Clinical trial results:
A Long-term, Open-label, Non-comparative Study to Evaluate the Safety and Efficacy of a Modigraf® Based Immunosuppression Regimen in Paediatric Solid Allograft Recipients

Summary

EudraCT number	2009-012259-21
Trial protocol	ES GB DE BE FR
Global end of trial date	02 April 2017

Results information

Result version number	v3 (current)
This version publication date	29 July 2018
First version publication date	28 March 2018
Version creation reason	• New data added to full data set Results updated for consistency

Trial information

Trial identification

Sponsor protocol code	F506-CL-0404

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01371344
WHO universal trial number (UTN)	-
Other trial identifiers	Acronym: PROGRESSION

Notes:

Sponsors

Sponsor organisation name	Astellas Pharma Europe, Ltd
Sponsor organisation address	2000 Hillswood Drive, Chertsey, United Kingdom, KT16 0RS
Public contact	Clinical Trial Disclosure, Astellas Pharma Europe, Ltd, Astellas.resultsdisclosure@astellas.com
Scientific contact	Clinical Trial Disclosure, Astellas Pharma Europe, Ltd, Astellas.resultsdisclosure@astellas.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	02 April 2017
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	02 April 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The study had 2 parts: Part A (F506-CL-0404A) and Part B (F506-CL-0404B). The objective of F506-CL-0404A was to monitor the safety of and efficacy of Modigraf® (tacrolimus granules) in stable paediatric allograft recipients.

The objective of F506-CL-0404B was to monitor dose changes and tacrolimus whole blood trough levels after conversion from a tacrolimus granules based immunosuppression regimen to a Prograf® (tacrolimus capsules) based immunosuppression regimen.

Part A was completed as planned, however the study was terminated during Part B due to low enrollment in Part B.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 June 2011
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	Belgium: 3
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Germany: 5
Country: Number of subjects enrolled	Poland: 1
Country: Number of subjects enrolled	Spain: 26
Country: Number of subjects enrolled	United Kingdom: 9
Worldwide total number of subjects	47
EEA total number of subjects	47

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)	17
Children (2-11 years)	29
Adolescents (12-17 years)	1
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Children aged ≤ 12 years were enrolled at 11 sites in a total of 6 countries: UK (2 sites), Spain (3 sites), Germany (2 sites), Belgium (1 site), Poland (1 site) and France (2 sites).

Pre-assignment

Screening details:

Pediatric participants who had undergone liver, kidney or heart transplantation and who had previously participated F506-CL-0403 study were enrolled in Part A of this study. Participants who participated in Part A or F506-CL-0403 and who were converted to receive tacrolimus capsules were enrolled in Part B.

Period 1

Period 1 title	Part A
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Part A: Heart Transplant (Tacrolimus granules)

Arm description:

In Part A of the study, participants who were heart transplant recipients received tacrolimus granules-based immunosuppressive regimen twice daily for a maximum of 1 year or until commercial availability of tacrolimus granules in the participant's country.

Arm type	Experimental
Investigational medicinal product name	Tacrolimus granules
Investigational medicinal product code	FK506
Other name	Modigraf®
Pharmaceutical forms	Granules for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Participants received the same dose regimen of tacrolimus granules as they were receiving at the end of the F506-CL-0403 study, and the first dose was administered on day 1. Subsequent oral tacrolimus doses were adjusted by the investigator based on clinical evidence of efficacy and occurrence of adverse events and observing the recommended whole blood trough level range of 5 to 20 ng/ml. The tacrolimus granules for oral suspension were available in sachets containing either 0.2 mg or 1 mg tacrolimus granules per sachet.

Arm title	Part A: Liver Transplant (Tacrolimus granules)

Arm description:

In Part A of the study, participants who were liver transplant recipients received tacrolimus granules-based immunosuppressive regimen twice daily for a maximum of 1 year or until commercial availability of tacrolimus granules in the participant's country.

Arm type	Experimental
Investigational medicinal product name	Tacrolimus granules
Investigational medicinal product code	FK506
Other name	Modigraf®
Pharmaceutical forms	Granules for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Participants received the same dose regimen of tacrolimus granules as they were receiving at the end of the F506-CL-0403 study, and the first dose was administered on day 1. Subsequent oral tacrolimus doses were adjusted by the investigator based on clinical evidence of efficacy and occurrence of adverse events and observing the recommended whole blood trough level range of 5 to 20 ng/ml. The tacrolimus granules for oral suspension were available in sachets containing either 0.2 mg or 1 mg tacrolimus

granules per sachet.

