Clinical trial results:
Einfluss von Rituximab-Induktion und Lebendspende auf Immunregulation und Viruskontrolle nach Nierentransplantation - eine prospektive Pilotstudie
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Impact of Rituximab Induction and Living Donation on Immunoregulation and Virus Control in Renal Transplantation – a Prospective Pilot Study

Summary

EudraCT number	2009-012198-36
Trial protocol	DE
Global end of trial date	18 June 2019

Results information

Result version number	v1 (current)
This version publication date	31 May 2023
First version publication date	31 May 2023

Trial information

Trial identification

Sponsor protocol code	NTx-RTx-LD-001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01136395
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Justus-Liebig-Universität Gießen
Sponsor organisation address	Ludwigstraße 23, Gießen, Germany, 35390
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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	07 June 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 June 2019
Global end of trial reached?	Yes
Global end of trial date	18 June 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

1. Extent and duration of B cell and B cell subset depletion after rituximab administration in peripheral blood and iliac lymph nodes.
2. Impact of of rituximab administration on BKV replication.
3. Safety of rituximab.

Protection of trial subjects:

All patients treated with rituximab intravenously (iv) previously received 100mg prednisolone iv, an antihistamine iv, and metamizole 1g iv to prevent side effects of rituximab administration. Rituximab was administered under monitor control and using the infusion rates prescribed in the technical information.

Background therapy:

Induction therapy: rATG (rabbit ATG) was used, if panel reactive antibodies (PRA) were ≥20% and when antibody-mediated rejection occured in a previos transplant, respectively. Otherwise, basiliximab was used in all three patient groups as an induction therapy.

Steroid dosing was used according to the local protocol.
In group 1 intravenous IgG was administered at a dose of 0.5g/kg 4 days before blood group incompatible live kidney transplantation .
In groups 2 and 3, the same total dose of IgG was administered at the time points day 0 (before Tx), day 1 and 2, with an additional day 4 if necessary.

Maintenance immunosuppression with Tacr/MPS/steroids in groups 2 (LD ABOc) and 3 (DD NTx) were used according to the following protocol:
- initial Tacr dose (Prograf®) 0.15 mg/kg/d (exception: reduced initial daily dose in e.g. hepatic insufficiency), switch to once-daily administration of Tacr-MR (Advagraf®) 7-14 days after transplantation.
-Tacr target level: through level initially 10-15 ng/ml (up to week 6), 5-10 ng/ml (after week 6), 5-8 ng/ml (from 4th month).
- MPS (Myfortic®) 2x720mg per day, starting before transplantation; dose reduction to 3x360mg (2x540mg) or 2x360mg MPS (depending on measured MPA-AUC. Target: 30-60 mgxl/h.
Maintenance immunosuppression in group 1 (LD ABOi): Immunosuppressive therapy with Tacr/MPS/steroids was performed in the same way as in groups 2 and 3. However, immunosuppression with Tacr and MPS (starting dose 2x720 mg per day) was started 1 day pretransplant immunoadsorption treatment.

Evidence for comparator:

No comparator products were used.

Actual start date of recruitment	06 January 2010
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy, Scientific research
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 85
Worldwide total number of subjects	85
EEA total number of subjects	85

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	79
From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Consecutive adult patients (age at least 18 years) who were able to give consent were informed in writing and verbally about this clinical study and asked for their written informed consent. A recruitment period of approximately 3 years after amendment was planned for the inclusion of 90 (30 per group) patients.

Pre-assignment

Screening details:

Inclusion criteria:
- Kidney transplantation after deceased donation (allocation: Eurotransplant) and after living donation (blood group compatible and blood group incompatible), respectively.
- Immunized and non-immunized transplant recipients.
- Age of recipients at least 18 years.
- Separate precautions for women of childbearing age.

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment group 1 (LD ABOi)

Arm description:

Group 1 (LD ABOi): The investigational therapy with rituximab MABTHERA® (not approved in the context of kidney transplantation) was only be administered in this treatment arm. Patients usually received a single dose of 375mg/m2 of rituximab as an infusion 4 weeks prior to the planned transplantation. If there was no complete B cell depletion in peripheral blood (< 8 CD19+ cells/µl) or if the isoagglutinin titers did not drop sufficiently under immunoadsorption treatment (target titer 1:4), a second or even third administration of MABTHERA® 375 mg/m2 prior to transplantation could be administered. If necessary, an additional administration within the first two weeks after transplantation was allowed, the target isoagglutinine titers could otherwise not be kept within the target range after transplantation.

Arm type	Experimental
Investigational medicinal product name	Rituximab
Investigational medicinal product code	EU/1/98/067/001-002
Other name	
Pharmaceutical forms	Solution for solution for infusion
Routes of administration	Concentrate for solution for infusion

Dosage and administration details:

Patients in treatment arm 1 (LD ABOi) received rituximab MABTHERA® at a dose of 375 mg/m2 usually once 4 weeks prior to planned transplantation. A second or third dose prior to transplantation was allowed if complete B-cell depletion in the peripheral blood was not achieved or if isoagglutinine titer did not drop sufficiently.

MABTHERA® was administered via a separate access under monitor supervision. Thereby 30min before administration 100mg prednisolone i.v., 1g metamizole (e.g. Novalgin®) i.v. and an antihistamine (e.g., 1 amp Fenistil®) i.v. was administered.
MABTHERA® was administered at a defined infusion rate (each 30min) : 50mg/h - 100mg/h - 150mg/h - 200mg/h - 250mg/h - 300mg/h - 350mg/h - further 400mg/h. This
results in an infusion time of 3.5h for e.g. 700mg MABTHERA®, and 4h for 900mg. In case of repeated infusions, infusion rates could be enhanced according to the package insert.

Arm title	Treatment group 2 (LD ABOc)

Arm description:	
Group 2 (LD ABOc): Kidney transplantation after living donation, blood group compatible, no administration of rituximab, no administration of any other comparator.	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	Treatment group 3 (DD NTx)
Arm description:	
Group 3 (DD NTx): deceased donor renal transplantation, blood group compatible, allocation via Eurotransplant (via ETKAS programs, European Seniors Program, or other special programs); no administration of Rituximab or any other comparator substance.	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	Treatment group 1 (LD ABOi)	Treatment group 2 (LD ABOc)	Treatment group 3 (DD NTx)
Started	25	30	30
Completed	18	26	27
Not completed	7	4	3
Adverse event, serious fatal	3	-	3
Consent withdrawn by subject	1	-	-
Adverse event, non-fatal	2	-	-
graft loss(acute/chronic ab related rejection)	1	-	-
Graft loss (Non adherence)	-	1	-
Lost to follow-up	-	1	-
MPGN1 Recurrence	-	2	-

Baseline characteristics

Reporting groups	
Reporting group title	Treatment group 1 (LD ABOi)

Reporting group description:

Group 1 (LD ABOi): The investigational therapy with rituximab MABTHERA® (not approved in the context of kidney transplantation) was only be administered in this treatment arm. Patients usually received a single dose of 375mg/m2 of rituximab as an infusion 4 weeks prior to the planned transplantation. If there was no complete B cell depletion in peripheral blood (< 8 CD19+ cells/µl) or if the isoagglutinin titers did not drop sufficiently under immunoadsorption treatment (target titer 1:4), a second or even third administration of MABTHERA® 375 mg/m2 prior to transplantation could be administered. If necessary, an additional administration within the first two weeks after transplantation was allowed, the target isoagglutinine titers could otherwise not be kept within the target range after transplantation.

Reporting group title	Treatment group 2 (LD ABOc)

Reporting group description:

Group 2 (LD ABOc): Kidney transplantation after living donation, blood group compatible, no administration of rituximab, no administration of any other comparator.

Reporting group title	Treatment group 3 (DD NTx)

Reporting group description:

Group 3 (DD NTx): deceased donor renal transplantation, blood group compatible, allocation via Eurotransplant (via
ETKAS programs, European Seniors Program, or other special programs); no administration of Rituximab or any other comparator substance.

Reporting group values	Treatment group 1 (LD ABOi)	Treatment group 2 (LD ABOc)	Treatment group 3 (DD NTx)
Number of subjects	25	30	30
Age categorical			
Age at the time of inclusion to the study			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	23	27	29
From 65-84 years	2	3	1
85 years and over	0	0	0
Age continuous			
Age at the time of inclusion to the study			
Units: years			
arithmetic mean	50.36	44.6	52.07
standard deviation	± 10.13	± 14.05	± 7.5
Gender categorical			
Units: Subjects			
Female	6	8	11
Male	19	22	19

Reporting group values	Total		

Number of subjects	85		
Age categorical			
Age at the time of inclusion to the study			
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)	79		
From 65-84 years	6		
85 years and over	0		
Age continuous			
Age at the time of inclusion to the study			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	25		
Male	60		

Subject analysis sets	
Subject analysis set title	Patients with rituximab treatment
Subject analysis set type	Full analysis
Subject analysis set description:	
Patients who received rituximab in the course of the study	
Subject analysis set title	Patients without rituximab treatment
Subject analysis set type	Full analysis
Subject analysis set description:	
Patients who did not receive rituximab in the course of the study	
Subject analysis set title	AB0i renal transplant patients
Subject analysis set type	Full analysis
Subject analysis set description:	
To ensure comparability of patientgroups with regard to reporting of serious adverse events only the two living renal transplant groups were compared.	
Subject analysis set title	AB0c renal transplant patients
Subject analysis set type	Full analysis
Subject analysis set description:	
To ensure comparability of patientgroups with regard to reporting of serious adverse events only the two living renal transplant groups were compared.	

Reporting group values	Patients with rituximab treatment	Patients without rituximab treatment	AB0i renal transplant patients
Number of subjects	30	54	24
Age categorical			
Age at the time of inclusion to the study			
Units: Subjects			
In utero			

Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous			
Age at the time of inclusion to the study			
Units: years arithmetic mean standard deviation	 50.36 ± 10.13	 48.33 ± 11.87	 ±
Gender categorical Units: Subjects			
Female Male			

Reporting group values	AB0c renal transplant patients		
Number of subjects	30		
Age categorical			
Age at the time of inclusion to the study			
Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous			
Age at the time of inclusion to the study			
Units: years arithmetic mean standard deviation	 ±	 	
Gender categorical Units: Subjects			
Female Male			

End points

End points reporting groups

Reporting group title	Treatment group 1 (LD ABOi)

Reporting group description:

Group 1 (LD ABOi): The investigational therapy with rituximab MABTHERA® (not approved in the context of kidney transplantation) was only be administered in this treatment arm. Patients usually received a single dose of 375mg/m2 of rituximab as an infusion 4 weeks prior to the planned transplantation. If there was no complete B cell depletion in peripheral blood (< 8 CD19+ cells/µl) or if the isoagglutinin titers did not drop sufficiently under immunoadsorption treatment (target titer 1:4), a second or even third administration of MABTHERA® 375 mg/m2 prior to transplantation could be administered. If necessary, an additional administration within the first two weeks after transplantation was allowed, the target isoagglutinine titers could otherwise not be kept within the target range after transplantation.

Reporting group title	Treatment group 2 (LD ABOc)

Reporting group description:

Group 2 (LD ABOc): Kidney transplantation after living donation, blood group compatible, no administration of rituximab, no administration of any other comparator.

Reporting group title	Treatment group 3 (DD NTx)

Reporting group description:

Group 3 (DD NTx): deceased donor renal transplantation, blood group compatible, allocation via Eurotransplant (via
ETKAS programs, European Seniors Program, or other special programs); no administration of Rituximab or any other comparator substance.

Subject analysis set title	Patients with rituximab treatment
Subject analysis set type	Full analysis

Subject analysis set description:

Patients who received rituximab in the course of the study

Subject analysis set title	Patients without rituximab treatment
Subject analysis set type	Full analysis

Subject analysis set description:

Patients who did not receive rituximab in the course of the study

Subject analysis set title	AB0i renal transplant patients
Subject analysis set type	Full analysis

Subject analysis set description:

To ensure comparability of patientgroups with regard to reporting of serious adverse events only the two living renal transplant groups were compared.

Subject analysis set title	AB0c renal transplant patients
Subject analysis set type	Full analysis

Subject analysis set description:

To ensure comparability of patientgroups with regard to reporting of serious adverse events only the two living renal transplant groups were compared.

Primary: B cell depletion and repopulation in peripheral blood

End point title	B cell depletion and repopulation in peripheral blood

End point description:

Depletion and repopulation of B cells in peripheral blood was investigated by flow cytometric analysis of whole blood at the defined investigation time points. Indicated values are Mean values and SEM of cells/µ were indicated.
Only in treatment group 1(AB0i) an additional measurement was performed before rituximab administration. The determined baseline concentration of B cells (CD19+ cells) at this time was 107 (± 13) B cells/µl.

End point type	Primary

End point timeframe:

Analysis was performed at the time points before rituximab administration (pre RTx), before transplantation (pre tpl) and 3 months (3 mo), 6 months (6 mo), 1 year, 2 years, 3 years, 4 years, and 5 years after transplantation.

End point values	Treatment group 1 (LD ABOi)	Treatment group 2 (LD ABOc)	Treatment group 3 (DD NTx)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	25[1]	30[2]	30[3]	
Units: cells/microlitre				
arithmetic mean (standard error)				
CD19 B cells/µl before transplantation	2 (± 1)	117 (± 13)	130 (± 13)	
CD19 B cells/µl 3 month after transplantation	1 (± 0)	170 (± 24)	150 (± 23)	
CD19 B cells/µl 6 month after transplantation	1 (± 1)	122 (± 18)	123 (± 21)	
CD19 B cells/µl 1 year after transplantation	7 (± 2)	92 (± 14)	87 (± 13)	
CD19 B cells/µl 2 years after transplantation	53 (± 15)	110 (± 14)	112 (± 13)	
CD19 B cells/µl 3 years after transplantation	79 (± 17)	134 (± 17)	125 (± 16)	
CD19 B cells/µl 4 years after transplantation	120 (± 24)	150 (± 21)	148 (± 17)	
CD19 B cells/µl 5 years after transplantation	149 (± 34)	176 (± 27)	151 (± 17)	

Notes:

[1] - pre RTx 25, pre tpl 23, 3 mo 22, 6 mo 20, 1 year 22, 2 years 21, 3 years 20, 4 years 18, 5 years 18

[2] - pre RTx nd, pre tpl 30, 3 mo 30, 6 mo 28, 1 year 29, 2 years 29, 3 years 29, 4 years 25, 5 years 25

[3] - pre RTx nd, pre tpl 30, 3 mo 30, 6 mo 30, 1 year 30, 2 years 29, 3 years 28, 4 years 26, 5 years 26

Statistical analyses

Statistical analysis title	Statistical comparison of the three patient groups
Comparison groups	Treatment group 1 (LD ABOi) v Treatment group 2 (LD ABOc) v Treatment group 3 (DD NTx)
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	Kruskal-wallis

Primary: Memory B cell depletion and repopulation in peripheral blood

End point title	Memory B cell depletion and repopulation in peripheral blood

End point description:

Depletion and repopulation of memory B cells (CD27+ CD19+) B cell subpopulation in peripheral blood was investigated by flow cytometric analysis of whole blood at the defined investigation time points. Indicated values are Mean values and SEM of cells/µl.
Only in treatment group 1(AB0i) an additional measurement was performed before rituximab

administration. The established baseline memory B cell concentration (CD27+ CD19+) at this time point was 17 (± 3) cells/µl.

End point type	Primary

End point timeframe:

Analysis was performed at the time points before rituximab administration (pre RTx), before transplantation (pre tpl) and 3 months (3 mo), 6 months (6 mo), 1 year, 2 years, 3 years, 4 years, and 5 years after transplantation.

End point values	Treatment group 1 (LD ABOi)	Treatment group 2 (LD ABOc)	Treatment group 3 (DD NTx)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	25[4]	30[5]	30[6]	
Units: cells/µl				
arithmetic mean (standard error)				
Memory B cells/µl before transplantation	0 (± 0)	15 (± 2)	22 (± 6)	
Memory B cells/µl 3 month after transplantation	0 (± 0)	38 (± 5)	38 (± 8)	
Memory B cells/µl 6 month after transplantation	0 (± 0)	28 (± 4)	33 (± 7)	
Memory B cells/µl 1 year after transplantation	1 (± 0)	19 (± 4)	17 (± 3)	
Memory B cells/µl 2 years after transplantation	2 (± 0)	19 (± 4)	15 (± 3)	
Memory B cells/µl 3 years after transplantation	2 (± 0)	15 (± 4)	16 (± 2)	
Memory B cells/µl 4 years after transplantation	6 (± 2)	17 (± 5)	14 (± 2)	
Memory B cells/µl 5 years after transplantation	9 (± 5)	20 (± 5)	11 (± 2)	

Notes:

[4] - pre RTx 25, pre tpl 23, 3 mo 22, 6 mo 20, 1 year 22, 2 years 21, 3 years 20, 4 years 18, 5 years 18

[5] - pre RTx nd, pre tpl 30, 3 mo 30, 6 mo 28, 1 year 29, 2 years 29, 3 years 29, 4 years 25, 5 years 25

[6] - pre RTx nd, pre tpl 30, 3 mo 30, 6 mo 30, 1 year 30, 2 years 29, 3 years 28, 4 years 26, 5 years 26

Statistical analyses

Statistical analysis title	Statistical comparison of the three patient groups
Comparison groups	Treatment group 1 (LD ABOi) v Treatment group 2 (LD ABOc) v Treatment group 3 (DD NTx)
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	Kruskal-wallis
Confidence interval	
sides	2-sided
Variability estimate	Standard error of the mean

Primary: Naive B cell depletion and repopulation in peripheral blood

End point title	Naive B cell depletion and repopulation in peripheral blood

End point description:

Depletion and repopulation of naive B cells (CD27- CD19+ B cell subpopulation) in peripheral blood was investigated by flow cytometric analysis of whole blood at the defined investigation time points. Indicated values are Mean values and SEM of cells/µ were indicated.
Only in treatment group 1(AB0i) an additional measurement was performed before rituximab administration.. The determined baseline concentration of naive B cells (CD27- CD19+ B cell subpopulation) at this time point was 86 (± 9) cells/µl.

End point type	Primary

End point timeframe:

Analysis was performed at the time points before rituximab administration (pre RTx), before transplantation (pre tpl) and 3 months (3 mo), 6 months (6 mo), 1 year, 2 years, 3 years, 4 years, and 5 years after transplantation.

End point values	Treatment group 1 (LD ABOi)	Treatment group 2 (LD ABOc)	Treatment group 3 (DD NTx)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	25[7]	30[8]	30[9]	
Units: cells/µl				
arithmetic mean (standard error)				
Naive B cells/µl before transplantation	0 (± 0)	97 (± 12)	99 (± 11)	
Naive B cells/µl 3 month after transplantation	0 (± 0)	128 (± 20)	108 (± 18)	
Naive B cells/µl 6 month after transplantation	1 (± 1)	92 (± 14)	95 (± 18)	
Naive B cells/µl 1 year after transplantation	5 (± 2)	70 (± 11)	66 (± 10)	
Naive B cells/µl 2 years after transplantation	48 (± 14)	87 (± 11)	96 (± 12)	
Naive B cells/µl 3 years after transplantation	71 (± 16)	116 (± 15)	107 (± 15)	
Naive B cells/µl 4 years after transplantation	106 (± 23)	129 (± 18)	129 (± 14)	
Naive B cells/µl 5 years after transplantation	134 (± 29)	143 (± 22)	129 (± 15)	

Notes:

[7] - pre RTx 25, pre tpl 23, 3 mo 22, 6 mo 20, 1 year 22, 2 years 21, 3 years 20, 4 years 18, 5 years 18

[8] - pre RTx nd, pre tpl 30, 3 mo 30, 6 mo 28, 1 year 29, 2 years 29, 3 years 29, 4 years 25, 5 years 25

[9] - pre RTx nd, pre tpl 30, 3 mo 30, 6 mo 30, 1 year 30, 2 years 29, 3 years 28, 4 years 26, 5 years 26

Statistical analyses

Statistical analysis title	Statistical comparison of the three patient groups
Comparison groups	Treatment group 1 (LD ABOi) v Treatment group 2 (LD ABOc) v Treatment group 3 (DD NTx)

Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	Kruskal-wallis

Primary: Short-lived plasma cell depletion and repopulation in peripheral blood

End point title	Short-lived plasma cell depletion and repopulation in peripheral blood

End point description:

Depletion and repopulation of short lived B cells (CD19+ CD38+ CD138- B cell subpopulation) in peripheral blood was investigated by flow cytometric analysis of whole blood at the defined investigation time points. Indicated values are Mean values and SEM of cells/µ were indicated.
Indicated values are Mean values and SEM of cells/µ were indicated.
Only in treatment group 1(AB0i) an additional measurement was performed before rituximab administration. The determined baseline concentration of short lived B cells (CD19+ CD38+ CD138-) at this time was 77 (± 9) cells/µl.

End point type	Primary

End point timeframe:

Analysis was performed at the time points before rituximab administration (pre RTx), before transplantation (pre tpl) and 3 months (3 mo), 6 months (6 mo), 1 year, 2 years, 3 years, 4 years, and 5 years after transplantation.

End point values	Treatment group 1 (LD ABOi)	Treatment group 2 (LD ABOc)	Treatment group 3 (DD NTx)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	25[10]	30[11]	30[12]	
Units: cells/µl				
arithmetic mean (standard error)				
Short lived plasma cells/µl before transplantation	0 (± 0)	89 (± 12)	97 (± 13)	
Short lived plasma cells/µl 3 month after tx	0 (± 0)	119 (± 17)	112 (± 19)	
Short lived plasma cells/µl 6 month after tx	1 (± 1)	90 (± 13)	93 (± 17)	
Short lived plasma cells/µl 1 year after tx	5 (± 1)	63 (± 9)	62 (± 11)	
Short lived plasma cells/µl 2 years after tx	41 (± 13)	73 (± 8)	80 (± 11)	
Short lived plasma cells/µl 3 years after tx	53 (± 13)	88 (± 11)	84 (± 12)	
Short lived plasma cells/µl 4 years after tx	88 (± 17)	97 (± 13)	100 (± 14)	
Short lived plasma cells/µl 5 years after tx	108 (± 25)	116 (± 17)	99 (± 12)	

Notes:

[10] - pre RTx 25, pre tpl 23, 3 mo 22, 6 mo 20, 1 year 22, 2 years 21, 3 years 20, 4 years 18, 5 years 18
[11] - pre RTx nd, pre tpl 30, 3 mo 30, 6 mo 28, 1 year 29, 2 years 29, 3 years 29, 4 years 25, 5 years 25
[12] - pre RTx nd, pre tpl 30, 3 mo 30, 6 mo 30, 1 year 30, 2 years 29, 3 years 28, 4 years 26, 5 years

Statistical analyses

Statistical analysis title	Statistical comparison of the three patient groups
Comparison groups	Treatment group 1 (LD ABOi) v Treatment group 2 (LD ABOc) v Treatment group 3 (DD NTx)
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	Kruskal-wallis

Primary: Flow cytometric analysis of regional lymph nodes at the time of transplantation

End point title	Flow cytometric analysis of regional lymph nodes at the time of transplantation

End point description:

Regional lymph nodes were harvested from patients during transplantation and prepared for cytometric analysis. The percentages of the examined lymphocyte populations in the lymph nodes were determinedby flow cytometry.
SLPC = Short Lived Plasma Cell

End point type	Primary

End point timeframe:

The regional lymph nodes to be examined were collected during kidney transplantation and analyzed as soon as possible by flow cytometry.

End point values	Treatment group 1 (LD ABOi)	Treatment group 2 (LD ABOc)	Treatment group 3 (DD NTx)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	24	15	
Units: percent				
arithmetic mean (standard error)				
Nk cells in % of lymphocytes	2.2 (± 0.2)	1.8 (± 0.2)	2.7 (± 0.4)	
T cells in % of lymphocytes	53.2 (± 3.8)	61.4 (± 2.5)	55.6 (± 3.6)	
CD4+ T cells in % of lymphocytes	44.2 (± 3.2)	50.9 (± 2.3)	46.0 (± 2.6)	
CD25+/CD127- in % of CD4+ cells (Treg cells)	6.3 (± 2.4)	4.4 (± 1.3)	5.1 (± 2.2)	
CD8+ T cells in % of lymphocytes	10.3 (± 1.0)	12.1 (± 1.4)	9.6 (± 0.7)	
CD19+ T cells in % of lymphocytes	38.0 (± 4.1)	32.4 (± 2.3)	36.0 (± 3.2)	
Memory B cells(CD27+ CD19+ cells) % of lymphocytes	33.8 (± 3.9)	25.6 (± 2.7)	27.3 (± 2.8)	
Naive B cells(CD27- CD19+ cells) % of lymphocytes	3.9 (± 0.9)	6.9 (± 1.2)	8.7 (± 1.8)	

Mature B cells(CD22+ CD19+ cells) % of lymphocytes	39.0 (± 4.2)	32.5 (± 2.3)	35.9 (± 3.2)	
SLPC (CD19+ CD38+ CD138- cells)in % of lymphocytes	8.7 (± 1.6)	16.5 (± 1.5)	18.1 (± 2.3)	

Statistical analyses

Statistical analysis title	Comparison of all groups studied
Statistical analysis description:	
Comparison of lymphocyte subpopulations in regional lymph nodes between the three patient groups.	
Comparison groups	Treatment group 1 (LD ABOi) v Treatment group 2 (LD ABOc) v Treatment group 3 (DD NTx)
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	Kruskal-wallis

Statistical analysis title	Comparison of living donor groups
Statistical analysis description:	
Comparison of lymphocyte subpopulations in regional lymph nodes between the two live renal transplant groups.	
Comparison groups	Treatment group 1 (LD ABOi) v Treatment group 2 (LD ABOc)
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Secondary: Frequency of severe infectious diseases in AB0i and AB0c patient groups.

End point title	Frequency of severe infectious diseases in AB0i and AB0c patient groups.
End point description:	
Incidence of severe infectious diseases in AB0i versus AB0c lifing renal transplant patients.	
End point type	Secondary
End point timeframe:	
From the time of kidney transplantation up to 2 years after transplantation.	

End point values	AB0i renal transplant patients	AB0c renal transplant patients		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24	30		
Units: Percent of all / number of all				
Severe infection disease (number of all)	11	6		
Severe infection disease (percent)	46	20		

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of BK viremia

End point title	Incidence of BK viremia

End point description:

Incidence of BK viremia (1, 2, 3, 4 and 5 years posttransplant, respectively) in patients who received rituximab versus those who did not.

End point type	Secondary

End point timeframe:

From the time of renal transplantation to 5 years after transplantation.

End point values	Patients with rituximab treatment	Patients without rituximab treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	54		
Units: percent				
number (not applicable)				
Incidence of BK viremia 0-1 years	31	7		
Incidence of BK viremia 0-2 years	31	11		
Incidence of BK viremia 0-3 years	31	13		
Incidence of BK viremia 0-4 years	33	13		
Incidence of BK viremia 0-5 years	33	13		

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of BK virus nephropathy

End point title	Incidence of BK virus nephropathy

End point description:

Incidence of BK virus nephropathy 0-5 years posttransplant in patients who received rituximab versus those who did not.

End point type	Secondary

End point timeframe:

From the time of renal transplantation to 5 years after transplantation.

End point values	Patients with rituximab treatment	Patients without rituximab treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	53		
Units: percent				
number (not applicable)				
Incidence of BK virus nephropathy 0-5 years	7	6		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were documented in all study participants from before rituximab administration or transplantation until 5 years after transplantation. This covers the period from January 2010 to May 2019.

Adverse event reporting additional description:

AEs were identified during routine examinations of study participants at the time points before rituximab administration, before transplantation and at 3 months, 6 months, 1 year, 2 years, 3 years, 4 years, and 5 years after transplantation, as well as during necessary unscheduled visits of study participants to our outpatient clinic.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Reporting group 1 (LD ABOi-NTX)
Reporting group description: -	
Reporting group title	Reporting group 2 (LD ABOc-NTx)
Reporting group description: -	
Reporting group title	Reporting group 3 (DD-NTx)

Reporting group description: -

Serious adverse events	Reporting group 1 (LD ABOi-NTX)	Reporting group 2 (LD ABOc-NTx)	Reporting group 3 (DD-NTx)
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 25 (84.00%)	21 / 30 (70.00%)	26 / 30 (86.67%)
number of deaths (all causes)	3	0	3
number of deaths resulting from adverse events	3	0	3
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post transplant lymphoproliferative disorder	Additional description: Suspected relationship to Tacrolimus and myfortic		
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (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 cell carcinoma			

subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Arterial occlusive disease			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (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
Thrombophlebitis			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (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
Infarction	Additional description: Non-site specific necrosis and vascular insufficiency NEC, multiple infarctions with consecutive sepsis, the main event was categorized as clotting disorders due to a antiphospholipid antibody syndrome (without relevant clinical events pretransplant)		
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Peripheral artery occlusion			
subjects affected / exposed	2 / 25 (8.00%)	0 / 30 (0.00%)	0 / 30 (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
Surgical and medical procedures			
Arteriovenous fistula operation			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal polypectomy			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

General disorders and administration site conditions			
Hernia			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impaired healing			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Transplant rejection			
subjects affected / exposed	6 / 25 (24.00%)	2 / 30 (6.67%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 6	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaphylactic shock			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (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
Reproductive system and breast disorders			
Pleural effusion			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (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
Organising pneumonia	Additional description: Suspected relationship to Tacrolimus and Myfortic		
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (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
Psychiatric disorders			

Suicide attempt			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Weight decreased	Additional description: suspected relationship to Tacrolimus		
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Arteriovenous graft site stenosis			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	2 / 30 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Complications of transplanted kidney			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incisional hernia			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haematoma			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural bleeding			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	2 / 30 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative lymphocele			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Radius fracture			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal transplant failure			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seroma			
subjects affected / exposed	6 / 25 (24.00%)	1 / 30 (3.33%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 6	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shunt aneurysm			
subjects affected / exposed	2 / 25 (8.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxicity to various agents	Additional description: everolimus intoxication (diarrhea)		
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (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
Shunt thrombosis			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (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 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (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
Arterial injury			

subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Graft complication			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (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
Tendon rupture			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Congenital cystic kidney disease			
subjects affected / exposed	0 / 25 (0.00%)	2 / 30 (6.67%)	0 / 30 (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
Hydrocele			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	2 / 30 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction	Additional description: Non STEMI		
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	2 / 30 (6.67%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia	Additional description: high potassium (6.4 mmol/l) due to suspected renal tub acidosis (Tacr associated)		

subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	2 / 30 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Myocardial infarction			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden cardiac death			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Coronary artery disease			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (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
Nervous system disorders			
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	2 / 30 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haemorrhage			
subjects affected / exposed	1 / 25 (4.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Apoplexy			

subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (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
Posterior reversible encephalopathy syndrome			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (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			
Agranulocytosis	Additional description: Suspected relationship to Myfortic		
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (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
Eye disorders			
Vitreous haemorrhage			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (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			
Abdominal hernia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal tenderness			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Diarrhoea			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fistula of small intestine			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mechanical ileus			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric perforation	Additional description: Association with Myfortic and steroids may be possible		
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (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
Gastrointestinal polyp haemorrhage			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			

Cholecystitis acute			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (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
Steatohepatitis	Additional description: Suspected relationship to Tacrolimus and Myfortic		
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (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
Cholestasis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Glomerulonephritis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postrenal failure			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal artery stenosis			
subjects affected / exposed	2 / 25 (8.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal mass			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureteric stenosis			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glomerulonephritis			

membranoproliferative			
subjects affected / exposed	1 / 25 (4.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephropathy toxic	Additional description: Graft deterioration due to tacrolimus nephrotoxicity		
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (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
Nephrotic syndrome			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (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
Acute kidney injury			
subjects affected / exposed	3 / 25 (12.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureteral necrosis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (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 obstruction			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (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
Endocrine disorders			
Hyperparathyroidism tertiary			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Tendon pain			

subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar spinal stenosis			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (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
Arthritis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (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
Spinal osteoarthritis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (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
Infections and infestations			
Bronchitis	Additional description: Suspected relationship to Tacrolimus and Myfortic in reporting group 3		
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus colitis	Additional description: Suspected relationship to Tacrolimus and Myfortic		
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus enterocolitis	Additional description: Suspected relationship to Tacrolimus and Myfortic. Additional bacterial infections might have been favoured by suppressed cellular immunity.		
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus gastroenteritis	Additional description: Suspected relationship to Tacrolimus and Myfortic		
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			

subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis intestinal haemorrhagic			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periumbilical abscess			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia	Additional description: Reporting group 3 (DD): Suspected relationship to Tacrolimus and Myfortic, Reporting group 1 (LDi): Suspected relationship to Tacrolimus		
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polyomavirus-associated nephropathy	Additional description: Suspected relationship to Tacolimus and Myfortic		
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	2 / 30 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound infection	Additional description: Suspected relationship to Tacrolimus and Myfortic		
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute	Additional description: Suspected relationship to Tacrolimus and Myfortic		
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal graft infection	Additional description: Suspected relationship to Tacrolimus and Myfortic		

subjects affected / exposed	6 / 25 (24.00%)	1 / 30 (3.33%)	3 / 30 (10.00%)
occurrences causally related to treatment / all	0 / 6	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shunt infection			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis	Additional description: Suspected relationship to Tacrolimus and Myfortic		
subjects affected / exposed	8 / 25 (32.00%)	2 / 30 (6.67%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 8	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspergilloma			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (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
Cystitis	Additional description: Suspected relationship to Tacrolimus and Myfortic		
subjects affected / exposed	1 / 25 (4.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus infection			
subjects affected / exposed	1 / 25 (4.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis viral			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (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
Erysipelas	Additional description: Suspected relationship to Myfortic		
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (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
Gastroenteritis			

subjects affected / exposed	1 / 25 (4.00%)	2 / 30 (6.67%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infected seroma	Additional description: Reorting group 3 (DD): Suspected relationship to Myfortic		
subjects affected / exposed	1 / 25 (4.00%)	1 / 30 (3.33%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal tuberculosis	Additional description: Suspected relationship to Tacrolimus and Myfortic		
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (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 cyst infection	Additional description: Suspected relationship to Tacrolimus and Myfortic		
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (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
Cholecystitis infective			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (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
Clostridium colitis	Additional description: Suspected relationship to Tacrolimus and Myfortic		
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis intestinal perforated			
subjects affected / exposed	2 / 25 (8.00%)	0 / 30 (0.00%)	0 / 30 (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
Sepsis	Additional description: Suspected relationship to Tacrolimus and Myfortic		
subjects affected / exposed	2 / 25 (8.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Wound infection fungal			

subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (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

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

Non-serious adverse events	Reporting group 1 (LD ABOi-NTX)	Reporting group 2 (LD ABOc-NTx)	Reporting group 3 (DD-NTx)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 25 (84.00%)	28 / 30 (93.33%)	28 / 30 (93.33%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Haemangioma			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Neuroma			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Basal cell carcinoma			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	2 / 25 (8.00%)	1 / 30 (3.33%)	3 / 30 (10.00%)
occurrences (all)	2	1	4
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Pelvic venous thrombosis			
subjects affected / exposed	1 / 25 (4.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	1	1	0
Thrombophlebitis			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0

Thrombosis			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Surgical and medical procedures			
Vascular anastomosis			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Implant site extravasation			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	3 / 30 (10.00%)
occurrences (all)	3	0	3
Injection site thrombosis			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Treatment noncompliance			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Unevaluable event			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Impaired healing			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	2	0	0
Oedema peripheral			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Chronic allograft nephropathy			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Transplant rejection			
subjects affected / exposed	4 / 25 (16.00%)	3 / 30 (10.00%)	3 / 30 (10.00%)
occurrences (all)	4	3	3
Reproductive system and breast disorders			
Menstruation irregular			

subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Prostatitis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Cough			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Haemoptysis			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Dyspnoea exertional			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 25 (0.00%)	2 / 30 (6.67%)	1 / 30 (3.33%)
occurrences (all)	0	2	1
Adjustment disorder with depressed mood			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Anxiety			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Confusional state			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	2	0	0
Insomnia			

subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Somatic symptom disorder			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Substance-induced psychotic disorder			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Investigations			
Intraocular pressure increased			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Immunosuppressant drug level decreased			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Graft ischaemia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Graft thrombosis			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Incisional hernia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Muscle rupture			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Peroneal nerve injury			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Shunt aneurysm			

subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Shunt thrombosis			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Transplant failure			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	2 / 30 (6.67%)
occurrences (all)	0	0	2
Ureteric anastomosis complication			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Alcohol poisoning			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Joint injury			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Peroneal nerve palsy postoperative			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Rib fracture			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Transfusion reaction			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Epicondylitis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Meniscus injury			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Post procedural haemorrhage			
subjects affected / exposed	2 / 25 (8.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	2	0	0
Procedural nausea			

subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Reactive gastropathy			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Shunt occlusion			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Upper limb fracture			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Urethral injury			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Congenital, familial and genetic disorders			
Hypertrophic cardiomyopathy			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Acute myocardial infarction			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Aortic valve incompetence			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Atrioventricular block			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Atrial fibrillation			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			

Neuropathy peripheral			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Tremor			
subjects affected / exposed	2 / 25 (8.00%)	1 / 30 (3.33%)	1 / 30 (3.33%)
occurrences (all)	2	1	1
Cognitive disorder			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Polyneuropathy			
subjects affected / exposed	2 / 25 (8.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	4	1	0
Syncope			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Autonomic neuropathy			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Leukopenia			
subjects affected / exposed	6 / 25 (24.00%)	2 / 30 (6.67%)	0 / 30 (0.00%)
occurrences (all)	9	2	0
Polycythaemia			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Thrombocytopenia			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			

Inner ear disorder			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Vertigo			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	3 / 30 (10.00%)
occurrences (all)	0	0	3
Diarrhoea			
subjects affected / exposed	6 / 25 (24.00%)	7 / 30 (23.33%)	3 / 30 (10.00%)
occurrences (all)	8	7	3
Gastric ulcer			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Haematochezia			
subjects affected / exposed	2 / 25 (8.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	2	0	1
Malabsorption			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	2 / 30 (6.67%)
occurrences (all)	1	0	2
Nausea			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Toothache			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Abdominal pain upper			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Food poisoning			
subjects affected / exposed	1 / 25 (4.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	1	1	0
Haemorrhoids			

subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Intestinal obstruction			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Gastric disorder			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Gastritis erosive			
subjects affected / exposed	2 / 25 (8.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	2	0	0
Haemorrhoidal haemorrhage			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Actinic keratosis			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Alopecia			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	2 / 30 (6.67%)
occurrences (all)	0	1	2
Night sweats			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Skin necrosis			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Angioedema			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Acute kidney injury			

subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Renal haematoma			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Renal tubular acidosis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Urinary retention			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Glomerulonephritis membranoproliferative			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Renal infarct			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Bladder tamponade			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Endocrine disorders			
Goitre			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Gouty arthritis			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Intervertebral disc protrusion			
subjects affected / exposed	1 / 25 (4.00%)	1 / 30 (3.33%)	1 / 30 (3.33%)
occurrences (all)	1	1	1
Back pain			

subjects affected / exposed	1 / 25 (4.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	1	1	0
Joint stiffness			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Bacterial infection			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Bronchitis			
subjects affected / exposed	4 / 25 (16.00%)	5 / 30 (16.67%)	1 / 30 (3.33%)
occurrences (all)	7	5	1
Cytomegalovirus gastroenteritis			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Cytomegalovirus infection reactivation			
subjects affected / exposed	1 / 25 (4.00%)	3 / 30 (10.00%)	3 / 30 (10.00%)
occurrences (all)	1	3	3
Diverticulitis			
subjects affected / exposed	1 / 25 (4.00%)	1 / 30 (3.33%)	2 / 30 (6.67%)
occurrences (all)	2	1	2
Gastroenteritis			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Gastrointestinal infection			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Herpes zoster			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	2
Nasopharyngitis			

subjects affected / exposed	5 / 25 (20.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	5	0	1
Oral candidiasis			
subjects affected / exposed	5 / 25 (20.00%)	2 / 30 (6.67%)	1 / 30 (3.33%)
occurrences (all)	5	2	1
Pneumonia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Polyomavirus viraemia			
subjects affected / exposed	6 / 25 (24.00%)	6 / 30 (20.00%)	5 / 30 (16.67%)
occurrences (all)	6	6	5
Renal graft infection			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Urinary tract infection			
subjects affected / exposed	5 / 25 (20.00%)	5 / 30 (16.67%)	5 / 30 (16.67%)
occurrences (all)	6	8	9
Urinary tract infection bacterial			
subjects affected / exposed	0 / 25 (0.00%)	2 / 30 (6.67%)	1 / 30 (3.33%)
occurrences (all)	0	2	1
Urinary tract infection enterococcal			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	2
Cytomegalovirus colitis			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Cytomegalovirus enterocolitis			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Cytomegalovirus infection			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Epididymitis			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Erysipelas			

subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Gingivitis			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Oral herpes			
subjects affected / exposed	1 / 25 (4.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	1	1	0
Paronychia			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Polyomavirus-associated nephropathy			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Renal cyst infection			
subjects affected / exposed	0 / 25 (0.00%)	2 / 30 (6.67%)	0 / 30 (0.00%)
occurrences (all)	0	2	0
Sinusitis			
subjects affected / exposed	1 / 25 (4.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	1	1	0
Soft tissue infection			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	2 / 25 (8.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	2	1	0
Bacterial prostatitis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
BK virus infection			
subjects affected / exposed	2 / 25 (8.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	2	0	0
Clostridium difficile colitis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0

Device related infection			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Onychomycosis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal candidiasis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Tonsillitis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Hypocalcaemia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
New onset diabetes after transplantation			
subjects affected / exposed	0 / 25 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Diabetes mellitus			
subjects affected / exposed	1 / 25 (4.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	1	1	0
Hypercalcaemia			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	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

None reported