Clinical trial results:
A Phase II Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Efficacy of Intravenous IdeS after Administration of Ascending Doses in Chronic Kidney Disease Patients

Summary

EudraCT number	2013-005417-13
Trial protocol	SE
Global end of trial date	13 February 2015

Results information

Result version number	v1
This version publication date	18 April 2019
First version publication date	18 April 2019

Trial information

Trial identification

Sponsor protocol code	13-HMedIdeS-02

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02224820
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, clinicalstudyinfo@hansabiopharma.com
Scientific contact	Clinical Trials Information, 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	25 June 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 February 2015
Global end of trial reached?	Yes
Global end of trial date	13 February 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To find an IdeS dosing scheme which in the majority of the patients results in HLA antibody levels which are acceptable for transplantation. This will be measured as an MFI less than 1100 as measured in a single antigen bead (SAB) assay, within 24 hours from dosing

Protection of trial subjects:

Dosing was staggered with at least 7 days between patients in the group. The investigator decided the number of doses for each patient (max 2) and the decision was based on both safety and efficacy.
There were to be at least 14 days between dosing of the first patient in a higher dose group and dosing of the last patient in the previous dose group.
Dose escalation to a higher group was to be based on safety and efficacy evaluation of previous dose groups. Proceeding to a higher dose group always required that the previous full group (2-4 patients) was evaluated by the Data Monitoring Committee (DMC).

Background therapy:

Patients were premedicated with the corticosteroid methylprednisolone (Solu-Medrol®) and the antihistamine loratadine (Loratadin®) before IdeS infusions.
All patients received prophylactic antibiotics until their serum total IgG was 3 g/L or more.

Evidence for comparator: -

Actual start date of recruitment	10 June 2014
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: 8
Worldwide total number of subjects	8
EEA total number of subjects	8

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)	7
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was performed at Uppsala University Hospital in Sweden. Enrolled patients were diagnosed with Chronic Kidney Disease in dialysis and on the waiting list for a kidney transplant.
Patients were recruited between 10-Jun-2014 and 12-Dec-2014.

Pre-assignment

Screening details:

In total, 10 patients were assessed for eligibility. Eight (8) patients were enrolled and started treatment.

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	Group 1

Arm description:

0.12 mg/kg of IdeS once or twice within 48 hours

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

Dosage and administration details:

0.12 mg/kg milligram(s)/kilogram intravenously once or twice within 48 hours

Arm title	Group 2

Arm description:

0.25 mg/kg IdeS once or twice within 48 hours

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

Dosage and administration details:

0.25 mg/kg milligram(s)/kilogram intravenously once or twice within 48 hours

Number of subjects in period 1	Group 1	Group 2
Started	3	5
Completed	3	4
Not completed	0	1
Adverse event, non-fatal	-	1

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	8	8	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn - gestational age < 37 wk	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)	7	7	
From 65 to 84 years	1	1	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	50.5		
standard deviation	± 11.9	-	
Gender categorical Units: Subjects			
Male	3	3	
Female	5	5	
Weight Units: kilogram(s)			
arithmetic mean	74.5		
standard deviation	± 14.5	-	
Height Units: cm			
arithmetic mean	172.3		
standard deviation	± 9.7	-	

Subject analysis sets

Subject analysis set title	SAS
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety analysis set (SAS) included all patients that received any amount of study medication.

Subject analysis set title	FAS
Subject analysis set type	Full analysis

Subject analysis set description:

The full analysis set (FAS) consisted of all patients in the safety analysis set (SAS) who had a measurement of anti-HLA antibody level within 24 hours from dosing.
The FAS was used for presenting efficacy data.

Subject analysis set title	PPS
Subject analysis set type	Per protocol

Subject analysis set description:

The per protocol set (PPS) was intended to consist of all patients who received at least one dose of IdeS and had evaluable PK data, and was determined by the PK analyst. The full criteria for the PPS, regarding protocol deviations that warranted exclusions, was specified when all data on protocol violations/deviations were available.
The PPS was used for the pharmacokinetics (PK) and pharmacodyamics (PD) evaluations.

Reporting group values	SAS	FAS	PPS
Number of subjects	8	8	7
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn - gestational age < 37 wk	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)	7	7	6
From 65 to 84 years	1	1	1
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	50.5	50.5	51.1
standard deviation	± 11.9	± 11.9	± 12.7
Gender categorical Units: Subjects			
Male	3	3	3
Female	5	5	4
Weight Units: kilogram(s)			
arithmetic mean	74.5	74.5	71.4
standard deviation	± 14.5	± 14.5	± 12.5
Height Units: cm			
arithmetic mean	172.3	172.3	172.7
standard deviation	± 9.7	± 9.7	± 10.4

End points

End points reporting groups

Reporting group title	Group 1
Reporting group description:	
0.12 mg/kg of IdeS once or twice within 48 hours	
Reporting group title	Group 2
Reporting group description:	
0.25 mg/kg IdeS once or twice within 48 hours	
Subject analysis set title	SAS
Subject analysis set type	Safety analysis
Subject analysis set description:	
The safety analysis set (SAS) included all patients that received any amount of study medication.	
Subject analysis set title	FAS
Subject analysis set type	Full analysis
Subject analysis set description:	
The full analysis set (FAS) consisted of all patients in the safety analysis set (SAS) who had a measurement of anti-HLA antibody level within 24 hours from dosing. The FAS was used for presenting efficacy data.	
Subject analysis set title	PPS
Subject analysis set type	Per protocol
Subject analysis set description:	
The per protocol set (PPS) was intended to consist of all patients who received at least one dose of IdeS and had evaluable PK data, and was determined by the PK analyst. The full criteria for the PPS, regarding protocol deviations that warranted exclusions, was specified when all data on protocol violations/deviations were available. The PPS was used for the pharmacokinetics (PK) and pharmacodyamics (PD) evaluations.	

Primary: Mean fluorescent intensity of less than 1100 within 24 hours

End point title	Mean fluorescent intensity of less than 1100 within 24 hours[1]
End point description:	
The primary endpoint in the study was efficacy defined as the IdeS dosing scheme resulting in HLA antibody levels acceptable for transplantation. It was analyzed using serial analysis for antibodies. Results from the single antigen bead (SAB) HLA assay were combined with results from the complement fixating anti-HLA assay (C1q). The acceptance criterion for transplantation was defined as a mean fluorescence intensity (MFI) of <1100, within 24 h from dosing. A responder was defined as a patient for whom all pre-dose MFI values that were >1100 had the 90th percentile MFI <1100 within 24 h after IdeS treatment.	
End point type	Primary
End point timeframe:	
From IdeS dosing up to 24 h after IdeS administration: (i) single antigen bead (SAB) HLA: pre-dose, 1h, 2h, 6h, and 24h post-dose (ii) complementing fixating anti-HLA assay (C1q): pre-dose, 1h and 24 h post-dose	

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	Group 1	Group 2	FAS	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	3	5[2]	8[3]	
Units: Number of responders				
SAB HLA	0	3	3	
C1q	3	3	6	

Notes:

[2] - The C1q analysis íncluded 3 patients only due to high background for 1 p and dose interrupted for 1p

[3] - The C1q analysis íncluded 6 patients only due to high background for 1 p and dose interrupted for 1p

Statistical analyses

No statistical analyses for this end point

Secondary: Safety

End point title	Safety

End point description:

A summary of repored Adverse Events (AE)s from the study is included.
Please refer to the "Adverse Event" section for details on the specific AEs reported from this clinical study.

End point type	Secondary

End point timeframe:

AEs were collected from the time-point the patient was admitted to the clinical trial unit and throughout the study including the follow-up period (i.e. up to day 64).

End point values	Group 1	Group 2	SAS	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	3	5	8	
Units: Number of AEs				
Adverse Events	23	53	76	
Related Adverse Events	8	19	27	
Serious Adverse Events	1	4	5	

Statistical analyses

No statistical analyses for this end point

Secondary: PK profile of IdeS: Cmax

End point title	PK profile of IdeS: Cmax

End point description:

Cmax = Maximum observed plasma concentration of IdeS following dosing (non-compartmental analysis)

End point type	Secondary

End point timeframe:

Immediately before IdeS dosing up to 21 days

End point values	Group 1	Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	4		
Units: µg/mL				
arithmetic mean (standard deviation)	2.24 (± 0.08)	6.39 (± 1.02)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK profile of IdeS: tmax

End point title	PK profile of IdeS: tmax
End point description:	
Tmax = Time of occurrence of Cmax (non-compartmental analysis)	
End point type	Secondary
End point timeframe:	
Immediately before IdeS dosing up to 21 days	

End point values	Group 1	Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	4		
Units: hour				
arithmetic mean (standard deviation)	0.92 (± 0.93)	0.94 (± 0.77)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK profile of IdeS: AUC

End point title	PK profile of IdeS: AUC
End point description:	
AUC = Area under the plasma concentration vs time curve from time 0 to infinity (non-compartmental analysis)	
End point type	Secondary
End point timeframe:	
Immediately before IdeS dosing up to day 21	

End point values	Group 1	Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	4		
Units: h x µg/mL				
arithmetic mean (standard deviation)	110 (± 27)	487 (± 30)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK profile of IdeS: t1/2

End point title	PK profile of IdeS: t1/2

End point description:

t1/2 = Terminal half-life (non-compartmental analysis)

End point type	Secondary

End point timeframe:

Up to day 21

End point values	Group 1	Group 2	PPS	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	3	4	7	
Units: hour				
arithmetic mean (standard deviation)	54 (± 7)	135 (± 111)	100 (± 90)	

Statistical analyses

No statistical analyses for this end point

Secondary: PK Profile of IdeS: CL

End point title	PK Profile of IdeS: CL

End point description:

CL = Clearance (non-compartmental analysis)

End point type	Secondary

End point timeframe:

Immediately before IdeS dosing up to 21 days

End point values	Group 1	Group 2	PPS	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	3	4	7	
Units: mL/h/Kg				
arithmetic mean (standard deviation)	1.14 (± 0.32)	0.66 (± 0.33)	0.86 (± 0.39)	

Statistical analyses

No statistical analyses for this end point

Secondary: PK Profile of IdeS: Vz

End point title	PK Profile of IdeS: Vz

End point description:

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

End point type	Secondary

End point timeframe:

Immediately berfore IdeS dosing up to 21 days

End point values	Group 1	Group 2	PPS	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	3	4	7	
Units: L/kg				
arithmetic mean (standard deviation)	0.088 (± 0.015)	0.092 (± 0.019)	0.090 (± 0.016)	

Statistical analyses

No statistical analyses for this end point

Secondary: PD Profile of IdeS: Cleavage of IgG

End point title	PD Profile of IdeS: Cleavage of IgG

End point description:

The efficacy of IdeS treatment on IgG was investigated using an enzyme-linked immunosorbent assay (ELISA) at different time-points after dosing. This assay determines the sum of intact IgG and single chain cleaved IgG (scIgG) in serum. In addition a turbimetirc assay and a qualitative sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) analysis were done (results not included).
The mean concentration of IgG at selected timepoints after dosing is presented to follow the progress of the IgG cleaving process.
Individual IgG concentrations at all time-points are listed in Appendix 16.2, List 16.2.6.7.

End point type	Secondary

End point timeframe:

1 dose: pre-dose, 14min, 0.5, 1, 2, 4, 6, 8, 24, 48, 72h, 7, 14, 21, 28, and 64d after dosing
2 doses: 1st dose as above until 24h, then pre-2nd dose, 14min, 0.5, 1, 2, 4, 6, 8, 24, 48, 72h, 7, 14, 21, 28, and 64d after dosing

End point values	Group 1	Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	4[4]		
Units: microgram(s)/millilitre				
arithmetic mean (full range (min-max))				
Concentration pre-1st dose	11000 (6800 to 13800)	9300 (7900 to 10700)		
Concentration at 6h (1st dose)	2200 (1000 to 4100)	130 (37 to 300)		
Concentration at 24h (1st dose)	610 (350 to 940)	23 (5 to 41)		
Concentration at 6h (2nd dose)	43 (14 to 58)	13 (5 to 25)		
Concentration at 24 h (2nd dose)	21 (14 to 26)	5 (5 to 5)		

Notes:

[4] - Please observe that 2 patients only received 2 doses

Attachments (see zip file)	IgG PD conc./cleavage/Appendix 16.2.6.7_IgG/Appendix

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogencity of IdeS: Anti-drug antibodies (ADAs)

End point title	Immunogencity of IdeS: Anti-drug antibodies (ADAs)

End point description:

The serum concentration of ant-IdeS IgG was measured.
The number of patients with anti-IdeS IgG present at screening and 64 days after IdeS dosing are presented together with the number of patients that had a peak concentration of anti-IdeS IgG lon day 14 after dosing.
Individual anti-IdeS IgG concentrations at all sampling time-points are listed in Appendix 16.2, List 16.2.6.6.

End point type	Secondary

End point timeframe:

1 dose: Screening, pre-dose, 24h after dose, 5d, 7d, 14d, 21d, 28d, and 64 d after dose
2 doses: Screening, pre-dose, 24h after 1st dose, 24 h after 2nd dose, 5d, 7d, 14d, 21d, 28d, and 64d after dose

End point values	Group 1	Group 2	PPS	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	3	4	7	
Units: Number of patients				
ADAs at Screening	3	4	7	
ADAs at Day 64	3	4	7	
Peak concentration of ADAs at Day 14	2	4	6	

Attachments (see zip file)	ADA; IgG/Appendix 16.2.6.6_ImmunoCAP_IgG/Appendix

Statistical analyses

No statistical analyses for this end point

Secondary: Reduction of PRA levels in cytotoxic sera screen after IdeS treatment

End point title	Reduction of PRA levels in cytotoxic sera screen after IdeS treatment

End point description:

Samples were analyzed for complement dependent cytotoxicity (CDC) against a panel of T- and B-cells to determine the level of panel reactivity (PRA) in percentage (%).
Number of patients with a reduction in T/B PRA (%) 1 hour after IdeS dosing is presented.

End point type	Secondary

End point timeframe:

1 dose: pre-dose, 1h, 2h, 6h, 24h, 7d, 14d, 28d, and 64d after dosing
2 doses: pre-dose, 1h, 2h, 6h, 24hafter first dose, then 1h, 2h, 6h, 24h, 7d, 14d, 28d, and 64d after second dosing

End point values	Group 1	Group 2	PPS	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	3	4[5]	7[6]	
Units: Number of patients				
Reduced T/B PRA 1 h after 1st dose	3	4	7	
Reduced T/B PRA 1 h after 2nd dose	3	2	5	

Notes:

[5] - Please note that 2 patients only had 2 doses of IdeS

[6] - Please note that 5 patients only had 2 doses of IdeS

Statistical analyses

No statistical analyses for this end point

Secondary: PK profile of IdeS: Alpha t1/2 and Beta t1/2

End point title	PK profile of IdeS: Alpha t1/2 and Beta t1/2

End point description:

2-compartment analysis
Alpha t1/2 = half-life for the distribution phase
Beta t1/2 = half-life for the elimination phase
Harmonic mean values were calculated for alpha and beta half-lives as ln2/mean alpha and ln2/mean beta, respectively.

End point type	Secondary

End point timeframe:

Immediately before IdeS dosing up to 21 days

End point values	Group 1	Group 2	PPS	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	3[7]	4[8]	7[9]	
Units: hour				
arithmetic mean (full range (min-max))				
Alpha t1/2	4.03 (2.38 to 7.77)	6.26 (3.22 to 11.2)	5.06 (2.38 to 11.2)	
Beta t1/2	53.7 (47.2 to 59.8)	88.9 (49.2 to 301)	69.3 (47.2 to 301)	

Notes:

[7] - Harmonic means are presented rather than arithmetic means

[8] - Harmonic means are presented rather than arithmetic means

[9] - Harmonic means are presented rather than arithmetic means

Statistical analyses

No statistical analyses for this end point

Secondary: PK profile of IdeS: Vss

End point title	PK profile of IdeS: Vss

End point description:

Vss = Volume of distribution during steady state (non-compartmental analysis)

End point type	Secondary

End point timeframe:

Immediately before IdeS dosing up to 21 days

End point values	Group 1	Group 2	PPS	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	3	4	7	
Units: L/kg				
arithmetic mean (standard deviation)	0.083 (± 0.014)	0.084 (± 0.019)	0.083 (± 0.015)	

Statistical analyses

No statistical analyses for this end point

Secondary: Results in FACS crossmatch test against available donor cells

End point title	Results in FACS crossmatch test against available donor cells

End point description:

Samples were analyzed for reactivity against T and B lymphocytes from available donors using flow-cytometry.
FACS crossmatch test was performed only for the one patient that was kidney transplanted during the course of the study.

End point type	Secondary

End point timeframe:

6h and 24h after each dose of IdeS

End point values	Group 1	Group 2	PPS	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	1[10]	0[11]	1[12]	
Units: Number of patients				
Positive T and B crossmatch 6h after 1st dose	1		1	
Negative T and B crossmatch 6h after 1st dose	0		0	
Positive T and B crossmatch 24h after 1st dose	1		1	
Negative T and B crossmatch 24h after 1st dose	0		0	
Positive T and B crossmatch 6h after 2nd dose	0		0	
Negative T and B crossmatch 6h after 2nd dose	1		1	
Positive T and B crossmatch 24h after 2nd dose	0		0	
Negative T and B crossmatch 24h after 2nd dose	1		1	

Notes:

[10] - 1 patient only was transplanted. There were no available donor cells for the other patients.

[11] - There were no available donor cells for the other patients.

[12] - 1 patient only was transplanted. There were no available donor cells for the other patients.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From the time of admission until last visit, 64 days after treatment	
Adverse event reporting additional description:	
Adverse events included all clinical laboratory tests, vital signs and ECGs jugded as clinically significant.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups	
Reporting group title	Group 1
Reporting group description:	
0.12 mg/kg IdeS once or twice within 48 hours	
Reporting group title	Group 2
Reporting group description:	
0.25 mg/kg IdeS once or twice in 48 hours	
Reporting group title	Safety analysis set
Reporting group description:	
The safety analysis set (SAS) included all patients that received any amount of study medication.	

Serious adverse events	Group 1	Group 2	Safety analysis set
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)	3 / 5 (60.00%)	4 / 8 (50.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Respiratory, thoracic and mediastinal disorders			
Increased bronchial secretion			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	1 / 8 (12.50%)
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			
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Upper respiratory tract infection			

subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 5 (20.00%)	2 / 8 (25.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	2 / 2
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	Group 1	Group 2	Safety analysis set
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	5 / 5 (100.00%)	8 / 8 (100.00%)
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 3 (33.33%)	1 / 5 (20.00%)	2 / 8 (25.00%)
occurrences (all)	1	1	2
Haematoma			
subjects affected / exposed	1 / 3 (33.33%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Feeling cold			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Feeling hot			

subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Infusion site pain			
subjects affected / exposed	2 / 3 (66.67%)	0 / 5 (0.00%)	2 / 8 (25.00%)
occurrences (all)	2	0	2
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 5 (40.00%)	2 / 8 (25.00%)
occurrences (all)	0	2	2
Immune system disorders			
Kidney transplant rejection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Anxiety			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	1 / 8 (12.50%)
occurrences (all)	1	1	1
Insomnia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 3 (33.33%)	1 / 5 (20.00%)	2 / 8 (25.00%)
occurrences (all)	1	1	2
Aspartate aminotransferas increased			
subjects affected / exposed	1 / 3 (33.33%)	1 / 5 (20.00%)	2 / 8 (25.00%)
occurrences (all)	1	2	3
Blood phosphorus increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1

C-reactive protein increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Donor specific antibody present			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Weight increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 3 (33.33%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Infusion related reaction			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 3 (33.33%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Sinus tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Nervous system disorders			
Dizziness postural			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	1 / 8 (12.50%)
occurrences (all)	0	2	2
Headache			
subjects affected / exposed	1 / 3 (33.33%)	1 / 5 (20.00%)	2 / 8 (25.00%)
occurrences (all)	1	2	3
Dysgeuisa			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Tremor			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	1 / 8 (12.50%)
occurrences (all)	0	1	1

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 5 (40.00%)	2 / 8 (25.00%)
occurrences (all)	0	2	2
Leucocytosis			
subjects affected / exposed	1 / 3 (33.33%)	1 / 5 (20.00%)	2 / 8 (25.00%)
occurrences (all)	1	1	2
Leukopenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Eye disorders			
Scleral haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Visual impairment			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	2 / 3 (66.67%)	0 / 5 (0.00%)	2 / 8 (25.00%)
occurrences (all)	2	0	2
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Dyspepsia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	2 / 5 (40.00%)	2 / 8 (25.00%)
occurrences (all)	0	2	2
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 3 (33.33%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1

Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Infections and infestations			
Herpex simplex infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Clostridium difficile infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Hordeolum			
subjects affected / exposed	1 / 3 (33.33%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Nasopharyngitis			
subjects affected / exposed	1 / 3 (33.33%)	1 / 5 (20.00%)	2 / 8 (25.00%)
occurrences (all)	1	1	2
Influenza			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Oral candidas			
subjects affected / exposed	0 / 3 (0.00%)	2 / 5 (40.00%)	2 / 8 (25.00%)
occurrences (all)	0	2	2
Tonsillitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Metabolism and nutrition disorders			
Hyperkalaemia			

subjects affected / exposed	1 / 3 (33.33%)	1 / 5 (20.00%)	2 / 8 (25.00%)
occurrences (all)	2	2	4
Hyponatraemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Iron deficiency			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Hyperglycaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1

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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/28767349