Arm title	Part A: Kidney Transplant (Tacrolimus granules)

Arm description:

In Part A of the study, participants who were kidney transplant recipients received tacrolimus granules-based immunosuppressive regimen twice daily for a maximum of 1 year or until commercial availability of tacrolimus granules in the participant's country.

Arm type	Experimental
Investigational medicinal product name	Tacrolimus granules
Investigational medicinal product code	FK506
Other name	Modigraf®
Pharmaceutical forms	Granules for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Participants received the same dose regimen of tacrolimus granules as they were receiving at the end of the F506-CL-0403 study, and the first dose was administered on day 1. Subsequent oral tacrolimus doses were adjusted by the investigator based on clinical evidence of efficacy and occurrence of adverse events and observing the recommended whole blood trough level range of 5 to 20 ng/ml. The tacrolimus granules for oral suspension were available in sachets containing either 0.2 mg or 1 mg tacrolimus granules per sachet.

Number of subjects in period 1	Part A: Heart Transplant (Tacrolimus granules)	Part A: Liver Transplant (Tacrolimus granules)	Part A: Kidney Transplant (Tacrolimus granules)
Started	17	18	12
Completed	16	11	10
Not completed	1	7	2
Other	-	1	-
Withdrawal of Consent	-	3	1
Intolerable Adverse Event	-	1	1
Retransplantation	-	2	-
Lost to follow-up	1	-	-

Period 2

Period 2 title	Part B
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Part B: All Participants (Tacrolimus capsules)

Arm description:

In Part B of the study, participants who were heart, kidney or liver transplant recipients and who were converted from tacrolimus granules-based immunosuppression regimen, received tacrolimus capsules twice daily for 1 month and thereafter received commercially available tacrolimus capsules.

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

Dosage and administration details:

Participants received an initial daily dose of tacrolimus capsules that is identical to the daily dose of tacrolimus granules prior to conversion to tacrolimus capsules and was administered on day 1. Subsequent oral tacrolimus doses were adjusted based on clinical evidence of efficacy and occurrence of adverse events, and observed the recommended whole blood trough level range of 5 to 20 ng/ml. Tacrolimus capsules contained 0.5 mg, 1 mg or 5 mg of tacrolimus per capsule.

Number of subjects in period 2[1]	Part B: All Participants (Tacrolimus capsules)
Started	5
Completed	6

Joined	1
Joined from F506-CL-0403	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Part A and Part B are independent of each other, where: (1) Participants can be enrolled in Part A only, and may not be enrolled in Part B; (2) Participants can be can be enrolled in Part A and subsequently to Part B; or (3) Participants can directly be enrolled into Part B only.

Baseline characteristics

Reporting groups	
Reporting group title	Part A: Heart Transplant (Tacrolimus granules)
Reporting group description:	
In Part A of the study, participants who were heart transplant recipients received tacrolimus granules-based immunosuppressive regimen twice daily for a maximum of 1 year or until commercial availability of tacrolimus granules in the participant's country.	
Reporting group title	Part A: Liver Transplant (Tacrolimus granules)
Reporting group description:	
In Part A of the study, participants who were liver transplant recipients received tacrolimus granules-based immunosuppressive regimen twice daily for a maximum of 1 year or until commercial availability of tacrolimus granules in the participant's country.	
Reporting group title	Part A: Kidney Transplant (Tacrolimus granules)
Reporting group description:	
In Part A of the study, participants who were kidney transplant recipients received tacrolimus granules-based immunosuppressive regimen twice daily for a maximum of 1 year or until commercial availability of tacrolimus granules in the participant's country.	

Reporting group values	Part A: Heart Transplant (Tacrolimus granules)	Part A: Liver Transplant (Tacrolimus granules)	Part A: Kidney Transplant (Tacrolimus granules)
Number of subjects	17	18	12
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	5.3	2.3	5.4
standard deviation	± 4.1	± 2.8	± 3.0
Gender categorical Units:			
Male	13	10	9
Female	4	8	3
Race Units: Subjects			
White	17	18	11
Black or African American	0	0	0
Asian	0	0	1
Other	0	0	0

Reporting group values	Total		
Number of subjects	47		
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean			
standard deviation	-		

Gender categorical Units:			
Male	32		
Female	15		
Race Units: Subjects			
White	46		
Black or African American	0		
Asian	1		
Other	0		

End points

End points reporting groups

Reporting group title	Part A: Heart Transplant (Tacrolimus granules)

Reporting group description:

In Part A of the study, participants who were heart transplant recipients received tacrolimus granules-based immunosuppressive regimen twice daily for a maximum of 1 year or until commercial availability of tacrolimus granules in the participant's country.

Reporting group title	Part A: Liver Transplant (Tacrolimus granules)

Reporting group description:

In Part A of the study, participants who were liver transplant recipients received tacrolimus granules-based immunosuppressive regimen twice daily for a maximum of 1 year or until commercial availability of tacrolimus granules in the participant's country.

Reporting group title	Part A: Kidney Transplant (Tacrolimus granules)

Reporting group description:

In Part A of the study, participants who were kidney transplant recipients received tacrolimus granules-based immunosuppressive regimen twice daily for a maximum of 1 year or until commercial availability of tacrolimus granules in the participant's country.

Reporting group title	Part B: All Participants (Tacrolimus capsules)

Reporting group description:

In Part B of the study, participants who were heart, kidney or liver transplant recipients and who were converted from tacrolimus granules-based immunosuppression regimen, received tacrolimus capsules twice daily for 1 month and thereafter received commercially available tacrolimus capsules.

Primary: Part A: Number of Participants with Acute Rejection Episodes

End point title	Part A: Number of Participants with Acute Rejection Episodes[1]

End point description:

Rejection episodes/acute rejections were indicated by clinical and/or laboratory signs, and were classified according to their rejection specific treatment: •Spontaneously Resolving Acute Rejection: not treated with new or increased corticosteroid medication, antibodies or any other medication and resolved, irrespective of any tacrolimus dose changes; •Corticosteroid Sensitive Acute Rejection: treated with new or increased corticosteroid medication only and which has resolved, irrespective of any tacrolimus dose changes; •Corticosteroid Resistant Acute Rejection: did not resolve following treatment with corticosteroids; - Resolved with further treatment: any acute rejection with an end date AND a treatment other than corticosteroid used; - Unresolved with further treatment: any acute rejection with no end date AND a treatment other than corticosteroid used; - Unresolved with no further treatment: any acute rejection with no end date AND ONLY corticosteroid treatment was used. SAF.

End point type	Primary

End point timeframe:

Up to 12 months

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As this is a single-arm study, there were no pre-determined hypothetical or comparative statistical analyses performed in Part A of the study.

End point values	Part A: Heart Transplant (Tacrolimus granules)	Part A: Liver Transplant (Tacrolimus granules)	Part A: Kidney Transplant (Tacrolimus granules)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	18	12	
Units: Participants				
Spontaneously Resolving Acute Rejection	1	0	0	

Corticosteroid Sensitive Acute Rejection	3	2	0	
Corticosteroid Resistant Acute Rejections	0	1	0	
Other Acute Rejections	1	0	1	

Statistical analyses

No statistical analyses for this end point

Primary: Part A: Severity of BPARs

End point title	Part A: Severity of BPARs[2]

End point description:

The severity of BPARs was categorized with specific criteria by organ: For kidney transplant participants, according to Banff '97 Diagnostic categories for renal allograft biopsies – Banff '07 update (C4d deposition, Acute antibody-mediated rejection I, II, and III, Acute T cell mediated rejection IA, IB, IIA, IIB and III); for liver transplant participants, according to 1997 Banff Schema for Grading of Liver Allograft Rejection - Rejection Activity Index score (sum of grades: 1-mild, 2-moderate, 3-severe; range from 0-9); for heart, according to Standardized Nomenclature of the International Society of Heart and Lung Transplantation - Standardised Cardiac Biopsy Grading: Acute Cellular Rejection 2004 (mild, moderate, severe). The analysis population was the Safety Analysis Set (SAF), which consisted of participants took at least 1 dose of study drug. Categories not applicable to the reporting groups are denoted as "99999."

End point type	Primary

End point timeframe:

Up to 12 months

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As this is a single-arm study, there were no pre-determined hypothetical or comparative statistical analyses performed in Part A of the study.

End point values	Part A: Heart Transplant (Tacrolimus granules)	Part A: Liver Transplant (Tacrolimus granules)	Part A: Kidney Transplant (Tacrolimus granules)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	18	12	
Units: Participants				
Heart: Mild	2	99999	99999	
Heart: Moderate	0	99999	99999	
Heart: Severe	0	99999	99999	
Liver RAI Score 0-2	99999	0	99999	
Liver RAI Score 3	99999	0	99999	
Liver RAI Score 4-5	99999	0	99999	
Liver RAI Score 6-7	99999	2	99999	
Liver RAI Score 8-9	99999	1	99999	
Kidney: C4d deposition	99999	99999	0	
Kidney: Acute antibody-mediated rejection I	99999	99999	0	
Kidney: Acute antibody-mediated rejection II	99999	99999	0	
Kidney: Acute antibody-mediated rejection III	99999	99999	0	
Kidney: T-cell mediated rejection IA	99999	99999	0	
Kidney: T-cell mediated rejection IB	99999	99999	0	

Kidney: T-cell mediated rejection IIA	99999	99999	0	
Kidney: T-cell mediated rejection IIB	99999	99999	0	
Kidney: T-cell mediated rejection III	99999	99999	0	

Statistical analyses

No statistical analyses for this end point

Primary: Part A: Patient Survival

End point title	Part A: Patient Survival[3]

End point description:

Patient survival was reported as the number of deaths that occurred during Part A of the study. The analysis population was the SAF.

