Clinical trial results:
A Phase 2 Pilot, Multicenter, Single Arm Study to Evaluate the Efficacy, Safety, Tolerability, and Pharmacokinetics of GSK1070806 plus Standard of Care for the Prevention of Delayed Graft Function in Adult Subjects After Renal Transplantation

Summary

EudraCT number	2015-002812-33
Trial protocol	GB ES
Global end of trial date	06 March 2018

Results information

Result version number	v1
This version publication date	15 April 2018
First version publication date	15 April 2018

Trial information

Trial identification

Sponsor protocol code	204824

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom,
Public contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,

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	Interim
Date of interim/final analysis	23 June 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 March 2017
Global end of trial reached?	Yes
Global end of trial date	06 March 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess the frequency of delayed graft function (DGF) in donation after circulatory death (DCD) renal transplant recipients treated with GSK1070806

Protection of trial subjects:

This study uses standard of care (SoC) aligning study tasks with SoC tasks and visit schedule to mitigate participant study-burden. Additionally, participants are required to use additional anti-infective protocols due to the potential of GSK1070806 to increase immunosuppression.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 August 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	United Kingdom: 6
Worldwide total number of subjects	7
EEA total number of subjects	7

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)	5
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was a single arm study to evaluate the efficacy, safety, tolerability, and pharmacokinetics (PK) of GSK1070806 plus standard of care (SOC) for the prevention of delayed graft function in adult participants after renal transplantation. The results presented are based on the Interim Analysis.

Pre-assignment

Screening details:

A total of 7 participants were screened for the study, and all of them received study treatment. The study enrolled participants in 4 centers across 2 countries (Spain and United Kingdom).

Period 1

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

Arms

Arm title	GSK1070806 3 mg/kg IV

Arm description:

Participants received a single dose of 3 milligram per kilogram (mg/kg) intravenous (IV) infusion of GSK1070806 administered prior to kidney allograft reperfusion. Participants also received a combination immunosuppression comprised of basiliximab; mycophenolate mofetil (MMF) or aziothioprine; tacrolimus; and corticosteroids based on the clinical judgment of the investigator.

Arm type	Experimental
Investigational medicinal product name	GSK1070806
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received a single dose of 3 milligram per kilogram (mg/kg) intravenous (IV) infusion of GSK1070806 administered prior to kidney allograft reperfusion.

Number of subjects in period 1	GSK1070806 3 mg/kg IV
Started	7
Completed	6
Not completed	1
Consent withdrawn by subject	1

Baseline characteristics

Reporting groups	
Reporting group title	GSK1070806 3 mg/kg IV

Reporting group description:

Participants received a single dose of 3 milligram per kilogram (mg/kg) intravenous (IV) infusion of GSK1070806 administered prior to kidney allograft reperfusion. Participants also received a combination immunosuppression comprised of basiliximab; mycophenolate mofetil (MMF) or aziothioprine; tacrolimus; and corticosteroids based on the clinical judgment of the investigator.

Reporting group values	GSK1070806 3 mg/kg IV	Total	
Number of subjects	7	7	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 58.7 ± 13.46	 -	
Gender categorical Units: Subjects			
Female Male	0 7	0 7	
Race/Ethnicity, Customized Units: Subjects			
White-White/Caucasian/European Heritage	7	7	

End points

End points reporting groups

Reporting group title	GSK1070806 3 mg/kg IV

Reporting group description:

Participants received a single dose of 3 milligram per kilogram (mg/kg) intravenous (IV) infusion of GSK1070806 administered prior to kidney allograft reperfusion. Participants also received a combination immunosuppression comprised of basiliximab; mycophenolate mofetil (MMF) or aziothioprine; tacrolimus; and corticosteroids based on the clinical judgment of the investigator.

Primary: Number of participants requiring dialysis during the first 7 days post transplant

End point title	Number of participants requiring dialysis during the first 7 days post transplant[1]

End point description:

The requirement of dialysis (except as needed for hyperkalaemia during the first 24 hours [hrs]) were used to assess the frequency of delayed graft function (DGF) in donation after circulatory death (DCD) renal transplant recipients treated with GSK1070806. For DGF related endpoints, the 'Analysis Population' (AP) is defined as participants in the 'All Subjects' Population who have been declared to have DGF or have reached 7 days. For other endpoints, the AP is defined as participants having Baseline and at least one post-Baseline assessment.

End point type	Primary

End point timeframe:

Up to Day 7

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: There are no statistical data to report.

End point values	GSK1070806 3 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	7[2]			
Units: Participants				
Participants	5			

Notes:

[2] - AP Population

Statistical analyses

No statistical analyses for this end point

Secondary: Serum creatinine at Baseline and over time post transplant

End point title	Serum creatinine at Baseline and over time post transplant

End point description:

Blood samples were to be collected to measure serum creatinine at the indicated timepoints to assess graft function in DCD renal transplant recipients treated with GSK1070806. Baseline value was the latest pre-dose assessment value. Data will be posted by July 2018.

End point type	Secondary

End point timeframe:

Up to 12 months

End point values	GSK1070806 3 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[3]			
Units: Micromoles per liter				
arithmetic mean (standard deviation)	()			

Notes:

[3] - AP Population

Statistical analyses

No statistical analyses for this end point

Secondary: Urine volume at Baseline and over time post transplant

End point title	Urine volume at Baseline and over time post transplant

End point description:

Urine volume at Baseline and over time post transplant was to be measured to assess graft function in DCD renal transplant recipients treated with GSK1070806. Baseline value was the latest pre-dose assessment value. All Subjects Population comprised of participants who received the dose of study medication. Data will be posted by July 2018.

End point type	Secondary

End point timeframe:

Up to Day 7

End point values	GSK1070806 3 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[4]			
Units: Milliliter				
arithmetic mean (standard deviation)	()			

Notes:

[4] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants in the first 7 days with: primary non function, functional DGF, intermediate graft function, immediate graft function

End point title	Number of participants in the first 7 days with: primary non function, functional DGF, intermediate graft function, immediate graft function

End point description:

Number of participants in the first 7 days with primary non function, functional DGF, intermediate graft function and immediate graft function were to be evaluated to access graft function in DCD renal transplant recipients treated with GSK1070806. Data will be posted by July 2018.

End point type	Secondary

End point timeframe:

Up to Day 7

End point values	GSK1070806 3 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[5]			
Units: Participants				

Notes:

[5] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with episodes of biopsy-proven acute rejection

End point title	Number of participants with episodes of biopsy-proven acute rejection

End point description:

Number of participants with episodes of biopsy-proven acute rejection were to be evaluated to assess the effect of GSK1070806 on acute rejection risk, and rejection/Pharmacodynamic (PD) biomarkers. Data will be posted by July 2018.

End point type	Secondary

End point timeframe:

Up to 12 months

End point values	GSK1070806 3 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[6]			
Units: Participants				

Notes:

[6] - AP Population

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Interferon gamma-induced Protein 10 (IP-10) and Serum Monokine Induced Gamma interferon (Mig) levels at Baseline and over time post transplant

End point title	Serum Interferon gamma-induced Protein 10 (IP-10) and Serum Monokine Induced Gamma interferon (Mig) levels at Baseline and over time post transplant

End point description:

The interferon-gamma -inducible chemokine IP10 and the interferon-gamma -inducible chemokine Mig have been identified as an early predictive marker of antibody-mediated kidney graft rejection. Baseline value was the latest pre-dose assessment value. Data will be posted by July 2018.

End point type	Secondary

End point timeframe:

Up to 12 months

End point values	GSK1070806 3 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[7]			
Units: Participants				

Notes:

[7] - AP Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with dialysis events in the first 30 days post-transplant

End point title	Number of participants with dialysis events in the first 30 days post-transplant

End point description:

Number of participants with dialysis events in the first 30 days post transplant was evaluated to assess the effect of GSK1070806 on dialysis dependency and graft survival.

End point type	Secondary

End point timeframe:

Up to 30 days

End point values	GSK1070806 3 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	7[8]			
Units: Participants				
Participants	5			

Notes:

[8] - AP Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who are dialysis independent at visits up to 12 months post-transplant

End point title	Number of participants who are dialysis independent at visits up to 12 months post-transplant

End point description:

Number of participants who are dialysis independent at visits up to 12 months post transplant was to be evaluated to assess the effect of GSK1070806 on dialysis dependency and graft survival. Data will be posted by July 2018.

End point type	Secondary

End point timeframe:

Up to 12 months

End point values	GSK1070806 3 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[9]			
Units: Participants				

Notes:

[9] - AP Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with adverse event (AE) and serious adverse event (SAE)

End point title	Number of participants with adverse event (AE) and serious adverse event (SAE)

End point description:

AE is any untoward medical occurrence in a participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Any untoward event resulting in death, life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, congenital anomaly/birth defect or any other situation according to medical or scientific judgment were categorized as SAE. Data will be posted by July 2018.

End point type	Secondary

End point timeframe:

Up to 12 months

End point values	GSK1070806 3 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	7[10]			
Units: Participants				
Any AE	7			
Any SAE	6			

Notes:

[10] - AP Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants having any emergent hematology results of Potential Clinical Importance

End point title	Number of participants having any emergent hematology results of Potential Clinical Importance

End point description:

Hematology parameters included platelet counts, red blood cells (RBC) count, hemoglobin, hematocrit, mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), white blood cells (WBC) count with differential neutrophils, lymphocytes, monocytes, eosinophils, and basophils. Number of participants with potential clinical importance (high or low) results in any of these parameters are presented.

End point type	Secondary

End point timeframe:

Up to 12 months

End point values	GSK1070806 3 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	6[11]			
Units: Participants				
High	2			
Low	6			

Notes:

[11] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants having any emergent clinical chemistry results of Potential Clinical Importance

End point title	Number of participants having any emergent clinical chemistry results of Potential Clinical Importance

End point description:

Clinical chemistry parameters included analysis of urea, creatinine, glucose, potassium, sodium, calcium, Gamma-Glutamyl Transferase (GGT), alanine aminotransferase (ALT), alkaline phosphatise, bilirubin, total protein and albumin levels. Number of participants with potential clinical importance (high or low) results in any of these parameters are presented.

End point type	Secondary

End point timeframe:

Up to 12 months

End point values	GSK1070806 3 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	6[12]			
Units: Participants				
High	4			
Low	6			

Notes:

[12] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants having any abnormality of Potential Clinical Importance of vital signs results

End point title	Number of participants having any abnormality of Potential Clinical Importance of vital signs results

End point description:

Vital signs parameters included analysis of systolic and diastolic blood pressure, heart rate and body temperature. Number of participants with any abnormality of potential clinical importance (high or low) in any of these vitals signs are presented.

End point type	Secondary

End point timeframe:

Up to 12 months

End point values	GSK1070806 3 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	7[13]			
Units: Participants				
High	4			
Low	3			

Notes:

[13] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants having infections

End point title	Number of participants having infections

End point description:

Number of participants having infections was to be summarized. Data will be posted by July 2018.

End point type	Secondary

End point timeframe:

Up to 12 months

End point values	GSK1070806 3 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[14]			
Units: Participants				

Notes:

[14] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Secondary: Serum concentrations of GSK1070806

End point title	Serum concentrations of GSK1070806

End point description:

Serial blood samples were to be collected to evaluate PK of GSK1070806 at pre-dose, 0.75 hours, 4-8 hours, 24 hours, 168 hours (or at discharge) after kidney reperfusion, Day 30, Day 90, 6 and 12 months. PK Population included participants in the 'All Subjects' Population for whom a serum PK sample is obtained and analyzed for GSK1070806. Data will be posted by July 2018.

End point type	Secondary

End point timeframe:

Pre-dose, 0.75 hours, 4-8 hours, 24 hours, 168 hours (or at discharge) after kidney reperfusion, Day 30, Day 90, 6 and 12 months

End point values	GSK1070806 3 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[15]			
Units: Nanograms per milliliter				
arithmetic mean (standard deviation)	()			

Notes:

[15] - PK Population

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum plasma concentration (Cmax) of GSK1070806

End point title	Maximum plasma concentration (Cmax) of GSK1070806

End point description:

Serial blood samples were collected to evaluate PK of GSK1070806 at pre-dose, 0.75 hours, 4-8 hours, 24 hours, 168 hours (or at discharge) after kidney reperfusion, Day 30, Day 90, 6 and 12 months. Data will be posted by July 2018.

End point type	Secondary

End point timeframe:

Pre-dose, 0.75 hours, 4-8 hours, 24 hours, 168 hours (or at discharge) after kidney reperfusion, Day 30, Day 90, 6 and 12 months

End point values	GSK1070806 3 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[16]			
Units: Micrograms per milliliter				
geometric mean (geometric coefficient of variation)	()			

Notes:

[16] - PK Population

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the plasma concentration time curve (AUC) from time 0 to 168 hours (AUC[0-168]) and AUC from time 0 to 672 hours (AUC[0-672]) of GSK1070806

End point title	Area under the plasma concentration time curve (AUC) from time 0 to 168 hours (AUC[0-168]) and AUC from time 0 to 672 hours (AUC[0-672]) of GSK1070806

End point description:

Blood samples were to be collected to evaluate PK of GSK1070806 at pre-dose, 0.75 hours, 4-8 hours, 24 hours, 168 hours (or at discharge) after kidney reperfusion, Day 30, Day 90, 6 and 12 months. Data will be posted by July 2018.

End point type	Secondary

End point timeframe:

Pre-dose, 0.75 hours, 4-8 hours, 24 hours, 168 hours (or at discharge) after kidney reperfusion, Day 30, Day 90, 6 and 12 months

End point values	GSK1070806 3 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[17]			
Units: Hour*milligrams per milliliter				
geometric mean (geometric coefficient of variation)	()			

Notes:

[17] - PK Population

Statistical analyses

No statistical analyses for this end point

Secondary: Serum levels of free, total, and GSK1070806 bound Interleukin 18 (IL-18) levels at Baseline and over time post-transplant

End point title	Serum levels of free, total, and GSK1070806 bound Interleukin 18 (IL-18) levels at Baseline and over time post-transplant

End point description:

IL-18 is itself rapidly secreted from intracellular stores following inflammasome mediated-activation. The appearance of IL-18 marks the initiation of the inflammatory response leading to further injury. Baseline value was the latest pre-dose assessment value. Data will be posted by July 2018.

End point type	Secondary

End point timeframe:

Pre-dose, 0.75 hours, 4-8 hours, Day 1, Day 2, at discharge, Day 30, Day 90, 6 and 12 months

End point values	GSK1070806 3 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[18]			
Units: Picograms per milliliter				
arithmetic mean (standard deviation)	()			

Notes:

[18] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with positive result in anti-GSK1070806 antibodies (ADAs)

End point title	Number of participants with positive result in anti-GSK1070806 antibodies (ADAs)

End point description:

Serum samples were to be collected to test for the presence of antibodies against GSK1070806 at indicated time points. The presence of anti-GSK1070806 binding antibodies were to be assessed using a validated electrochemiluminescent (ECL) immunoassay. Data will be posted by July 2018.

End point type	Secondary

End point timeframe:

Pre-dose, Day 30, Day 90, 6 and 12 months

End point values	GSK1070806 3 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[19]			
Units: Participants				

Notes:

[19] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Secondary: ADA titer before and after GSK1070806 administration

End point title	ADA titer before and after GSK1070806 administration

End point description:

Serum samples were to be collected to test for the presence of antibodies against GSK1070806 at indicated time points. The presence of ADA titre was to be assessed using a validated ECL immunoassay. Data will be posted by July 2018.

End point type	Secondary

End point timeframe:

Pre-dose, Day 30, Day 90, 6 and 12 months

End point values	GSK1070806 3 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[20]			
Units: Nanograms per milliliter				
arithmetic mean (standard deviation)	()			

Notes:

[20] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

On-treatment serious adverse events (SAEs) and non-serious AEs were defined as events occurring from the first dose until 12 months.

Adverse event reporting additional description:

SAEs and Non-serious AEs were collected for All Subjects Population, comprised of participants who received the dose of study medication.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	2.0

Reporting groups

Reporting group title	GSK1070806 3 mg/kg IV

Reporting group description:

Participants received a single dose of 3 milligram per kilogram (mg/kg) intravenous (IV) infusion of GSK1070806 administered prior to kidney allograft reperfusion. Participants also received a combination immunosuppression comprised of basiliximab; mycophenolate mofetil (MMF) or aziothioprine; tacrolimus; and corticosteroids based on the clinical judgment of the investigator.

Serious adverse events	GSK1070806 3 mg/kg IV		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 7 (85.71%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Transplant dysfunction			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Ventricular fibrillation			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Ureteral stent removal			

subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Hernia			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Kidney transplant rejection			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Prostatomegaly			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Respiratory arrest			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			

Ureteric obstruction			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	GSK1070806 3 mg/kg IV		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 7 (100.00%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 7 (28.57%)		
occurrences (all)	2		
Surgical and medical procedures			
Renal transplant biopsy			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
General disorders and administration site conditions			
Catheter site haemorrhage			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Immune system disorders			
Kidney transplant rejection			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal			

disorders			
Wheezing			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Epistaxis			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Investigations			
Blood creatine increased			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Blood potassium decreased			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Blood sodium decreased			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Body temperature decreased			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Candida test positive			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Haemoglobin increased			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Wound dehiscence			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Wound evisceration			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Nervous system disorders			
Tremor			

subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 7 (57.14%)		
occurrences (all)	4		
Leukopenia			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Neutropenia			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Thrombocytopenia			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	2 / 7 (28.57%)		
occurrences (all)	2		
Constipation			
subjects affected / exposed	3 / 7 (42.86%)		
occurrences (all)	3		
Abdominal pain			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Dyspepsia			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Inguinal hernia			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Frequent bowel movements			

subjects affected / exposed occurrences (all) Lip swelling subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1 1 / 7 (14.29%) 1 1 / 7 (14.29%) 1		
Skin and subcutaneous tissue disorders Nail discolouration subjects affected / exposed occurrences (all) Decubitus ulcer subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all) Urticaria subjects affected / exposed occurrences (all)	 1 / 7 (14.29%) 1 1 / 7 (14.29%) 1 1 / 7 (14.29%) 2 1 / 7 (14.29%) 1		
Renal and urinary disorders Urinary retention subjects affected / exposed occurrences (all) Renal disorder subjects affected / exposed occurrences (all) Ureteric stenosis subjects affected / exposed occurrences (all) Urine - vancomycin resistent enterococcus positive subjects affected / exposed occurrences (all)	 2 / 7 (28.57%) 4 1 / 7 (14.29%) 1 1 / 7 (14.29%) 1 1 / 7 (14.29%) 1		
Infections and infestations			

Urinary tract infection subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 4			
Escherichia urinary tract infection subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1			
Influenza subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1			
Lower respiratory tract infection subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 2			
Postoperative wound infection subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1			
Pyelonephritis acute subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1			
Metabolism and nutrition disorders Acidosis subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 2			
Diabetes mellitus subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1			
Fluid overload subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1			
Hyperkalaemia subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1			
Hypoglycaemia subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1			
Hypoalbuminaemia				

subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	2		
Hypophosphataemia			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Hypomagnesaemia			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 February 2016	Amendment 01: Updates to clarify select safety criteria; completion of abbreviations table.
09 August 2016	Amendment 02: Eligibility Criteria: Allowance of second kidney transplant recipients for enrollment, removal of upper age limits, addition of definition for 'surgical damage' related to transplant organ retrieval; and clarifications to interim analysis and DCD categorization type.
22 March 2017	Amendment 03: Dose escalation: clarifications based on data from patients receiving 3 mg/kg dose to escalate to higher dose.
04 May 2017	Amendment 04: Eligibility Criteria: Additional exclusion criteria have been added to reduce the chance of enrolling participants with high cardiac risk profiles. Dose escalation: Based on emergent efficacy and pharmacokinetic-pharmacodynamics (PKPD) data, the number of participants required to be treated prior to a decision to escalate dose has been reduced, and stopping criteria following dose escalation have been amended.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported