Sponsor organisation address	Carl-Neuberg-Str. 1, Hannover, Germany, 30625
Public contact	Stabsstelle Zentrum für Klinische Studien, Hannover Medical School, EudraCT@mh-hannover.de
Scientific contact	Stabsstelle Zentrum für Klinische Studien, Hannover Medical School, EudraCT@mh-hannover.de

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	24 March 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 March 2019
Global end of trial reached?	Yes
Global end of trial date	26 March 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Prolongation of kidney function and reduced viral infections after solid organ transplantation by monitoring of virus-specific T cells followed by therapeutic intervention. The primary endpoint is eGFR (Cystatin C, Filler) 2 years after transplantation

Protection of trial subjects:

The clinical trial was conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki and with the standards of International Conference on Harmonisation (ICH) Good Clinical Practice (GCP). A continuous risk assessment was performed during the study

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 April 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 64
Worldwide total number of subjects	64
EEA total number of subjects	64

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)	64
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

All children after kidney transplantation will be asked for participation within the first 4 weeks after transplantation.

Pre-assignment

Screening details:

Eligibility will be determined based upon the inclusion and exclusion criteria

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	non intervention group

Arm description:

In the control group and the intervention group the immunosuppressive medication will be steered in the 'normal' target range of trough levels due to the standard protocol. In case of the control group the physician decides the application rate of the immunosuppressive medication in the normal target range of trough levels arbitrarily

Arm type	Active comparator
Investigational medicinal product name	Sandimmune® Optoral
Investigational medicinal product code	
Other name	Ciclosporine A
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Ciclosporine A (CsA)-start dose is 400 mg/m²/d in two doses (maximal dose 250mg/dose), dose will be adopted to target C0-levels of 200-250 ng/ml for the first 4 weeks after transplantation, then CsA will be reduced by 50% to a target C0-level of 50-100 ng/ml (HPLC) (a tolerance of \pm 10% in the target C0-level is allowed for a period of 8 weeks) when administered together with Everolimus. Target doses are reduced to 30-75 ng/ml (a tolerance of \pm 10% in the target C0-level is allowed for a period of 8 weeks) six months after transplantation.

Sandimmun® Optoral will be given on a twice-daily schedule at approximately 12-hours intervals in the morning and in the evening for the complete study duration of 23 months.

Investigational medicinal product name	Certican
Investigational medicinal product code	
Other name	Everolimus
Pharmaceutical forms	Tablet, Tablet and powder for oral solution
Routes of administration	Oral use

Dosage and administration details:

Patients will be treated with Everolimus, starting four weeks after transplantation with 0.8 mg/m² Everolimus b.i.d. (maximal dose 1.5 mg/dose). Target trough levels are 3-6 ng/ml (HPLC) in the first five months and 2-5 ng/ml thereafter.

Dosing should be adjusted in all patients if the Everolimus whole blood trough level is below 3 ng/ml or above 6 ng/ml (a tolerance of \pm 10% in the target C0-level is allowed for a period of 8 weeks) and below 2 ng/ml or above 5 ng/ml (a tolerance of \pm 10% in the target C0-level is allowed for a period of 8 weeks) six months after transplantation.

Blood for Everolimus trough levels will be obtained from all patients. Blood should be drawn 15 minutes before the administration of the morning dose of Everolimus. For the C0 samples the date of sampling should be recorded on the Immunosuppressive Therapies CRF.

Investigational medicinal product name	Valcyte
Investigational medicinal product code	
Other name	Valganciclovir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

In case of CMV-infection/-reactivation with relevant CMV-DNA-detection, in both groups an antiviral therapy with Valganciclovir will be performed. In the non-intervention group Valganciclovir will be given for 3 months

The dosing of Valganciclovir will be calculated according to the following:

Dose (mg) = GFR x 7 x BSA (body surface area), applied in one single dose per day; maximum dose 1 x 900 mg. If the calculated GFR exceeds 150ml/min/1,73m², dose is calculated with a GFR of 150ml/min/1,73m².

Arm title	intervention-group
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Arm description:

In the intervention group immunosuppressive therapy should be adopted due to the levels of virus-specific T cells as a direct measure of the intensity of immunosuppression in addition to classical trough level monitoring. Antiviral management should be based on the individual virus-specific immune defense assessed by the amount of virus-specific T cells.

Arm type	Experimental
Investigational medicinal product name	Sandimmune® Optoral
Investigational medicinal product code	
Other name	Ciclosporine A
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Ciclosporine A (CsA)-start dose is 400 mg/m²/d in two doses (maximal dose 250mg/dose), dose will be adopted to target C0-levels of 200-250 ng/ml for the first 4 weeks after transplantation, then CsA will be reduced by 50% to a target C0-level of 50-100 ng/ml (HPLC) (a tolerance of ± 10% in the target C0-level is allowed for a period of 8 weeks) when administered together with Everolimus. Target doses are reduced to 30-75 ng/ml (a tolerance of ± 10% in the target C0-level is allowed for a period of 8 weeks) six months after transplantation.

Sandimmun® Optoral will be given on a twice-daily schedule at approximately 12-hours intervals in the morning and in the evening for the complete study duration of 23 months.

Investigational medicinal product name	Certican
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Dosage and administration details:

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Dosing should be adjusted in all patients if the Everolimus whole blood trough level is below 3 ng/ml or above 6 ng/ml (a tolerance of ± 10% in the target C0-level is allowed for a period of 8 weeks) and below 2 ng/ml or above 5 ng/ml (a tolerance of ± 10% in the target C0-level is allowed for a period of 8 weeks) six months after transplantation.

Blood for Everolimus trough levels will be obtained from all patients. Blood should be drawn 15 minutes before the administration of the morning dose of Everolimus. For the C0 samples the date of sampling should be recorded on the Immunosuppressive Therapies CRF.

Investigational medicinal product name	Valcyte
Investigational medicinal product code	
Other name	Valganciclovir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

In case of CMV-infection/-reactivation with relevant CMV-DNA-detection, in both groups an antiviral therapy with Valganciclovir will be performed. In the intervention group, Valganciclovir therapy will only be carried out until there is a sufficient and stable number of CMV-specific CD4 T cells without DNA-detection.

The dosing of Valganciclovir will be calculated according to the following:

Dose (mg) = GFR x 7 x BSA (body surface area), applied in one single dose per day; maximum dose 1 x 900 mg. If the calculated GFR exceeds 150ml/min/1,73m², dose is calculated with a GFR of 150ml/min/1,73m².

Number of subjects in period 1	non intervention group	intervention-group
Started	33	31
Completed	30	25
Not completed	3	6
patient died by drowning in a bath tub	1	-
disease relapse	1	1
rejection	1	5

Baseline characteristics

Reporting groups

Reporting group title	non intervention group
Reporting group description:	
In the control group and the intervention group the immunosuppressive medication will be steered in the 'normal' target range of trough levels due to the standard protocol. In case of the control group the physician decides the application rate of the immunosuppressive medication in the normal target range of trough levels arbitrarily	
Reporting group title	intervention-group
Reporting group description:	
In the intervention group immunosuppressive therapy should be adopted due to the levels of virus-specific T cells as a direct measure of the intensity of immunosuppression in addition to classical trough level monitoring. Antiviral management should be based on the individual virus-specific immune defense assessed by the amount of virus-specific T cells.	

Reporting group values	non intervention group	intervention-group	Total
Number of subjects	33	31	64
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
median	11.33	11.92	
full range (min-max)	1.75 to 16.42	1.58 to 16.17	-
Gender categorical			
Units: Subjects			
Female	14	13	27
Male	19	18	37

End points

End points reporting groups

Reporting group title	non intervention group
Reporting group description: In the control group and the intervention group the immunosuppressive medication will be steered in the 'normal' target range of trough levels due to the standard protocol. In case of the control group the physician decides the application rate of the immunosuppressive medication in the normal target range of trough levels arbitrarily	
Reporting group title	intervention-group
Reporting group description: In the intervention group immunosuppressive therapy should be adopted due to the levels of virus-specific T cells as a direct measure of the intensity of immunosuppression in addition to classical trough level monitoring. Antiviral management should be based on the individual virus-specific immune defense assessed by the amount of virus-specific T cells.	

Primary: eGFR (Cystatin C, Filler) 2 years after transplantation

End point title	eGFR (Cystatin C, Filler) 2 years after transplantation
End point description:	
End point type	Primary
End point timeframe: 2 years after transplantation	

End point values	non intervention group	intervention-group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	31		
Units: eGFR filler				
number (confidence interval 95%)				
population A	61.49 (44.84 to 78.14)	62.27 (45.78 to 79.66)		
population B	60.78 (45.99 to 75.56)	66.19 (45.99 to 75.56)		
population C	59.35 (44.52 to 74.18)	61.91 (44.52 to 74.18)		

Statistical analyses

Statistical analysis title	eGFR filler 2 years after transplantation
Comparison groups	non intervention group v intervention-group

Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7743
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.15
upper limit	13.55
Variability estimate	Standard deviation
Dispersion value	22.51

Secondary: Death and relapse

End point title	Death and relapse
End point description:	
End point type	Secondary
End point timeframe:	
during participation in the study , over the whole time	

End point values	non intervention group	intervention- group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	31		
Units: death and relapse	2	2		

Statistical analyses

No statistical analyses for this end point

Secondary: histological evidence of acute rejection and type

End point title	histological evidence of acute rejection and type
End point description:	
Protocol defined biopsy (6 months after transplantation) was performed on 51 patients. For one patient in the non-intervention group (Center No.=1, Subject No.=11), the sample material was insufficient for histological assessment. In the protocol defined biopsies, only acute rejections were detected.	
End point type	Secondary
End point timeframe:	
over the whole duration of the study	

End point values	non intervention group	intervention- group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	24		
Units: rejections				
Borderline	11	8		
Banff type IA	3	4		
Banff type IB	2	0		
Banff type IIA	1	1		
Total	17	13		

Statistical analyses

Statistical analysis title	chi squared test
Comparison groups	intervention-group v non intervention group
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.4186
Method	Chi-squared

Secondary: CMV DNA

End point title	CMV DNA
End point description:	
Number of patients with CMV-DNA \geq the cut-off value of 1000 copies/ml	
End point type	Secondary
End point timeframe:	
over the duration of the study	

End point values	non intervention group	intervention- group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	31		
Units: number of patients with CMV DNA	2	2		

Statistical analyses

Statistical analysis title	Fishers exact test
Comparison groups	non intervention group v intervention-group
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 1
Method	Fisher exact

Secondary: ADV DNA

End point title	ADV DNA
End point description:	Number of patients with ADV-DNA \geq the cut-off value of 1000 copies/ml
End point type	Secondary
End point timeframe:	over the duration of the study

End point values	non intervention group	intervention-group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	31		
Units: number of patients with ADV DNA	1	1		

Statistical analyses

Statistical analysis title	Fishers exact test
Comparison groups	non intervention group v intervention-group
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 1
Method	Fisher exact

Secondary: HSV DNA

End point title	HSV DNA
End point description:	Number of patients with HSV-DNA \geq the cut-off value of 1000 copies/ml
End point type	Secondary
End point timeframe:	over the duration of the study participation

End point values	non intervention group	intervention- group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	31		
Units: number of patients with HSV DNA	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: EBV DNA

End point title	EBV DNA
End point description:	
Number of patients with EBV-DNA \geq the cut-off value of 1000 copies/ml	
End point type	Secondary
End point timeframe:	
during the duration of the study participation	

End point values	non intervention group	intervention- group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	31		
Units: number of patients with EBV DNA	14	7		

Statistical analyses

Statistical analysis title	chi squared test
Comparison groups	non intervention group v intervention-group
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.00911
Method	Chi-squared

Secondary: dose of study medication Everolimus

End point title	dose of study medication Everolimus
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End point description:

The analysis of the dose of the study medications is performed on 55 patients who completed the treatment regimen according to the study protocol (population B). Mean daily dose/m² (mg/m²) from month 7 after transplantation to the end of the study is calculated for each patient and compared descriptively between the treatment groups using two-sided t-tests. For one patient (Center No.=3 & Subject No.=5) who did not participate Visit 9 (Month 7), data from Visit 10 (Month 8) until the end of the study are utilised in the analyses.

End point type	Secondary
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End point timeframe:

Mean daily dose/m² (mg/m²) from month 7 after transplantation to the end of the study is calculated for each patient and compared descriptively between the treatment groups

End point values	non intervention group	intervention-group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	25		
Units: mg/m ²				
number (not applicable)	1.15	0.82		

Statistical analyses

Statistical analysis title	Mean difference
Comparison groups	non intervention group v intervention-group
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0039
Method	t-test, 2-sided

Secondary: trough blood level of study medication Everolimus

End point title	trough blood level of study medication Everolimus
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End point description:

The analysis of the trough blood level of the study medications is performed on 55 patients who completed the treatment regimen according to the study protocol (population B). Mean trough blood level (µg/L) from month 7 after transplantation to the end of the study is calculated for each patient and compared between the treatment groups using t tests. For one patient (Center No.=3 & Subject No.=5) who did not participate Visit 9 (Month 7), data from Visit 10 (Month 8) until the end of the study are utilised in the analyses.

End point type	Secondary
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End point timeframe:

from month 7 after transplantation to the end of the study is calculated for each patient

End point values	non intervention group	intervention-group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	25		
Units: micrograms/L				
number (not applicable)	4.47	3.46		

Statistical analyses

Statistical analysis title	t test
Comparison groups	intervention-group v non intervention group
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.0001
Method	t-test, 2-sided

Secondary: dose of study medication Ciclosporin A

End point title	dose of study medication Ciclosporin A
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End point description:

The analysis of the dose of the study medications is performed on 55 patients who completed the treatment regimen according to the study protocol (population B). Mean daily dose/m2 (mg/m2) from month 7 after transplantation to the end of the study is calculated for each patient and compared descriptively between the treatment groups using two-sided t-tests. For one patient (Center No.=3 & Subject No.=5) who did not participate Visit 9 (Month 7), data from Visit 10 (Month 8) until the end of the study are utilised in the analyses.

End point type	Secondary
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End point timeframe:

Mean daily dose/m2 (mg/m2) from month 7 after transplantation to the end of the study

End point values	non intervention group	intervention-group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	25		
Units: mg/m2				
number (not applicable)	88.38	78.43		

Statistical analyses

Statistical analysis title	t test
Comparison groups	non intervention group v intervention-group

Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.1283
Method	t-test, 2-sided

Secondary: through blood level of Ciclosporin A

End point title	through blood level of Ciclosporin A
End point description:	
The analysis of the trough blood level of the study medications is performed on 55 patients who completed the treatment regimen according to the study protocol (population B). Mean trough blood level (µg/L) from month 7 after transplantation to the end of the study is calculated for each patient and compared between the treatment groups using t tests. For one patient (Center No.=3 & Subject No.=5) who did not participate Visit 9 (Month 7), data from Visit 10 (Month 8) until the end of the study are utilised in the analyses.	
End point type	Secondary
End point timeframe:	
Mean trough blood level (µg/L) from month 7 after transplantation to the end of the study	

End point values	non intervention group	intervention-group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	25		
Units: micrograms/L				
number (not applicable)	64.05	47.36		

Statistical analyses

Statistical analysis title	t test
Comparison groups	non intervention group v intervention-group
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.0001
Method	t-test, 2-sided

Secondary: Glucocorticoids

End point title	Glucocorticoids
End point description:	
The analysis of the therapy with glucocorticoids is performed on 55 patients who completed the treatment regimen according to the study protocol (population B). The number of patients with oral therapy with glucocorticoids 2 years after transplantation is compared between the treatment groups using a descriptive chi-squared test.	

End point type	Secondary
End point timeframe:	
The number of patients with oral therapy with glucocorticoids 2 years after transplantation	

End point values	non intervention group	intervention-group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	25		
Units: number of patients with oral GCR-A	14	5		

Statistical analyses

Statistical analysis title	chi squared test
Comparison groups	non intervention group v intervention-group
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.0384
Method	Chi-squared

Secondary: clinically indicated biopsy

End point title	clinically indicated biopsy
End point description:	
End point type	Secondary
End point timeframe:	
over the duration of the study	

End point values	non intervention group	intervention-group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	11		
Units: indicated biopsy and rejection				
Borderline	7	1		
Banff type IA	2	3		
Banff type IB	7	4		
Banff type IIA	1	3		
Banff type IIB	1	0		
Banff type III	1	0		
Total	19	11		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AE occurring after study start. Medical conditions/diseases present before study start are only considered AE if they worsen after study start.

Adverse event reporting additional description:

Numbers in the non-serious adverse events section reflect all adverse events occurring during the study (non-serious and serious).

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	22.0
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Reporting groups

Reporting group title	intervention
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Reporting group description: -

Reporting group title	non-intervention
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Reporting group description: -

Serious adverse events	intervention	non-intervention	
Total subjects affected by serious adverse events			
subjects affected / exposed	25 / 31 (80.65%)	28 / 33 (84.85%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events			
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shock			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			

Drowning			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Face oedema			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Medical device site calcification			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	8 / 31 (25.81%)	11 / 33 (33.33%)	
occurrences causally related to treatment / all	8 / 10	15 / 15	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Kidney transplant rejection			
subjects affected / exposed	8 / 31 (25.81%)	14 / 33 (42.42%)	
occurrences causally related to treatment / all	1 / 14	2 / 20	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal transplant failure			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal			

disorders			
Cough			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperventilation			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthopnoea			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device malfunction			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood creatinine increased			
subjects affected / exposed	11 / 31 (35.48%)	7 / 33 (21.21%)	
occurrences causally related to treatment / all	13 / 21	9 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigation			

subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Abdominal injury			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous fistula thrombosis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Craniocerebral injury			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrostomy tube site complication			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal lymphocele			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shunt blood flow excessive			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulna fracture			

subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Hypertrophic cardiomyopathy			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss of consciousness			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Petit mal epilepsy			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	2 / 31 (6.45%)	3 / 33 (9.09%)	
occurrences causally related to treatment / all	1 / 2	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Papilloedema			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	2 / 31 (6.45%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	4 / 31 (12.90%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	4 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	1 / 31 (3.23%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			

subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	6 / 31 (19.35%)	2 / 33 (6.06%)	
occurrences causally related to treatment / all	4 / 7	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Ingrowing nail			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Focal segmental glomerulosclerosis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukocyturia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Micturition disorder			

subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal necrosis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral obstruction			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vesicoureteric reflux			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Diabetes insipidus			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abscess limb			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous fistula site infection			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteriuria			

subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	2 / 31 (6.45%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear infection			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterobacter sepsis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia urinary tract infection			
subjects affected / exposed	2 / 31 (6.45%)	2 / 33 (6.06%)	
occurrences causally related to treatment / all	2 / 2	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile infection			
subjects affected / exposed	3 / 31 (9.68%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	6 / 6	5 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	9 / 31 (29.03%)	2 / 33 (6.06%)	
occurrences causally related to treatment / all	7 / 9	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis adenovirus			

subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis rotavirus			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Human bocavirus infection			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Implant site infection			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	1 / 31 (3.23%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	1 / 31 (3.23%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parainfluenzae virus infection			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paronychia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	4 / 31 (12.90%)	3 / 33 (9.09%)	
occurrences causally related to treatment / all	2 / 4	5 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyomavirus-associated nephropathy			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	3 / 31 (9.68%)	2 / 33 (6.06%)	
occurrences causally related to treatment / all	4 / 4	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal abscess			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	0 / 31 (0.00%)	2 / 33 (6.06%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhinitis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	3 / 31 (9.68%)	2 / 33 (6.06%)	
occurrences causally related to treatment / all	2 / 3	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	4 / 31 (12.90%)	3 / 33 (9.09%)	
occurrences causally related to treatment / all	6 / 8	3 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection enterococcal			

subjects affected / exposed	2 / 31 (6.45%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	1 / 2	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection pseudomonal			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	9 / 31 (29.03%)	5 / 33 (15.15%)	
occurrences causally related to treatment / all	17 / 18	9 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	1 / 31 (3.23%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	8 / 31 (25.81%)	3 / 33 (9.09%)	
occurrences causally related to treatment / all	4 / 11	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fluid intake reduced			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fluid overload			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercreatininaemia			

subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	1 / 31 (3.23%)	2 / 33 (6.06%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	4 / 31 (12.90%)	2 / 33 (6.06%)	
occurrences causally related to treatment / all	4 / 7	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic acidosis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	intervention	non-intervention	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 31 (100.00%)	33 / 33 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Sebacous adenoma			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Skin papilloma			
subjects affected / exposed	3 / 31 (9.68%)	10 / 33 (30.30%)	
occurrences (all)	4	11	
Vascular disorders			

Arteriovenous fistula subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 33 (3.03%) 1	
Haematoma subjects affected / exposed occurrences (all)	5 / 31 (16.13%) 5	3 / 33 (9.09%) 3	
Hypertension subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	5 / 33 (15.15%) 6	
Lymphoedema subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 33 (3.03%) 1	
Shock subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 33 (3.03%) 1	
Venous thrombosis subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 33 (3.03%) 1	
Pregnancy, puerperium and perinatal conditions Umbilical granuloma subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 33 (3.03%) 1	
General disorders and administration site conditions Chest pain subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 3	0 / 33 (0.00%) 0	
Drowning subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 33 (3.03%) 1	
Face oedema subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	2 / 33 (6.06%) 2	
Fatigue subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 33 (3.03%) 1	
General physical health deterioration			

subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)
occurrences (all)	2	0
Generalised oedema		
subjects affected / exposed	2 / 31 (6.45%)	1 / 33 (3.03%)
occurrences (all)	2	1
Granuloma		
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)
occurrences (all)	1	0
Impaired healing		
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)
occurrences (all)	1	0
Injection site haematoma		
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)
occurrences (all)	1	0
Malaise		
subjects affected / exposed	1 / 31 (3.23%)	1 / 33 (3.03%)
occurrences (all)	2	1
Medical device pain		
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)
occurrences (all)	1	0
Medical device site calcification		
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Medical device site erythema		
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Medical device site granuloma		
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)
occurrences (all)	1	0
Medical device site inflammation		
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Oedema peripheral		
subjects affected / exposed	7 / 31 (22.58%)	8 / 33 (24.24%)
occurrences (all)	9	15
Pain		

subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Pyrexia			
subjects affected / exposed	18 / 31 (58.06%)	24 / 33 (72.73%)	
occurrences (all)	69	76	
Vaccination site pain			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Immune system disorders			
Immunodeficiency			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Kidney transplant rejection			
subjects affected / exposed	8 / 31 (25.81%)	14 / 33 (42.42%)	
occurrences (all)	14	20	
Renal transplant failure			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Seasonal allergy			
subjects affected / exposed	1 / 31 (3.23%)	1 / 33 (3.03%)	
occurrences (all)	1	1	
Reproductive system and breast disorders			
Adipomastia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Breast swelling			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Genital rash			
subjects affected / exposed	1 / 31 (3.23%)	1 / 33 (3.03%)	
occurrences (all)	1	1	
Gynaecomastia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Menorrhagia			

subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Scrotal erythema			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Bronchial obstruction			
subjects affected / exposed	1 / 31 (3.23%)	1 / 33 (3.03%)	
occurrences (all)	1	1	
Cough			
subjects affected / exposed	26 / 31 (83.87%)	19 / 33 (57.58%)	
occurrences (all)	61	38	
Dyspnoea			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Epistaxis			
subjects affected / exposed	2 / 31 (6.45%)	4 / 33 (12.12%)	
occurrences (all)	4	7	
Hyperventilation			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Nasal congestion			
subjects affected / exposed	2 / 31 (6.45%)	2 / 33 (6.06%)	
occurrences (all)	2	2	
Obstructive airways disorder			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Oropharyngeal pain			
subjects affected / exposed	7 / 31 (22.58%)	10 / 33 (30.30%)	
occurrences (all)	9	15	
Orthopnoea			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences (all)	2	0	
Pharyngeal erythema			

subjects affected / exposed	1 / 31 (3.23%)	1 / 33 (3.03%)	
occurrences (all)	1	1	
Pleural effusion			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	2	
Respiratory failure			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Rhinitis allergic			
subjects affected / exposed	2 / 31 (6.45%)	2 / 33 (6.06%)	
occurrences (all)	2	2	
Rhinorrhoea			
subjects affected / exposed	7 / 31 (22.58%)	7 / 33 (21.21%)	
occurrences (all)	10	12	
Tonsillar hypertrophy			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Behaviour disorder			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Depression			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Encopresis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Enuresis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Insomnia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Sleep disorder			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	

Product issues			
Device malfunction			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences (all)	2	0	
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Alanine aminotransferase increased			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Blood albumin decreased			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Blood bicarbonate increased			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Blood cholesterol increased			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Blood creatinine increased			
subjects affected / exposed	16 / 31 (51.61%)	13 / 33 (39.39%)	
occurrences (all)	34	24	
Enterococcus test positive			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Klebsiella test positive			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Investigation			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	

Liver function test increased subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 33 (0.00%) 0	
Mammogram abnormal subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 33 (3.03%) 1	
Weight decreased subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 33 (3.03%) 1	
Injury, poisoning and procedural complications			
Abdominal injury subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 33 (3.03%) 1	
Arteriovenous fistula thrombosis subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 33 (3.03%) 1	
Arthropod bite subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 33 (3.03%) 1	
Arthropod sting subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 33 (0.00%) 0	
Bone contusion subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 33 (3.03%) 1	
Complications of transplant surgery subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 33 (0.00%) 0	
Contusion subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	2 / 33 (6.06%) 2	
Craniocerebral injury subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 33 (3.03%) 1	
Fall			

subjects affected / exposed	2 / 31 (6.45%)	0 / 33 (0.00%)
occurrences (all)	2	0
Foot fracture		
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Forearm fracture		
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)
occurrences (all)	1	0
Gastrostomy tube site complication		
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)
occurrences (all)	1	0
Incision site haematoma		
subjects affected / exposed	2 / 31 (6.45%)	2 / 33 (6.06%)
occurrences (all)	2	2
Incisional hernia		
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Ligament sprain		
subjects affected / exposed	2 / 31 (6.45%)	0 / 33 (0.00%)
occurrences (all)	2	0
Ligament rupture		
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Muscle strain		
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Post procedural swelling		
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Postoperative wound complication		
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)
occurrences (all)	1	0
Procedural pain		
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Radius fracture		

subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Renal lymphocele			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Shunt aneurysm			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Shunt blood flow excessive			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Skin laceration			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Skin abrasion			
subjects affected / exposed	1 / 31 (3.23%)	1 / 33 (3.03%)	
occurrences (all)	1	1	
Stoma site pain			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Subcutaneous haematoma			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	2	
Suture related complication			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Ulna fracture			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Traumatic haematoma			
subjects affected / exposed	0 / 31 (0.00%)	2 / 33 (6.06%)	
occurrences (all)	0	2	
Vaccination complication			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	2	
Congenital, familial and genetic			

disorders			
Cryptorchism			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Hydrocele			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Hypertrophic cardiomyopathy			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Pericardial effusion			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	2	
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 31 (6.45%)	3 / 33 (9.09%)	
occurrences (all)	2	3	
Headache			
subjects affected / exposed	14 / 31 (45.16%)	15 / 33 (45.45%)	
occurrences (all)	22	31	
Loss of consciousness			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Migraine			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Petit mal epilepsy			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Tremor			
subjects affected / exposed	1 / 31 (3.23%)	2 / 33 (6.06%)	
occurrences (all)	1	2	
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	6 / 31 (19.35%)	8 / 33 (24.24%)	
occurrences (all)	7	8	
Hypochromic anaemia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Iron deficiency anaemia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Lymphadenopathy			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Neutropenia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Thrombocytopenia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	8 / 31 (25.81%)	2 / 33 (6.06%)	
occurrences (all)	8	2	
Middle ear effusion			
subjects affected / exposed	1 / 31 (3.23%)	2 / 33 (6.06%)	
occurrences (all)	1	3	
Tympanic membrane hyperaemia			
subjects affected / exposed	1 / 31 (3.23%)	2 / 33 (6.06%)	
occurrences (all)	1	2	
Vertigo			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Eye disorders			
Eyelid oedema			
subjects affected / exposed	3 / 31 (9.68%)	5 / 33 (15.15%)	
occurrences (all)	4	6	
Eye haematoma			

subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Papilloedema			
subjects affected / exposed	1 / 31 (3.23%)	1 / 33 (3.03%)	
occurrences (all)	1	2	
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Abdominal pain			
subjects affected / exposed	8 / 31 (25.81%)	3 / 33 (9.09%)	
occurrences (all)	10	5	
Abdominal pain upper			
subjects affected / exposed	11 / 31 (35.48%)	6 / 33 (18.18%)	
occurrences (all)	11	7	
Aphthous ulcer			
subjects affected / exposed	7 / 31 (22.58%)	8 / 33 (24.24%)	
occurrences (all)	9	21	
Ascites			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Chapped lips			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Constipation			
subjects affected / exposed	0 / 31 (0.00%)	2 / 33 (6.06%)	
occurrences (all)	0	3	
Diarrhoea			
subjects affected / exposed	17 / 31 (54.84%)	22 / 33 (66.67%)	
occurrences (all)	33	37	
Dyspepsia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Enteritis			
subjects affected / exposed	1 / 31 (3.23%)	1 / 33 (3.03%)	
occurrences (all)	2	1	

Flatulence		
subjects affected / exposed	3 / 31 (9.68%)	1 / 33 (3.03%)
occurrences (all)	4	1
Gastric ulcer		
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Gingival hypertrophy		
subjects affected / exposed	17 / 31 (54.84%)	17 / 33 (51.52%)
occurrences (all)	20	17
Gastrooesophageal reflux disease		
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)
occurrences (all)	1	0
Haemorrhoids		
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Lip blister		
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Mouth ulceration		
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Nausea		
subjects affected / exposed	5 / 31 (16.13%)	3 / 33 (9.09%)
occurrences (all)	5	4
Oesophagitis		
subjects affected / exposed	0 / 31 (0.00%)	2 / 33 (6.06%)
occurrences (all)	0	2
Oral disorder		
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Oral mucosal blistering		
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Post-tussive vomiting		
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1

Stomatitis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Toothache			
subjects affected / exposed	2 / 31 (6.45%)	0 / 33 (0.00%)	
occurrences (all)	2	0	
Umbilical hernia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	14 / 31 (45.16%)	21 / 33 (63.64%)	
occurrences (all)	35	42	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	6 / 31 (19.35%)	8 / 33 (24.24%)	
occurrences (all)	7	10	
Alopecia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Blister			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Dandruff			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Dermatitis			
subjects affected / exposed	0 / 31 (0.00%)	2 / 33 (6.06%)	
occurrences (all)	0	2	
Eczema			
subjects affected / exposed	1 / 31 (3.23%)	5 / 33 (15.15%)	
occurrences (all)	1	5	
Erythema			
subjects affected / exposed	1 / 31 (3.23%)	1 / 33 (3.03%)	
occurrences (all)	1	1	
Hirsutism			

subjects affected / exposed	0 / 31 (0.00%)	2 / 33 (6.06%)
occurrences (all)	0	2
Hyperkeratosis		
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Hypertrichosis		
subjects affected / exposed	18 / 31 (58.06%)	18 / 33 (54.55%)
occurrences (all)	18	18
Hypertrophic scar		
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)
occurrences (all)	1	0
Ingrowing nail		
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)
occurrences (all)	3	0
Keloid scar		
subjects affected / exposed	2 / 31 (6.45%)	0 / 33 (0.00%)
occurrences (all)	2	0
Papule		
subjects affected / exposed	0 / 31 (0.00%)	2 / 33 (6.06%)
occurrences (all)	0	2
Pruritus		
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Rash		
subjects affected / exposed	6 / 31 (19.35%)	2 / 33 (6.06%)
occurrences (all)	6	2
Rash papular		
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)
occurrences (all)	1	0
Scar pain		
subjects affected / exposed	2 / 31 (6.45%)	2 / 33 (6.06%)
occurrences (all)	2	2
Seborrhoeic dermatitis		
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)
occurrences (all)	1	0
Skin exfoliation		

subjects affected / exposed	2 / 31 (6.45%)	0 / 33 (0.00%)	
occurrences (all)	2	0	
Skin striae			
subjects affected / exposed	0 / 31 (0.00%)	3 / 33 (9.09%)	
occurrences (all)	0	3	
Swelling face			
subjects affected / exposed	0 / 31 (0.00%)	2 / 33 (6.06%)	
occurrences (all)	0	2	
Urticaria			
subjects affected / exposed	2 / 31 (6.45%)	0 / 33 (0.00%)	
occurrences (all)	2	0	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 31 (3.23%)	1 / 33 (3.03%)	
occurrences (all)	1	1	
Focal segmental glomerulosclerosis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Hydronephrosis			
subjects affected / exposed	1 / 31 (3.23%)	1 / 33 (3.03%)	
occurrences (all)	1	1	
Leukocyturia			
subjects affected / exposed	5 / 31 (16.13%)	4 / 33 (12.12%)	
occurrences (all)	6	7	
Micturition disorder			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Proteinuria			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences (all)	2	0	
Renal necrosis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Renal pain			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	

Urinary retention subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 33 (3.03%) 1	
Urethral obstruction subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 33 (0.00%) 0	
Vesicoureteric reflux subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 33 (3.03%) 1	
Endocrine disorders Cushing's syndrome subjects affected / exposed occurrences (all)	10 / 31 (32.26%) 10	8 / 33 (24.24%) 8	
Diabetes insipidus subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 33 (0.00%) 0	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	5 / 31 (16.13%) 5	3 / 33 (9.09%) 3	
Back pain subjects affected / exposed occurrences (all)	3 / 31 (9.68%) 4	2 / 33 (6.06%) 4	
Bone pain subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	1 / 33 (3.03%) 1	
Chronic kidney disease-mineral and bone disorder subjects affected / exposed occurrences (all)	3 / 31 (9.68%) 3	0 / 33 (0.00%) 0	
Coccydynia subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 33 (0.00%) 0	
Diastasis recti abdominis subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 33 (3.03%) 1	
Flank pain			

subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Muscle spasms			
subjects affected / exposed	8 / 31 (25.81%)	7 / 33 (21.21%)	
occurrences (all)	11	9	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal pain			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Myalgia			
subjects affected / exposed	1 / 31 (3.23%)	1 / 33 (3.03%)	
occurrences (all)	1	1	
Neck pain			
subjects affected / exposed	0 / 31 (0.00%)	2 / 33 (6.06%)	
occurrences (all)	0	2	
Pain in extremity			
subjects affected / exposed	5 / 31 (16.13%)	7 / 33 (21.21%)	
occurrences (all)	6	10	
Infections and infestations			
Abscess			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Abscess limb			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	6	
Acarodermatitis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Arteriovenous fistula site infection			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Bacterial infection			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences (all)	1	0	

Bacteriuria		
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	4
Body tinea		
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Bronchitis		
subjects affected / exposed	4 / 31 (12.90%)	2 / 33 (6.06%)
occurrences (all)	6	4
Candida infection		
subjects affected / exposed	3 / 31 (9.68%)	1 / 33 (3.03%)
occurrences (all)	3	1
Cellulitis		
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)
occurrences (all)	1	0
Conjunctivitis		
subjects affected / exposed	6 / 31 (19.35%)	1 / 33 (3.03%)
occurrences (all)	6	1
Cystitis		
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Ear infection		
subjects affected / exposed	3 / 31 (9.68%)	1 / 33 (3.03%)
occurrences (all)	3	1
Enterobacter sepsis		
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)
occurrences (all)	1	0
Epstein-Barr virus infection		
subjects affected / exposed	1 / 31 (3.23%)	1 / 33 (3.03%)
occurrences (all)	1	1
Escherichia urinary tract infection		
subjects affected / exposed	2 / 31 (6.45%)	2 / 33 (6.06%)
occurrences (all)	2	5
Eye infection		
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)
occurrences (all)	1	0

Eyelid boil		
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)
occurrences (all)	1	0
Fungal infection		
subjects affected / exposed	1 / 31 (3.23%)	1 / 33 (3.03%)
occurrences (all)	2	2
Febrile infection		
subjects affected / exposed	8 / 31 (25.81%)	6 / 33 (18.18%)
occurrences (all)	30	12
Furuncle		
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)
occurrences (all)	1	0
Gastroenteritis		
subjects affected / exposed	10 / 31 (32.26%)	4 / 33 (12.12%)
occurrences (all)	13	5
Gastroenteritis adenovirus		
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Gastroenteritis rotavirus		
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)
occurrences (all)	1	0
Gastrointestinal infection		
subjects affected / exposed	0 / 31 (0.00%)	2 / 33 (6.06%)
occurrences (all)	0	2
Hand-foot-and-mouth disease		
subjects affected / exposed	0 / 31 (0.00%)	2 / 33 (6.06%)
occurrences (all)	0	2
Herpes virus infection		
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)
occurrences (all)	1	0
Herpes zoster		
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)
occurrences (all)	1	0
Hordeolum		
subjects affected / exposed	0 / 31 (0.00%)	2 / 33 (6.06%)
occurrences (all)	0	2

Human bocavirus infection		
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)
occurrences (all)	1	0
Impetigo		
subjects affected / exposed	2 / 31 (6.45%)	0 / 33 (0.00%)
occurrences (all)	2	0
Implant site infection		
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Infected bite		
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Infection		
subjects affected / exposed	2 / 31 (6.45%)	5 / 33 (15.15%)
occurrences (all)	4	5
Influenza		
subjects affected / exposed	2 / 31 (6.45%)	1 / 33 (3.03%)
occurrences (all)	2	1
Lice infestation		
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Mastoiditis		
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Nasopharyngitis		
subjects affected / exposed	27 / 31 (87.10%)	26 / 33 (78.79%)
occurrences (all)	68	80
Oral candidiasis		
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Oral herpes		
subjects affected / exposed	4 / 31 (12.90%)	1 / 33 (3.03%)
occurrences (all)	8	1
Otitis externa		
subjects affected / exposed	1 / 31 (3.23%)	2 / 33 (6.06%)
occurrences (all)	1	2

Otitis media		
subjects affected / exposed	8 / 31 (25.81%)	6 / 33 (18.18%)
occurrences (all)	11	8
Parainfluenzae virus infection		
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)
occurrences (all)	1	0
Paronychia		
subjects affected / exposed	3 / 31 (9.68%)	4 / 33 (12.12%)
occurrences (all)	3	6
Periumbilical abscess		
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Pharyngitis		
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)
occurrences (all)	1	0
Pneumonia		
subjects affected / exposed	4 / 31 (12.90%)	3 / 33 (9.09%)
occurrences (all)	4	5
Polyomavirus-associated nephropathy		
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)
occurrences (all)	1	0
Postoperative wound infection		
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Pyelonephritis		
subjects affected / exposed	3 / 31 (9.68%)	2 / 33 (6.06%)
occurrences (all)	5	3
Renal abscess		
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Respiratory tract infection		
subjects affected / exposed	2 / 31 (6.45%)	5 / 33 (15.15%)
occurrences (all)	4	9
Rhinitis		

subjects affected / exposed	23 / 31 (74.19%)	19 / 33 (57.58%)
occurrences (all)	63	42
Sinusitis		
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)
occurrences (all)	1	0
Skin infection		
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)
occurrences (all)	1	0
Skin candida		
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)
occurrences (all)	1	0
Staphylococcal infection		
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Tinea versicolour		
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)
occurrences (all)	1	0
Tonsillitis		
subjects affected / exposed	0 / 31 (0.00%)	2 / 33 (6.06%)
occurrences (all)	0	2
Upper respiratory tract infection		
subjects affected / exposed	6 / 31 (19.35%)	7 / 33 (21.21%)
occurrences (all)	8	9
Urinary tract infection enterococcal		
subjects affected / exposed	2 / 31 (6.45%)	1 / 33 (3.03%)
occurrences (all)	2	2
Urinary tract infection		
subjects affected / exposed	12 / 31 (38.71%)	9 / 33 (27.27%)
occurrences (all)	33	24
Urinary tract infection pseudomonal		
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)
occurrences (all)	1	0
Urosepsis		
subjects affected / exposed	9 / 31 (29.03%)	6 / 33 (18.18%)
occurrences (all)	18	10
Viral infection		

subjects affected / exposed	1 / 31 (3.23%)	1 / 33 (3.03%)	
occurrences (all)	1	1	
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	1 / 31 (3.23%)	1 / 33 (3.03%)	
occurrences (all)	1	1	
Calcium deficiency			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences (all)	1	0	
Dehydration			
subjects affected / exposed	11 / 31 (35.48%)	3 / 33 (9.09%)	
occurrences (all)	15	3	
Fluid overload			
subjects affected / exposed	0 / 31 (0.00%)	2 / 33 (6.06%)	
occurrences (all)	0	2	
Fluid intake reduced			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Folate deficiency			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Hypercholesterolaemia			
subjects affected / exposed	2 / 31 (6.45%)	5 / 33 (15.15%)	
occurrences (all)	2	5	
Hypercreatininaemia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)	
occurrences (all)	0	1	
Hyperkalaemia			
subjects affected / exposed	2 / 31 (6.45%)	3 / 33 (9.09%)	
occurrences (all)	2	3	
Hypochloraemia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	
occurrences (all)	2	0	

Hyperlipidaemia		
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Hypertriglyceridaemia		
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Hypokalaemia		
subjects affected / exposed	1 / 31 (3.23%)	9 / 33 (27.27%)
occurrences (all)	1	9
Hyponatraemia		
subjects affected / exposed	5 / 31 (16.13%)	2 / 33 (6.06%)
occurrences (all)	9	4
Hypophosphataemia		
subjects affected / exposed	1 / 31 (3.23%)	1 / 33 (3.03%)
occurrences (all)	1	1
Hypovitaminosis		
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Hypovolaemia		
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)
occurrences (all)	1	0
Iron deficiency		
subjects affected / exposed	12 / 31 (38.71%)	13 / 33 (39.39%)
occurrences (all)	12	13
Metabolic acidosis		
subjects affected / exposed	3 / 31 (9.68%)	6 / 33 (18.18%)
occurrences (all)	3	6
Mineral deficiency		
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1
Obesity		
subjects affected / exposed	1 / 31 (3.23%)	2 / 33 (6.06%)
occurrences (all)	1	2
Pseudogynaecomastia		
subjects affected / exposed	0 / 31 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	1

Vitamin B complex deficiency subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 33 (3.03%) 1	
Vitamin D deficiency subjects affected / exposed occurrences (all)	6 / 31 (19.35%) 6	10 / 33 (30.30%) 10	
Zinc deficiency subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	3 / 33 (9.09%) 3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 January 2011	<ul style="list-style-type: none">• Restrict the study population to children after kidney transplantation• Add Valganciclovir to the study treatment regime• Correct the SAE/pregnancy reporting• Clarify some inconsistencies in the protocol and add some missing information
28 November 2011	<ul style="list-style-type: none">• Extension of study from monocentre to multicentre

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/25127887>

<http://www.ncbi.nlm.nih.gov/pubmed/33323473>