End point type	Primary

End point timeframe:

Up to 12 months

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As this is a single-arm study, there were no pre-determined hypothetical or comparative statistical analyses performed in Part A of the study.

End point values	Part A: Heart Transplant (Tacrolimus granules)	Part A: Liver Transplant (Tacrolimus granules)	Part A: Kidney Transplant (Tacrolimus granules)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	18	12	
Units: Participants				
Deaths	0	0	0	

Statistical analyses

No statistical analyses for this end point

Primary: Part A: Graft Survival

End point title	Part A: Graft Survival[4]

End point description:

Graft survival was reported as the number of participants who experienced graft loss. Graft loss was defined as retransplantation or death or return to pretransplantation treatment modality for 6 weeks or longer. Additionally, kidney transplanted participants with ongoing dialysis at the end of study were counted as participants with graft loss. The analysis population was the SAF.

End point type	Primary

End point timeframe:

Up to 12 months

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As this is a single-arm study, there were no pre-determined hypothetical or comparative statistical analyses performed in Part A of the study.

End point values	Part A: Heart Transplant (Tacrolimus granules)	Part A: Liver Transplant (Tacrolimus granules)	Part A: Kidney Transplant (Tacrolimus granules)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	18	12	
Units: Participants				
Graft losses	0	2	0	

Statistical analyses

No statistical analyses for this end point

Primary: Part A: Number of Participants with Adverse Events (AEs)

End point title	Part A: Number of Participants with Adverse Events (AEs)[5]

End point description:

Safety was assessed by AEs, which included abnormalities identified during a medical test (e.g. clinical laboratory tests, vital signs, etc.) if the abnormality induced clinical signs or symptoms, needed active intervention, interruption or discontinuation of study medication or was clinically significant. A serious AE (SAE) was an event resulting in death, persistent or significant disability/incapacity or congenital anomaly or birth defect, was life-threatening, required or prolonged hospitalization or was considered medically important. A treatment emergent adverse event (TEAE) was defined as an AE observed after investigational drug administration. The analysis population was the SAF.

End point type	Primary

End point timeframe:

From first dose of study drug up to 30 days after last dose of study drug (up to 13 months)

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As this is a single-arm study, there were no pre-determined hypothetical or comparative statistical analyses performed in Part A of the study.

End point values	Part A: Heart Transplant (Tacrolimus granules)	Part A: Liver Transplant (Tacrolimus granules)	Part A: Kidney Transplant (Tacrolimus granules)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	18	12	
Units: Participants				
Any TEAE	16	15	12	
Drug-related TEAEs	9	12	11	
Deaths	0	0	0	
Serious TEAEs	8	9	9	
Drug-related Serious TEAEs	3	2	7	
Deaths Resulting from AEs	0	0	0	
TEAEs Leading to Discontinuation of Study Drug	0	1	2	
Drug-related TEAEs Leading to Disc. of Study Drug	0	1	2	

Statistical analyses

No statistical analyses for this end point

Primary: Part A: Tacrolimus Mean Trough Levels

End point title	Part A: Tacrolimus Mean Trough Levels[6]

End point description:

The analysis population was the SAF. N indicates the number of participants with available data. Due to participants discontinuing the study drug at certain time points, data were not calculated and denoted as "99999."

End point type	Primary

End point timeframe:

Day 1, Months 1, 2, 3, 6, 9, 12 (prior to each study drug dosing)

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As this is a single-arm study, there were no pre-determined hypothetical or comparative statistical analyses performed in Part A of the study.

End point values	Part A: Heart Transplant (Tacrolimus granules)	Part A: Liver Transplant (Tacrolimus granules)	Part A: Kidney Transplant (Tacrolimus granules)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	18	12	
Units: ng/mL				
arithmetic mean (standard deviation)				
Day 1 [N=8, 15, 9]	8.76 (± 2.38)	11.68 (± 4.60)	11.71 (± 3.64)	
Month 1 [N=17, 18, 11]	11.74 (± 5.07)	9.80 (± 3.34)	7.11 (± 2.41)	
Month 2 [N=16, 12, 11]	9.80 (± 4.01)	9.15 (± 2.28)	5.65 (± 1.58)	
Month 3 [N=15, 11, 11]	9.29 (± 3.17)	12.82 (± 11.97)	6.50 (± 1.97)	
Month 6 [N=1, 1, 7]	5.30 (± 99999)	19.20 (± 99999)	7.37 (± 5.09)	
Month 9 [N=1, 0, 6]	3.40 (± 99999)	99999 (± 99999)	5.12 (± 0.99)	
Month 12 [N=0, 0, 6]	99999 (± 99999)	99999 (± 99999)	4.95 (± 0.65)	
Last Day on Study Drug [17, 18, 11]	8.30 (± 2.13)	11.73 (± 9.77)	5.13 (± 1.71)	

Statistical analyses

No statistical analyses for this end point

Primary: Part A: Number of Dose Adjustments

End point title	Part A: Number of Dose Adjustments[7]

End point description:

Study drug doses were adjusted based on clinical evidence of efficacy and occurrence of adverse events, and taking into consideration the recommended whole blood trough level range of 5-20 ng/ml. The analysis population was the SAF. N indicates the number of participants with available data. Due to participants discontinuing the study drug at certain time points, data were not calculated and are denoted as "99999."

End point type	Primary

End point timeframe:

Months 1, 2, 3, 6, 9, 12

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As this is a single-arm study, there were no pre-determined hypothetical or comparative statistical analyses performed in Part A of the study.

End point values	Part A: Heart Transplant (Tacrolimus granules)	Part A: Liver Transplant (Tacrolimus granules)	Part A: Kidney Transplant (Tacrolimus granules)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	18	10	
Units: dose adjustments				
arithmetic mean (standard deviation)				
Month 1 [N=17, 18, 8]	7.6 (± 5.3)	12.1 (± 8.5)	4.3 (± 3.3)	
Month 2 [N=10, 9, 5]	2.2 (± 1.4)	5.8 (± 4.3)	3.8 (± 5.7)	
Month 3 [N=1, 5, 6]	2.0 (± 99999)	3.2 (± 1.9)	1.2 (± 0.4)	
Month 6 [N=1, 0, 4]	2.0 (± 99999)	99999 (± 99999)	1.8 (± 1.0)	
Month 9 [N=0, 0, 2]	99999 (± 99999)	99999 (± 99999)	2.0 (± 0.0)	
Month 12 [N=0, 0, 1]	99999 (± 99999)	99999 (± 99999)	1.0 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Primary: Part B: Number of Participants with AEs

End point title	Part B: Number of Participants with AEs[8]

End point description:

Safety was assessed by AEs, which included abnormalities identified during a medical test (e.g. clinical laboratory tests, vital signs, etc.) if the abnormality induced clinical signs or symptoms, needed active intervention, interruption or discontinuation of study medication or was clinically significant. A SAE was an event resulting in death, persistent or significant disability/incapacity or congenital anomaly or birth defect, was life-threatening, required or prolonged hospitalization or was considered medically important. A TEAE was defined as an AE observed after investigational drug administration. The analysis population was the conversion analysis set was comprised of all participants enrolled in Part B who took at least 1 dose of study drug (tacrolimus capsules).

End point type	Primary

End point timeframe:

From first dose of study drug (tacrolimus capsules) up to 7 days after last dose (up to 38 days)

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As this is a single-arm study, there were no pre-determined hypothetical or comparative statistical analyses performed in Part B of the study.

End point values	Part B: All Participants (Tacrolimus capsules)			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: participants				

Any TEAE	4			
SAEs	0			
Drug-related AEs	1			

Statistical analyses

No statistical analyses for this end point

Primary: Part B: Tacrolimus Trough Levels Prior to and After Conversion

End point title	Part B: Tacrolimus Trough Levels Prior to and After

End point description:

The analysis population was the conversion analysis set. N indicates the number of participants with available data. Values prior to conversion were the last trough level prior to first dose of study drug (tacrolimus capsules). Values after conversion were the first trough level after first dose of study drug (tacrolimus capsules).

End point type	Primary

End point timeframe:

Day -1 up to 1 month

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As this is a single-arm study, there were no pre-determined hypothetical or comparative statistical analyses performed in Part B of the study.

End point values	Part B: All Participants (Tacrolimus capsules)			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: ng/mL				
median (full range (min-max))				
Prior to Conversion [N=4]	5.20 (3.1 to 7.1)			
After to Conversion [N=6]	5.55 (2.8 to 9.0)			

Statistical analyses

No statistical analyses for this end point

Primary: Part B: Number of Dose Adjustments

End point title	Part B: Number of Dose Adjustments[10]

End point description:

The analysis population was the conversion analysis set. Only participants with dose adjustments were included in the analysis.

End point type	Primary

End point timeframe:

From first dose of study drug up to 1 month

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As this is a single-arm study, there were no pre-determined hypothetical or comparative statistical analyses performed in Part B of the study.

End point values	Part B: All Participants (Tacrolimus capsules)			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: participants				
1 adjustment	1			
2 adjustments	0			
3 adjustments	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Number of Participants with Biopsy-proven Acute Rejection Episodes (BPARs)

End point title	Part A: Number of Participants with Biopsy-proven Acute Rejection Episodes (BPARs)

End point description:

BPAR episodes were defined as acute rejection episodes confirmed by biopsy, and were classified according to their rejection specific treatment: •Spontaneously Resolving Acute Rejection: not treated with new or increased corticosteroid medication, antibodies or any other medication and resolved, irrespective of any tacrolimus dose changes; •Corticosteroid Sensitive Acute Rejection: treated with new or increased corticosteroid medication only and which has resolved, irrespective of any tacrolimus dose changes; •Corticosteroid Resistant Acute Rejection: did not resolve following treatment with corticosteroids; - Resolved with further treatment: any acute rejection with an end date AND a treatment other than corticosteroid used; - Unresolved with further treatment: any acute rejection with no end date AND a treatment other than corticosteroid used; - Unresolved with no further treatment: any acute rejection with no end date AND ONLY corticosteroid treatment used. SAF.

End point type	Secondary

End point timeframe:

Up to 12 months

End point values	Part A: Heart Transplant (Tacrolimus granules)	Part A: Liver Transplant (Tacrolimus granules)	Part A: Kidney Transplant (Tacrolimus granules)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	18	12	
Units: participants				
number (not applicable)				
Spontaneously Resolving Acute Rejection	0	0	0	
Corticosteroid Sensitive Acute Rejection	2	2	0	
Corticosteroid Resistant Acute Rejection	0	1	0	

Other Acute Rejections	0	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Part A: From first dose of study drug (tacrolimus granules) up to 30 days after last dose of study drug (up to 13 months); Part B: From first dose of study drug (tacrolimus capsules) up to 7 days after last dose (up to 38 days)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.0

Reporting groups

Reporting group title	Part A: Heart Transplant (Tacrolimus granules)

Reporting group description:

In Part A of the study, participants who were heart transplant recipients received tacrolimus granules-based immunosuppressive regimen twice daily for a maximum of 1 year or until commercial availability of tacrolimus granules in the participant's country.

Reporting group title	Part A: Liver Transplant (Tacrolimus granules)

Reporting group description:

In Part A of the study, participants who were liver transplant recipients received tacrolimus granules-based immunosuppressive regimen twice daily for a maximum of 1 year or until commercial availability of tacrolimus granules in the participant's country.

Reporting group title	Part A: Kidney Transplant (Tacrolimus granules)

Reporting group description:

In Part A of the study, participants who were kidney transplant recipients received tacrolimus granules-based immunosuppressive regimen twice daily for a maximum of 1 year or until commercial availability of tacrolimus granules in the participant's country.

Reporting group title	Part B: All Participants (Tacrolimus capsules)

Reporting group description:

In Part B of the study, participants who were heart, kidney or liver transplant recipients and who were converted from tacrolimus granules-based immunosuppression regimen, received tacrolimus capsules twice daily for 1 month and thereafter received commercially available tacrolimus capsules.

Serious adverse events	Part A: Heart Transplant (Tacrolimus granules)	Part A: Liver Transplant (Tacrolimus granules)	Part A: Kidney Transplant (Tacrolimus granules)
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 17 (47.06%)	9 / 18 (50.00%)	9 / 12 (75.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Surgical and medical procedures			
Central venous catheter removal			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Social circumstances			

Treatment noncompliance			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Drug interaction			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	1 / 17 (5.88%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Biliary anastomosis complication			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Complications of transplanted liver			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal anastomotic leak			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Body temperature increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1

deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic enzyme increased			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac hypertrophy			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	2 / 17 (11.76%)	0 / 18 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0

deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Lung consolidation			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 17 (0.00%)	2 / 18 (11.11%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Neurotoxicity			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Convulsion			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Intra-abdominal haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholangitis			

subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic vein thrombosis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver disorder			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Oliguria			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acidosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			

Bacterial sepsis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	2 / 17 (11.76%)	1 / 18 (5.56%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis clostridial			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis norovirus			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal protozoal infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	2 / 12 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 12 (0.00%)

occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	2 / 12 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	9 / 10
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection bacterial			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part B: All Participants (Tacrolimus capsules)		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Surgical and medical procedures			
Central venous catheter removal			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Social circumstances			
Treatment noncompliance			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Drug interaction			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		

deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Biliary anastomosis complication				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Complications of transplanted liver				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal anastomotic leak				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tibia fracture				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
Body temperature increased				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood creatinine increased				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatic enzyme increased				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to	0 / 0			

treatment / all			
deaths causally related to treatment / all	0 / 0		
Transaminases increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac hypertrophy			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Supraventricular tachycardia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tachycardia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Lung consolidation			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary oedema			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Neurotoxicity			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Convulsion			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Intra-abdominal haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatic vein thrombosis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Liver disorder			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Oliguria			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal impairment			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acidosis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bacterial sepsis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cytomegalovirus infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		

deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis clostridial				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis viral				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis norovirus				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal protozoal infection				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Postoperative wound infection				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection bacterial			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Part A: Heart Transplant (Tacrolimus granules)	Part A: Liver Transplant (Tacrolimus granules)	Part A: Kidney Transplant (Tacrolimus granules)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 17 (94.12%)	15 / 18 (83.33%)	11 / 12 (91.67%)
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 17 (29.41%)	3 / 18 (16.67%)	2 / 12 (16.67%)
occurrences (all)	5	3	2
Diastolic hypertension			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Hypotension			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Thrombosis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Surgical and medical procedures			
Catheter removal			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Central venous catheter removal			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Immune system disorders			

Drug hypersensitivity			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Hypogammaglobulinaemia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Seasonal allergy			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
General disorders and administration site conditions			
Device occlusion			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
Chills			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Generalised oedema			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	1 / 17 (5.88%)	3 / 18 (16.67%)	1 / 12 (8.33%)
occurrences (all)	1	4	4
Psychiatric disorders			
Sleep disorder			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Vomiting psychogenic			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Genital pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			

Complications of transplanted kidney			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Complications of transplanted liver			
subjects affected / exposed	0 / 17 (0.00%)	2 / 18 (11.11%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Contusion			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Radius fracture			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Alanine aminotransferase increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Blood magnesium decreased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Blood creatinine increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
Body temperature increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Blood pressure increased			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Haemoglobin decreased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)

occurrences (all)	0	0	1
Platelet count decreased			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Immunosuppressant drug level increased			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Hypertrophic cardiomyopathy			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Pericardial effusion			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Ventricular tachycardia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 17 (5.88%)	1 / 18 (5.56%)	7 / 12 (58.33%)
occurrences (all)	1	1	8
Oropharyngeal pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Pneumothorax			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Pleural effusion			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Pulmonary haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Rhinorrhoea			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	4 / 12 (33.33%)

occurrences (all)	1	0	5
Upper respiratory tract inflammation			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Wheezing			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 17 (5.88%)	4 / 18 (22.22%)	2 / 12 (16.67%)
occurrences (all)	1	5	2
Haemolytic anaemia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Lymphadenopathy			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Neutropenia			
subjects affected / exposed	4 / 17 (23.53%)	3 / 18 (16.67%)	1 / 12 (8.33%)
occurrences (all)	4	5	1
Nervous system disorders			
Hypertonia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	2
Tremor			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Eye disorders			
Eye swelling			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Conjunctivitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1

Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Diarrhoea			
subjects affected / exposed	4 / 17 (23.53%)	3 / 18 (16.67%)	7 / 12 (58.33%)
occurrences (all)	4	5	13
Abdominal pain upper			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Mouth ulceration			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	1 / 17 (5.88%)	8 / 18 (44.44%)	6 / 12 (50.00%)
occurrences (all)	1	10	13
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Renal failure			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Nephropathy toxic			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)

occurrences (all)	0	0	1
Renal injury			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Renal impairment			
subjects affected / exposed	1 / 17 (5.88%)	3 / 18 (16.67%)	0 / 12 (0.00%)
occurrences (all)	1	3	0
Urinary retention			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Hepatobiliary disorders			
Bile duct obstruction			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Bile duct stenosis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Hepatotoxicity			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Hyperbilirubinaemia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Portal vein thrombosis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Alopecia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Dermatitis exfoliative			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0

Eczema			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Drug eruption			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Rash			
subjects affected / exposed	1 / 17 (5.88%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Swelling face			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 17 (0.00%)	2 / 18 (11.11%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Hyperphosphataemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Hyperkalaemia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Hypokalaemia			
subjects affected / exposed	0 / 17 (0.00%)	2 / 18 (11.11%)	1 / 12 (8.33%)
occurrences (all)	0	3	1
Hypomagnesaemia			
subjects affected / exposed	4 / 17 (23.53%)	6 / 18 (33.33%)	1 / 12 (8.33%)
occurrences (all)	4	6	1
Hyponatraemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	2 / 12 (16.67%)

occurrences (all)	0	0	2
Hypophosphataemia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Vitamin D deficiency			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Metabolic acidosis			
subjects affected / exposed	0 / 17 (0.00%)	7 / 18 (38.89%)	0 / 12 (0.00%)
occurrences (all)	0	8	0
Infections and infestations			
Biliary tract infection bacterial			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Abdominal infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Biliary tract infection fungal			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Clostridial infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Epstein-Barr virus infection			
subjects affected / exposed	0 / 17 (0.00%)	3 / 18 (16.67%)	0 / 12 (0.00%)
occurrences (all)	0	3	0
Device related infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis norovirus			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal candidiasis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Genital infection male			

subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Herpes zoster			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Human herpesvirus 6 infection			
subjects affected / exposed	0 / 17 (0.00%)	6 / 18 (33.33%)	0 / 12 (0.00%)
occurrences (all)	0	6	0
Lower respiratory tract infection bacterial			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	4 / 12 (33.33%)
occurrences (all)	0	1	4
Oral candidiasis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
Oral fungal infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Peritonitis bacterial			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Pneumonia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Respiratory tract infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	2 / 12 (16.67%)
occurrences (all)	2	0	2
Viral infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1

Non-serious adverse events	Part B: All Participants (Tacrolimus capsules)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 6 (33.33%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Diastolic hypertension			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypotension			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Thrombosis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Surgical and medical procedures			
Catheter removal			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Central venous catheter removal			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypogammaglobulinaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Seasonal allergy			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			

Device occlusion subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Chills subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Generalised oedema subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Pyrexia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Psychiatric disorders Sleep disorder subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Vomiting psychogenic subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Reproductive system and breast disorders Genital pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Injury, poisoning and procedural complications Complications of transplanted kidney subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Complications of transplanted liver subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Contusion subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Radius fracture subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		

Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Alanine aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Blood magnesium decreased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Blood creatinine increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Body temperature increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Blood pressure increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Haemoglobin decreased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Platelet count decreased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Immunosuppressant drug level increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Hypertrophic cardiomyopathy			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Pericardial effusion			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Ventricular tachycardia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Pneumothorax			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Pleural effusion			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Pulmonary haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Rhinorrhoea			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Upper respiratory tract inflammation			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Wheezing			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Haemolytic anaemia			
subjects affected / exposed	0 / 6 (0.00%)		

occurrences (all)	0		
Lymphadenopathy			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Neutropenia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Hypertonia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Tremor			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Eye disorders			
Eye swelling			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Conjunctivitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Abdominal pain upper			
subjects affected / exposed	1 / 6 (16.67%)		

occurrences (all)	1		
Mouth ulceration			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Renal failure			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Nephropathy toxic			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Renal injury			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Renal impairment			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Urinary retention			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hepatobiliary disorders			
Bile duct obstruction			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		

Bile duct stenosis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Hepatotoxicity subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Hyperbilirubinaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Portal vein thrombosis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Skin and subcutaneous tissue disorders Dermatitis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Alopecia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Dermatitis exfoliative subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Eczema subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Drug eruption subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Pruritus subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Rash subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Swelling face subjects affected / exposed	0 / 6 (0.00%)		

occurrences (all)	0		

Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hyperphosphataemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hyperkalaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypokalaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypomagnesaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hyponatraemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypophosphataemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Vitamin D deficiency			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Metabolic acidosis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Infections and infestations			

Biliary tract infection bacterial				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Abdominal infection				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Biliary tract infection fungal				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Clostridial infection				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Epstein-Barr virus infection				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Device related infection				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Gastroenteritis norovirus				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Gastrointestinal candidiasis				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Genital infection male				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Herpes zoster				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Human herpesvirus 6 infection				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Lower respiratory tract infection bacterial				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			

Nasopharyngitis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	2		
Oral candidiasis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Oral fungal infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Peritonitis bacterial			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Pneumonia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Viral infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

This study was terminated during Part B, due to low number of participants enrolled in Part B.

Notes: