Clinical trial results:
A Phase II Study to Evaluate the Efficacy of IdeS (IgG endopeptidase) to Desensitize Transplant Patients with a Positive Crossmatch Test

Summary

EudraCT number	2016-002064-13
Trial protocol	SE FR
Global end of trial date	03 July 2018

Results information

Result version number	v1 (current)
This version publication date	25 July 2019
First version publication date	25 July 2019

Trial information

Trial identification

Sponsor protocol code	15-HMedIdeS-06

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02790437
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Hansa Biopharma AB
Sponsor organisation address	Scheelevägen 22, Lund, Sweden, 223 63
Public contact	Clinical Trials Information, Hansa Biopharma AB, Hansa Biopharma AB, clinicalstudyinfo@hansabiopharma.com
Scientific contact	Clinical Trials Information, Hansa Biopharma AB, Hansa Biopharma AB, clinicalstudyinfo@hansabiopharma.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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	27 November 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 July 2018
Global end of trial reached?	Yes
Global end of trial date	03 July 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To asses the efficacy of imlifidase in creating a negative crossmatch test

Protection of trial subjects:

Patients who were not eligible for transplantation after imlifidase treatment were not transplanted and thus did not receive any induction therapy or immunosuppression.

All patients who received imlifidase were asked to remain in the study and followed up according to the study protocol even if they were not transplanted.

Patients who lost their graft during the study remained in the study and were followed up according to the study protocol and/or clinical practice at the study site.

After study completion, all patients were followed up regularly and interdisciplinary (by nephrologist and transplant surgeons) according to each centre’s follow-up routines for transplanted patients. The frequencies of outpatient visits were adjusted individually to the state of patient Health and transplant function.

Patients whose ADA levels had not returned to normal range at study completion were asked to return for a follow-up ADA sample at 12 months.

Background therapy:

Premedication: Glucocorticoids (methylprednisolone, 250 mg IV) and antihistamines (loratadine 10 mg orally or an equipotent antihistamine) before each imlifidase infusion.

Prophylactic antibiotics or sulphonamides: According to clinical practice at each site from the start of imlifidase treatment until the serum IgG level was back within normal range.

IVig and rituximab: High dose IVIg 10% solution 2 g/kg (maximum 140 g for >70 kg) 7 days after imlifidase treatment and 1 g rituximab (anti-CD20 antibody) 9 days after imlifidase treatment. If deemed necessary by the investigator, the IVIg dose could be split into two doses administered over days 6-8.

Immunosuppressing agents: According to clinical practice at each study site.

Induction therapy: If indicated, sites could use either ATGAM or alemtuzumab. Rabbit ATG could not be used since it is efficiently cleaved by imlifidase. Alemtuzumab could be administered 4 days after imlifidase at the earliest, based on limited experience. If alemtuzumab was used as induction therapy on day 4, pulse steroid treatment could be used up to day 4 to prevent T-cell mediated rejection.

Evidence for comparator:

N/A

Actual start date of recruitment	30 September 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Sweden: 2
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	United States: 14
Worldwide total number of subjects	19
EEA total number of subjects	5

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)	19
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited between 30-Sep-2016 and 28-Nov-2017 in US.
Patients were recruited between 21-Mar-2017 and 27-Nov-2017 in EEA.

Pre-assignment

Screening details:

A total of 21 patients were screened world-wide and 19 were enrolled in the study. One screening failure was reported from US and one from EEA.

Period 1

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

Blinding implementation details:

N/A

Arms

Are arms mutually exclusive?	Yes
Arm title	0.25 mg/kg

Arm description:

One IV infusion.

Arm type	Experimental
Investigational medicinal product name	Imlifidase
Investigational medicinal product code	
Other name	IdeS, IgG endopeptidase
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

After dilution imfilidase was administered as an IV infusion over at least 15 minutes using a syringe or an infusion bag, an infusion pump and a particle filter.

Arm title	2 x 0.25 mg/kg

Arm description:

Two IV infusions. The first dose on day 0 and as the desired effect was not achieved (i.e. a negative CXM test was not obtained) an additional imlifidase infusion was given within 2 days of the first infusion.

Arm type	Experimental
Investigational medicinal product name	Imlifidase
Investigational medicinal product code	
Other name	IdeS, IgG endopeptidase
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

After dilution imfilidase was administered as an IV infusion over at least 15 minutes using a syringe or an infusion bag, an infusion pump and a particle filter.

Number of subjects in period 1	0.25 mg/kg	2 x 0.25 mg/kg
Started	16	3
Completed	13	3
Not completed	3	0
Consent withdrawn by subject	1	-
Adverse event, non-fatal	1	-
Patient graft failure-nephrectomy	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	19	19	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	19	19	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	39.10		
standard deviation	± 10.80	-	
Gender categorical Units: Subjects			
Female	6	6	
Male	13	13	

End points

End points reporting groups

Reporting group title	0.25 mg/kg

Reporting group description:

One IV infusion.

Reporting group title	2 x 0.25 mg/kg

Reporting group description:

Two IV infusions. The first dose on day 0 and as the desired effect was not achieved (i.e. a negative CXM test was not obtained) an additional imlifidase infusion was given within 2 days of the first infusion.

Subject analysis set title	FAS
Subject analysis set type	Full analysis

Subject analysis set description:

FAS comprises data from all patients in the safety analysis set (SAS) with available post-dose efficacy data.
The FAS is used for presentation of efficacy endpoints

Subject analysis set title	SAS
Subject analysis set type	Safety analysis

Subject analysis set description:

The SAS comprises data from all patients dosed with any amount of study medication.

Subject analysis set title	PP
Subject analysis set type	Per protocol

Subject analysis set description:

The PP analysis set consists of all patients in the safety set who had at least one efficacy endpoint value. Data from patients with one or more major protocol deviations were excluded.
The PP analysis set is used for presentation of PK and PD endpoints.

Primary: Conversion of a positive crossmatch to a negative within 24h

End point title	Conversion of a positive crossmatch to a negative within 24h[1]

End point description:

Crossmatch was assessed using both FACS CXM and CDC CXM tests.
The FACS CXM is a multi-staining procedure where the recipient's serum is used to stain donor cells to identify the presence of donor specific antibodies (DSAs) in recipient's serum. T- and B-cells were identified using conjugated antibodies against CD3 and CD19, respectively. DSAs were identified using a conjugated anti-human antibody.
The CDC CXM test evaluates the cytotoxic capacity of the DSAs. The recipient's serum was mixed with donor cells prior to addition of complement. Fluorescent dyes were added to the mixture and the percentage of live/dead cells was scored using a fluorescent microscope. In case an anti-human globulin was used as an amplifier for the CDC CXM, the laboratory was also required to perform a non-amplified CDC CXM test.

The primary endpoint was met if at least one assay was positive pre-dose and the last assay within 24 h post-dose was negative.

End point type	Primary

End point timeframe:

Crossmatch (CXM) was assessed pre-dose and at up to 3 times within 24 h post dose (i.e. 2h, 6h and 24h post dose). If one or both the tests at 2 and 6 h were negative the patient proceeded to transplantation and no more CXM test was performed.

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: Data for the primary endpoint was summarized for FAS. No statistical significance testing was performed due to few patients in the two treatment arms. All endpoints were presented using descriptive statistics, individual listings and graphs.

End point values	FAS			
Subject group type	Subject analysis set			
Number of subjects analysed	19			
Units: CXM conversion within 24 h				
Yes	17			
No	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Donor Specific Antibodies (DSAs)

End point title	Donor Specific Antibodies (DSAs)

End point description:

DSA levels were measured using the single antigen beads (SAB) anti-HLA assay. The levels were determined as mean fluorescence intensity (MFI).
Positive DSA (i.e. HLA antibodies) were defined as a MFI value >3000.

End point type	Secondary

End point timeframe:

Pre-dose , 2h, 6 h, 24 h, 48 h, 96 h, 7 dys, 14 days, 28 days, 90 days and 180 days.

End point values	PP			
Subject group type	Subject analysis set			
Number of subjects analysed	18[2]			
Units: Number of patients with DSA (MFI>3000)				
Pre-dose	17			
2 h	7			
6 h	3			
24 h	3			
48 h	3			
96 h	6			
7 days	9			
14 days	13			
28 days	10			
90 days	8			
180 days	7			

Notes:

[2] - Except for Day 180 when the number of subjects was 17

Statistical analyses

No statistical analyses for this end point

Secondary: Kidney function - eGFR

End point title	Kidney function - eGFR

End point description:

Estimated glomerular filtration rate (eGFR) calculated as described by the MDRD equation is a measure of kidney function.
eGFR for a kidney with normal function is 90 mL/min/1.72m2. Kidney disease is characterised by a decreased eGFR value.

End point type	Secondary

End point timeframe:

Day 28, Day 90 and Day 180

End point values	PP			
Subject group type	Subject analysis set			
Number of subjects analysed	18[3]			
Units: Number of patients				
>60 mL/min/1.72m2 at Day 28	4			
>60 mL/min/1.72m2 at Day 90	6			
>60 mL/min/1.72m2 at Day 180	4			
30-59 mL/min/1.72m2 at Day 28	9			
30-59 mL/min/1.72m2 at Day 90	7			
30-59 mL/min/1.72m2 at Day 180	11			
<30 mL/min/1.72m2 at Day 28	5			
<30 mL/min/1.72m2 at Day 90	4			
<30 mL/min/1.72m2 at Day 180	2			

Notes:

[3] - Except for Day 90 and 180 when the number of subjects was 17 as 1 subject lost the graft Day 77

Statistical analyses

No statistical analyses for this end point

Secondary: Serum IgG concentration - PD

End point title	Serum IgG concentration - PD

End point description:

IgG concentration refers to the sum of intact IgG and single-cleaved IgG. Please note that IvIg was administered Day 7.

End point type	Secondary

End point timeframe:

Pre-dose to Day 180

End point values	0.25 mg/kg	2 x 0.25 mg/kg	PP	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	15[4]	3[5]	18[6]	
Units: IgG concentration				
geometric mean (geometric coefficient of variation)				
Pre-dose	10.11 (± 85.92)	8.35 (± 55.37)	9.79 (± 79.73)	

2 h	1.19 (± 91.05)	0.68 (± 165.87)	1.08 (± 100.51)	
6 h	0.55 (± 83.44)	0.38 (± 109.18)	0.52 (± 85.49)	
24 h	0.37 (± 79.14)	0.15 (± 42.46)	0.32 (± 83.92)	
48 h	0.51 (± 129.17)	0.17 (± 45.57)	0.43 (± 132.55)	
Day 7 pre-IVIg	0.64 (± 107.44)	0.2 (± 96.88)	0.53 (± 122.3)	
Day 7 post-IVIg	16.52 (± 49.9)	18.47 (± 23.91)	16.89 (± 45.05)	
Day 9	15.34 (± 85.32)	26.94 (± 50.82)	16.85 (± 83)	
Day 14	13.48 (± 55.67)	10.85 (± 53.42)	13 (± 54.34)	
Day 21	10.57 (± 58.67)	5.88 (± 88.3)	9.58 (± 66.04)	
Day 28	10.25 (± 69.85)	11.53 (± 66.45)	10.45 (± 67.16)	
Day 64	11.91 (± 71.52)	7.77 (± 45.82)	11.09 (± 69.02)	
Day 180	9.33 (± 42.58)	8.99 (± 0)	9.28 (± 39.21)	

Notes:

[4] - Data for 7 patients at Day 180

[5] - Data for 1 patient only at Day 180

[6] - Data for 8 patients at Day 180

Statistical analyses

No statistical analyses for this end point

Secondary: PK - Cmax

End point title	PK - Cmax

End point description:

Cmax = Maximum observed plasma concentration of imlifidase following dosing (Non-compartmental PK analysis)

End point type	Secondary

End point timeframe:

Pre-dose to Day 14

End point values	PP			
Subject group type	Subject analysis set			
Number of subjects analysed	18[7]			
Units: microgram(s)/millilitre				
geometric mean (geometric coefficient of variation)				
Cmax (first dose)	3.95 (± 25.2)			
Cmax (second dose)	4.13 (± 29.4)			

Notes:

[7] - Cmax (second dose) calculated for 3 subjects only who received a 2nd dose 11-13h after the first.

Statistical analyses

No statistical analyses for this end point

Secondary: PK - Tmax

End point title	PK - Tmax

End point description:

Tmax = time point for maximum observed plasma concentration of imlifidase following dosing (Non-compartmental PK analysis)

End point type	Secondary

End point timeframe:

Pre-dose to Day 14

End point values	PP			
Subject group type	Subject analysis set			
Number of subjects analysed	18[8]			
Units: hour				
arithmetic mean (standard deviation)				
Tmax (first dose)	2.21 (± 0.31)			
Tmax (second dose)	15.98 (± 5.50)			

Notes:

[8] - Tmax (second dose) - 3 subjects only who received a second dose 11-13h after the first dose

Statistical analyses

No statistical analyses for this end point

Secondary: PK - AUC

End point title	PK - AUC

End point description:

AUC = area under the plasma concentration vs time curve (Non-compartmental PK analysis)

End point type	Secondary

End point timeframe:

Pre-dose to Day 14

End point values	PP			
Subject group type	Subject analysis set			
Number of subjects analysed	9			
Units: h x microgram(s)/millilitre				
geometric mean (geometric coefficient of variation)	156.09 (± 45.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK - Alpha t1/2 and Beta t1/2

End point title	PK - Alpha t1/2 and Beta t1/2

End point description:

Alpha t1/2 = half-life during distribution phase, Beta t1/2 = half-life during elimination phase (Non-compartmental PK analysis)

End point type	Secondary

End point timeframe:

Pre-dose to Day 14

End point values	PP			
Subject group type	Subject analysis set			
Number of subjects analysed	9[9]			
Units: hour				
arithmetic mean (standard deviation)				
Alpha t1/2 Beta t1/2	4.58 (± 3.85) 76.30 (± 42.76)			

Notes:

[9] - Please note - Harmonic mean (SD) was used rather than arithmetic mean (SD)

Statistical analyses

No statistical analyses for this end point

Secondary: PK - CL

End point title	PK - CL

End point description:

CL = clearance (Non-compartmental PK analysis)

End point type	Secondary

End point timeframe:

Pre-dose to Day 14

End point values	PP			
Subject group type	Subject analysis set			
Number of subjects analysed	9			
Units: millilitre(s)/hour/kilogram				
geometric mean (geometric coefficient of variation)	1.60 (± 45.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK - Vss

End point title	PK - Vss

End point description:

Vss = Volume of distribution at steady state (Non-compartmental PK analysis)

End point type	Secondary

End point timeframe:

Pre-dose to Day 14

End point values	PP			
Subject group type	Subject analysis set			
Number of subjects analysed	9			
Units: litre(s)/kilogram				
geometric mean (geometric coefficient of variation)	0.14 (± 26.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK - Vz

End point title	PK - Vz

End point description:

Vz = Volume of distribution during the elimination phase (Non-compartmental PK analysis)

End point type	Secondary

End point timeframe:

Pre-dose to Day 14

End point values	PP			
Subject group type	Subject analysis set			
Number of subjects analysed	9			
Units: litre(s)/kilogram				
geometric mean (geometric coefficient of variation)	0.19 (± 27.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Safety - AEs

End point title	Safety - AEs

End point description:

End point type	Secondary

End point timeframe:

AEs were collected from the time of signing of the ICF until end of study, incl the follow-up period (=day 180)
Presented AEs include TEAEs and post-treatment AEs, i.e. all AEs occurring after first dose of IdeS until day 180

End point values	0.25 mg/kg	2 x 0.25 mg/kg	SAS	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	3	19	
Units: Number of AEs				
Adverse Events	332	63	395	
Serious Adverse Events	33	8	41	
AEs leading to study discontinuation	1	0	1	
AEs leading to death	0	0	0	
Severe AEs (Grade 3 and 4)	62	19	81	
Related AEs	6	1	7	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were collected from the time of signing of the ICF until end of study, incl the follow-up period
AEs reported in EudraCT include TEAEs and post-treatment AEs, i.e. all AEs occurring after admin of the IMP until end of study, incl the follow-up period

Adverse event reporting additional description:

Data on AEs were obtained if spontaneously reported by the patient, if reported in response to an open question from the study personnel or if revealed by observation.
A TEAE was defined as any AE occurring after the administration of the IMP and within the time of the residual drug effect period (i.e. 30 days after IMP administration).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	0.25 mg/kg
Reporting group description: -	
Reporting group title	2 x 0.25 mg/kg
Reporting group description: -	
Reporting group title	Total

Reporting group description: -

Serious adverse events	0.25 mg/kg	2 x 0.25 mg/kg	Total
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 16 (75.00%)	3 / 3 (100.00%)	15 / 19 (78.95%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Blood creatine increased			
subjects affected / exposed	1 / 16 (6.25%)	1 / 3 (33.33%)	2 / 19 (10.53%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Donor specific antibody present			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Infusion related reaction			

subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transplant failure			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weaning failure			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Axillary vein thrombosis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superior vena cava syndrome			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Thrombotic microangiopathy			
subjects affected / exposed	0 / 16 (0.00%)	1 / 3 (33.33%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Thrombosis in device			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Transplant rejection			

subjects affected / exposed	7 / 16 (43.75%)	2 / 3 (66.67%)	9 / 19 (47.37%)
occurrences causally related to treatment / all	1 / 8	0 / 2	1 / 10
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain lower			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	0 / 16 (0.00%)	1 / 3 (33.33%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Glomerulonephritis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephropathy toxic			

subjects affected / exposed	1 / 16 (6.25%)	1 / 3 (33.33%)	2 / 19 (10.53%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 3 (33.33%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Device related infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterococcal bacteraemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 16 (0.00%)	1 / 3 (33.33%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perinephric abscess			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			

subjects affected / exposed	2 / 16 (12.50%)	0 / 3 (0.00%)	2 / 19 (10.53%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	0.25 mg/kg	2 x 0.25 mg/kg	Total
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 16 (93.75%)	3 / 3 (100.00%)	18 / 19 (94.74%)
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Flushing			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Haematoma			
subjects affected / exposed	0 / 16 (0.00%)	1 / 3 (33.33%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Hypertension			
subjects affected / exposed	3 / 16 (18.75%)	0 / 3 (0.00%)	3 / 19 (15.79%)
occurrences (all)	3	0	3
Hypotension			
subjects affected / exposed	4 / 16 (25.00%)	0 / 3 (0.00%)	4 / 19 (21.05%)
occurrences (all)	5	0	5
Jugular vein thrombosis			

subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
General disorders and administration site conditions			
Administration site pain			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Application site pain			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Application site pruritus			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Breakthrough pain			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Catheter site haemorrhage			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Catheter site pain			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	2	0	2
Chest discomfort			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Chest pain			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Generalised oedema			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Haemorrhagic cyst			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Oedema			

subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Oedema peripheral			
subjects affected / exposed	2 / 16 (12.50%)	1 / 3 (33.33%)	3 / 19 (15.79%)
occurrences (all)	5	2	7
Pain			
subjects affected / exposed	2 / 16 (12.50%)	0 / 3 (0.00%)	2 / 19 (10.53%)
occurrences (all)	5	0	5
Peripheral swelling			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Pyrexia			
subjects affected / exposed	4 / 16 (25.00%)	0 / 3 (0.00%)	4 / 19 (21.05%)
occurrences (all)	4	0	4
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	2 / 16 (12.50%)	0 / 3 (0.00%)	2 / 19 (10.53%)
occurrences (all)	2	0	2
Hypogammaglobulinaemia			
subjects affected / exposed	2 / 16 (12.50%)	2 / 3 (66.67%)	4 / 19 (21.05%)
occurrences (all)	2	2	4
Transplant rejection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	2	0	2
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 16 (12.50%)	1 / 3 (33.33%)	3 / 19 (15.79%)
occurrences (all)	2	1	3
Dyspnoea			
subjects affected / exposed	2 / 16 (12.50%)	0 / 3 (0.00%)	2 / 19 (10.53%)
occurrences (all)	3	0	3
Hiccups			
subjects affected / exposed	2 / 16 (12.50%)	0 / 3 (0.00%)	2 / 19 (10.53%)
occurrences (all)	2	0	2
Laryngeal oedema			

subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Lung disorder			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Pulmonary oedema			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Throat irritation			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Throat lesion			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Psychiatric disorders			
Affective disorder			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Agitation			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Anxiety			
subjects affected / exposed	3 / 16 (18.75%)	0 / 3 (0.00%)	3 / 19 (15.79%)
occurrences (all)	3	0	3
Depression			
subjects affected / exposed	2 / 16 (12.50%)	0 / 3 (0.00%)	2 / 19 (10.53%)
occurrences (all)	2	0	2
Hallucination			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Insomnia			
subjects affected / exposed	3 / 16 (18.75%)	0 / 3 (0.00%)	3 / 19 (15.79%)
occurrences (all)	3	0	3
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Blood creatinine increased			
subjects affected / exposed	2 / 16 (12.50%)	1 / 3 (33.33%)	3 / 19 (15.79%)
occurrences (all)	2	1	3
Blood potassium decreased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Clostridium test positive			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Donor specific antibody present			
subjects affected / exposed	2 / 16 (12.50%)	1 / 3 (33.33%)	3 / 19 (15.79%)
occurrences (all)	2	1	3
Hepatitis B core antibody positive			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Respiratory rate decreased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Sapovirus test positive			
subjects affected / exposed	0 / 16 (0.00%)	1 / 3 (33.33%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Transaminases increased			
subjects affected / exposed	3 / 16 (18.75%)	1 / 3 (33.33%)	4 / 19 (21.05%)
occurrences (all)	4	1	5
Urine output decreased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 3 (33.33%)	1 / 19 (5.26%)
occurrences (all)	0	1	1

Injury, poisoning and procedural complications			
Allergic transfusion reaction			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	2	0	2
Complications of transplant surgery			
subjects affected / exposed	4 / 16 (25.00%)	0 / 3 (0.00%)	4 / 19 (21.05%)
occurrences (all)	4	0	4
Delayed graft function			
subjects affected / exposed	7 / 16 (43.75%)	1 / 3 (33.33%)	8 / 19 (42.11%)
occurrences (all)	7	1	8
Incision site pain			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Infusion related reaction			
subjects affected / exposed	2 / 16 (12.50%)	0 / 3 (0.00%)	2 / 19 (10.53%)
occurrences (all)	3	0	3
Procedural pain			
subjects affected / exposed	3 / 16 (18.75%)	0 / 3 (0.00%)	3 / 19 (15.79%)
occurrences (all)	4	0	4
Renal lymphocele			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Seroma			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	2	0	2
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Pericardial effusion			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Tachycardia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Nervous system disorders			

Headache			
subjects affected / exposed	2 / 16 (12.50%)	1 / 3 (33.33%)	3 / 19 (15.79%)
occurrences (all)	2	1	3
Hypoaesthesia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Presyncope			
subjects affected / exposed	0 / 16 (0.00%)	1 / 3 (33.33%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Tongue paralysis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Tremor			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	9 / 16 (56.25%)	2 / 3 (66.67%)	11 / 19 (57.89%)
occurrences (all)	11	4	15
Anaemia of chronic disease			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Leukopenia			
subjects affected / exposed	4 / 16 (25.00%)	0 / 3 (0.00%)	4 / 19 (21.05%)
occurrences (all)	5	0	5
Neutropenia			
subjects affected / exposed	4 / 16 (25.00%)	2 / 3 (66.67%)	6 / 19 (31.58%)
occurrences (all)	4	3	7
Thrombocytopenia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Thrombocytosis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 3 (33.33%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Eye disorders			

Diplopia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Vision blurred			
subjects affected / exposed	0 / 16 (0.00%)	1 / 3 (33.33%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 16 (6.25%)	1 / 3 (33.33%)	2 / 19 (10.53%)
occurrences (all)	1	1	2
Abdominal pain			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Abdominal pain lower			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Abdominal pain upper			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Constipation			
subjects affected / exposed	7 / 16 (43.75%)	2 / 3 (66.67%)	9 / 19 (47.37%)
occurrences (all)	12	3	15
Diarrhoea			
subjects affected / exposed	7 / 16 (43.75%)	0 / 3 (0.00%)	7 / 19 (36.84%)
occurrences (all)	9	0	9
Dyspepsia			
subjects affected / exposed	5 / 16 (31.25%)	0 / 3 (0.00%)	5 / 19 (26.32%)
occurrences (all)	7	0	7
Flatulence			
subjects affected / exposed	2 / 16 (12.50%)	0 / 3 (0.00%)	2 / 19 (10.53%)
occurrences (all)	3	0	3
Gastritis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Gastrooesophageal reflux disease			

subjects affected / exposed	3 / 16 (18.75%)	0 / 3 (0.00%)	3 / 19 (15.79%)
occurrences (all)	3	0	3
Impaired gastric emptying			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Intra-abdominal haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)	1 / 3 (33.33%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Nausea			
subjects affected / exposed	7 / 16 (43.75%)	1 / 3 (33.33%)	8 / 19 (42.11%)
occurrences (all)	7	1	8
Paraesthesia oral			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Perianal erythema			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Vomiting			
subjects affected / exposed	7 / 16 (43.75%)	0 / 3 (0.00%)	7 / 19 (36.84%)
occurrences (all)	9	0	9
Hepatobiliary disorders			
Hepatocellular injury			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Pruritus			
subjects affected / exposed	6 / 16 (37.50%)	0 / 3 (0.00%)	6 / 19 (31.58%)
occurrences (all)	8	0	8
Rash			
subjects affected / exposed	1 / 16 (6.25%)	1 / 3 (33.33%)	2 / 19 (10.53%)
occurrences (all)	1	2	3
Swelling face			

subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	4 / 16 (25.00%)	0 / 3 (0.00%)	4 / 19 (21.05%)
occurrences (all)	5	0	5
Bladder spasm			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Hypertonic bladder			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Micturition urgency			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Polyuria			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Proteinuria			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Renal cyst haemorrhage			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Endocrine disorders			
Hyperparathyroidism secondary			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 3 (33.33%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Back pain			
subjects affected / exposed	2 / 16 (12.50%)	0 / 3 (0.00%)	2 / 19 (10.53%)
occurrences (all)	2	0	2
Flank pain			

subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Muscle spasms			
subjects affected / exposed	3 / 16 (18.75%)	1 / 3 (33.33%)	4 / 19 (21.05%)
occurrences (all)	3	1	4
Osteoporosis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 3 (33.33%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Pain in extremity			
subjects affected / exposed	0 / 16 (0.00%)	1 / 3 (33.33%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Bronchitis viral			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Conjunctivitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Cytomegalovirus viraemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Ear infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Escherichia urinary tract infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Gastroenteritis			
subjects affected / exposed	1 / 16 (6.25%)	1 / 3 (33.33%)	2 / 19 (10.53%)
occurrences (all)	1	1	2
Nasopharyngitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 3 (33.33%)	1 / 19 (5.26%)
occurrences (all)	0	2	2

Perinephric abscess			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Pneumonia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Pseudomonas infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Pyuria			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Rhinitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Upper respiratory tract infection			
subjects affected / exposed	1 / 16 (6.25%)	1 / 3 (33.33%)	2 / 19 (10.53%)
occurrences (all)	1	1	2
Urinary tract infection			
subjects affected / exposed	2 / 16 (12.50%)	0 / 3 (0.00%)	2 / 19 (10.53%)
occurrences (all)	4	0	4
Viraemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Dehydration			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Diabetes mellitus			
subjects affected / exposed	3 / 16 (18.75%)	0 / 3 (0.00%)	3 / 19 (15.79%)
occurrences (all)	3	0	3
Fluid overload			

subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Fluid retention			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Gout			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Hyperglycaemia			
subjects affected / exposed	4 / 16 (25.00%)	0 / 3 (0.00%)	4 / 19 (21.05%)
occurrences (all)	5	0	5
Hyperkalaemia			
subjects affected / exposed	5 / 16 (31.25%)	2 / 3 (66.67%)	7 / 19 (36.84%)
occurrences (all)	6	4	10
Hyperphosphataemia			
subjects affected / exposed	2 / 16 (12.50%)	0 / 3 (0.00%)	2 / 19 (10.53%)
occurrences (all)	2	0	2
Hypertriglyceridaemia			
subjects affected / exposed	4 / 16 (25.00%)	3 / 3 (100.00%)	7 / 19 (36.84%)
occurrences (all)	5	3	8
Hypoalbuminaemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Hypocalcaemia			
subjects affected / exposed	4 / 16 (25.00%)	0 / 3 (0.00%)	4 / 19 (21.05%)
occurrences (all)	5	0	5
Hypoglycaemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Hypokalaemia			
subjects affected / exposed	3 / 16 (18.75%)	0 / 3 (0.00%)	3 / 19 (15.79%)
occurrences (all)	3	0	3
Hypomagnesaemia			
subjects affected / exposed	6 / 16 (37.50%)	3 / 3 (100.00%)	9 / 19 (47.37%)
occurrences (all)	8	5	13
Hyponatraemia			

subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Hypophosphataemia			
subjects affected / exposed	3 / 16 (18.75%)	1 / 3 (33.33%)	4 / 19 (21.05%)
occurrences (all)	3	1	4
Iron deficiency			
subjects affected / exposed	0 / 16 (0.00%)	1 / 3 (33.33%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Magnesium deficiency			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Metabolic acidosis			
subjects affected / exposed	5 / 16 (31.25%)	2 / 3 (66.67%)	7 / 19 (36.84%)
occurrences (all)	5	2	7
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Vitamin D deficiency			
subjects affected / exposed	1 / 16 (6.25%)	0 / 3 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 March 2017	- Information was added to the Risk/Benefit section. 2 patients had shown signs of serum sickness in an IdeS study in patients diagnosed with asymptomatic antibodymediated thrombotic thrombocytopenic purpura with low ADAMTS 13 activity. The 2 patients completed the study which was thereafter closed. 27 patients without concomitant immunosuppressive therapy have previously been given IdeS without signs of serum sickness why the sponsor cannot rule out that the underlying decease was a factor in the development of the signs. Based on all available safety information from non-clinical and clinical studies it was concluded that the overall benefit/risk profile of IdeS still appeared favorable. - Physical examination was added to the last visit (visit 12) - Biopsies were added at visit 2 (deceased donor and patient) and visit 12 (patient). Reason: Follow up on suspected rejections and other renal tissue damages are important information in the evaluation of kidney status. - The rescreening procedure was clarified - Exlusion criteria regarding HBV, HCV, CMV or EBV infections were updated to allow test results within 6 months. It was not determined feasible to await screening results given the turnaround time of the information for patients transplaned with a deceased donor kidney. - The exclusion criterion regarding thrombotic episodes was updated to include also patients with a history of a diagnosed hypercoagulable condition whithout a history of thrombotic episodes. - The protocol was updated to allow splitting the IVIg dose into 2 doses if deemed necessary by the investigator as the recommended dose may be too large to administer at one time for most patients. - The doses of methylprednisolone and loratadin were added. This information was inadvertently omitted in the previous version. In addition some clarifications to procedures (incl. updating of time windows) and editorial changes were done. This amendment was done to the US protocol
09 May 2017	This amendment was done to the French protocol. Please refer to the amendment dated 20-Mar-2017 for information on updates.
14 June 2017	This amendment was done to the Swedish protocol. Please refer to the amendment dated 20-Mar-2017 for information on updates.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported