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	v3
This version publication date	22 March 2019
First version publication date	15 April 2018
Version creation reason	

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	Final
Date of interim/final analysis	16 August 2018
Is this the analysis of the primary completion data?	No

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.

Pre-assignment

Screening details:

A total of 10 participants were screened for the study, and 7 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
Lost to follow-up	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			
All Participants	7	7	
Age continuous Units: years			
arithmetic mean	58.7		
standard deviation	± 13.46	-	
Gender categorical Units: Subjects			
Female	0	0	
Male	7	7	
Race/Ethnicity, Customized Units: Subjects			
White	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 hyperkalemia 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. 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. Statistical analysis was carried out using Bayesian methodology. The proportion of participants with DGF was 0.57, highest Posterior Density (HPD) 95% Credible interval (CI) (0.25,0.90). The posterior probability for the proportion of participants with DGF <30% was 0.07 (HPD 95% CI [0.00,1.00]). The posterior probability for the proportion of participants with DGF <50% was 0.34 (HPD 95% CI [0.00,1.00]).

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: Statistical details are presented in outcome measure description for this single arm endpoint.

End point values	GSK1070806 3 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	7[2]			
Units: Participants				
Participants	4			

Notes:

[2] - AP Population

Statistical analyses

No statistical analyses for this end point

Secondary: Serum creatinine at Baseline and Change from Baseline over time post transplant

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

End point description:

Blood samples were 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. Only those participants with data available at the specified time points were

analyzed (represented by n=X in the category titles). 99999 indicates data is not available as standard deviation could not be calculated due to n=1. The AP Population is defined as participants having Baseline and at least one post-Baseline assessment.

End point type	Secondary

End point timeframe:

Baseline and up to 12 months

End point values	GSK1070806 3 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	7[3]			
Units: Micromoles per liter				
arithmetic mean (standard deviation)				
Screening, n=7	679.0 (± 175.14)			
Day 0, n=7	-39.3 (± 160.09)			
Day 1, n=7	-44.7 (± 214.06)			
Day 2, n=7	-99.0 (± 304.29)			
Day 3, n=7	-36.7 (± 378.28)			
Day 4, n=7	-104.6 (± 378.79)			
Day 5, n=6	-57.2 (± 334.19)			
Day 6, n=6	-75.7 (± 308.22)			
Day 7, n=6	-43.5 (± 321.91)			
Day 8, n=5	-150.8 (± 293.48)			
Day 9, n=3	-24.0 (± 297.82)			
Day 10, n=3	-53.0 (± 395.94)			
Day 11, n=3	-97.0 (± 462.46)			
Day 12, n=2	110.0 (± 257.39)			
Day 13, n=2	38.0 (± 209.30)			
Day 14, n=2	4.0 (± 190.92)			
Day 15, n=2	-51.0 (± 172.53)			
Day 16, n=2	-61.5 (± 173.24)			
Day 17, n=2	-107.5 (± 143.54)			
Day 18, n=2	-145.0 (± 123.04)			
Day 19, n=2	-173.5 (± 95.46)			
Day 20, n=2	-183.5 (± 81.32)			

Day 21, n=1	-117.0 (± 99999)			
Day 22, n=1	-91.0 (± 99999)			
Day 23, n=1	-95.0 (± 99999)			
Day 24, n=1	-115.0 (± 99999)			
Day 25, n=1	-152.0 (± 99999)			
Day 26, n=1	-155.0 (± 99999)			
Day 27, n=1	-175.0 (± 99999)			
Day 28, n=1	-191.0 (± 99999)			
Day 30, n=7	-478.3 (± 225.47)			
Day 90, n=7	-489.9 (± 214.06)			
6 months, n=7	-467.4 (± 232.49)			
12 months, n=6	-490.5 (± 224.32)			

Notes:

[3] - AP Population

Statistical analyses

No statistical analyses for this end point

Secondary: Urine volume at Baseline and change from Baseline over time post transplant

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

End point description:

Urine volume at Baseline and over time post transplant was measured to assess graft function in DCD renal transplant recipients treated with GSK1070806. Baseline value was the latest pre-dose assessment value. Change from Baseline was post Baseline value minus Baseline value. All Subjects Population comprised of participants who received the dose of study medication. 99999 indicates data is not available as standard deviation could not be calculated due to n=1. Only those participants with data available at the specified time points were analyzed (represented by n=X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Pre-operative) and up to Day 28

End point values	GSK1070806 3 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	7[4]			
Units: Liter				
arithmetic mean (standard deviation)				
Day 0, n=4	-0.5150 (± 0.59533)			

Day 1, n=5	0.5862 (± 1.56917)			
Day 2, n=5	1.2820 (± 2.62989)			
Day 3, n=5	0.8840 (± 1.04040)			
Day 4, n=5	1.1480 (± 1.00442)			
Day 5, n=4	0.8270 (± 1.02297)			
Day 6, n=4	1.1168 (± 1.30252)			
Day 7, n=4	1.2985 (± 1.37212)			
Day 8, n=3	1.2090 (± 1.20354)			
Day 9, n=2	1.2135 (± 1.46866)			
Day 10, n=2	0.8585 (± 0.62720)			
Day 11, n=2	0.4985 (± 0.22840)			
Day 12, n=1	1.4000 (± 99999)			
Day 13, n=1	1.6900 (± 99999)			
Day 14, n=1	1.1800 (± 99999)			
Day 15, n=1	1.5500 (± 99999)			
Day 16, n=1	1.8500 (± 99999)			
Day 17, n=1	1.5000 (± 99999)			
Day 18, n=1	1.9000 (± 99999)			
Day 19, n=1	1.6000 (± 99999)			
Day 20, n=1	1.2500 (± 99999)			
Day 21, n=1	0.7500 (± 99999)			
Day 22, n=1	1.0500 (± 99999)			
Day 23, n=1	1.1500 (± 99999)			
Day 24, n=1	1.4500 (± 99999)			
Day 25, n=1	2.0500 (± 99999)			
Day 26, n=1	2.0000 (± 99999)			
Day 27, n=1	1.5500 (± 99999)			
Day 28, n=1	1.4600 (± 99999)			
Pre-operative, n=5	0.6700 (± 0.60581)			

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 evaluated to access graft function in DCD renal transplant recipients treated with GSK1070806.

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	7[5]			
Units: Participants				
Primary Non Function	1			
3 day Functional DGF	3			
7 day Functional DGF	5			
3 day Intermediate Graft Function	0			
7 day Intermediate Graft Function	1			
3 day Immediate Graft Function	1			
7 day Immediate Graft Function	0			

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 evaluated to assess the effect of GSK1070806 on acute rejection risk, and rejection/ Pharmacodynamics (PD) biomarkers. Only those participants with data available at the specified time points were analyzed.

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	2[6]			
Units: Participants	1			

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 Change from Baseline 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 Change from Baseline 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. Change from Baseline was calculated as post Baseline value minus Baseline value. Only those participants with data available at the specified time points were analyzed (represented by n=X in the category titles).

End point type	Secondary

End point timeframe:

Baseline and up to 12 months

End point values	GSK1070806 3 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	7[7]			
Units: Picograms per Liter				
arithmetic mean (standard deviation)				
IP-10, Baseline, n=7	518.83817 (± 269.010355)			
IP-10, Day 0, 0.75 hour, n=6	-48.36607 (± 178.371827)			
IP-10, Day 0, 4-8 hour, n=6	-262.30099 (± 176.415675)			
IP-10, Day 1, n=6	-214.27224 (± 198.587957)			
IP-10, Day 2, n=5	-91.07498 (± 397.795706)			
IP-10, Day 30, n=6	-215.96831 (± 350.419207)			
IP-10, Day 90, n=7	221.97286 (± 617.906913)			
IP-10, 6 months, n=7	145.05039 (± 846.080946)			
IP-10, 12 months, n=5	241.29317 (± 564.374462)			
Mig, Baseline, n=7	175.76865 (± 194.372235)			

Mig, Day 0, 0.75 hour, n=6	-14.02145 (± 32.535124)			
Mig, Day 0, 4-8 hour, n=6	-49.28436 (± 54.067623)			
Mig, Day 1, n=6	-67.61716 (± 61.009544)			
Mig, Day 2, n=5	-133.99600 (± 165.972042)			
Mig, Day 30, n=6	-159.17646 (± 207.921389)			
Mig, Day 90, n=7	-78.69081 (± 227.901113)			
Mig, 6 months, n=7	-43.68148 (± 325.518838)			
Mig, 12 months, n=5	-30.52711 (± 75.218188)			

Notes:

[7] - All Subjects 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. The AP Population is defined as participants having Baseline and at least one post-Baseline assessment.

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 evaluated to assess the effect of GSK1070806 on dialysis dependency and graft survival.

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[9]			
Units: Participants	2			

Notes:

[9] - All Subjects 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.

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 abnormality in hematology results of Potential Clinical Importance

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

End point description:

Blood samples were collected to evaluate hematology parameters. Number of participants with abnormality in any hematology parameter results of potential clinical importance (high or low) observed at any time post Baseline are presented. PCI (high or low) was considered if hematocrit (high:>0.54;low:change from baseline [CFB] 0.075 decrease), hemoglobin (high:180; low: CFB 25 decrease), lymphocytes (low: 0.8), neutrophil count (low: 1.5), platelet count (low: 100; high: 550), White blood cells (low: 3; high:20).

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[11]			
Units: Participants				
Lymphocytes, Low	7			
Hematocrit, High	1			
White Blood Cells, High	1			
White Blood Cells, Low	1			
Platelet Count, Low	1			
Total neutrophils, Low	1			

Notes:

[11] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Blood samples were collected to evaluate clinical chemistry parameters. Number of participants with abnormal chemistry results of potential clinical importance (high or low) in any of these parameters at any time post Baseline visit have been presented. PCI (high or low) was considered if albumin (low<30), calcium (low<2, high>2.75), creatinine (high: CHB>44.2 increase), glucose (low<3, high>9), magnesium (low<0.5, high>1.23), phosphorus (low<0.8, high>1.6), potassium (low<3, high>5.5), sodium (low: 130, high>150), Total carbon dioxide (CO2) (low:18, high>32), Alanine aminotransferase (ALT) (high>=2*upper limit of normal [ULN]), Aspartate aminotransferase (AST) (high: >=2*ULN), Alkaline phosphatase (ALP) (high:>=2*ULN), Total bilirubin (high: >2*ULN), Total bilirubin+ALT (high: 1.5*ULN total bilirubin with >=2*ULN ALT).

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[12]			
Units: Participants				
Albumin, Low	6			
Calcium, Low	7			
Glucose, High	5			
Potassium, Low	1			
Potassium, High	3			
Total Bilirubin, High	1			
Sodium, Low	2			
ALT, High	1			
ALP, High	1			
AST, High	1			

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 blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR) and body temperature. Number of participants with any abnormality of potential clinical importance (high or low) in any of these vitals signs at any time post Baseline visit have been presented. PCI (high or low) was considered if SBP (low: <85, high:>160), DBP (low: <45, high>100), HR (low: <40, high: >110) and temperature (low: <35.5, high: >37.5).

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				
SBP, High	5			
SBP, Low	1			
DBP, High	2			
DBP, Low	1			
HR, High	1			

Temperature, High	1			
Temperature, Low	2			

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 were summarized.

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[14]			
Units: Participants	5			

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 collected to evaluate PK of GSK1070806 at Pre-operative, 0.75 hours, 4-8 hours, 24 hours, 168 hours, Day 30, Day 90, 6 months and 12 months after kidney reperfusion. PK Population included participants in the 'All Subjects' Population for whom a serum PK sample is obtained and analyzed for GSK1070806. 99999 indicates data was not available as standard deviation is not calculated as most of the values at these time points were imputed. Only those participants with data available at the specified time points were analyzed (represented by n=X in the category titles).

End point type	Secondary

End point timeframe:

Pre-operative, 0.75 hours, 4-8 hours, 24 hours, 168 hours, Day 30, Day 90, 6 months and 12 months after kidney reperfusion

End point values	GSK1070806 3 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	7[15]			
Units: Nanograms per milliliter				
arithmetic mean (standard deviation)				
Pre-operative, n=7	0.0 (± 99999)			
0.75 hours, n=6	58783.3 (± 11287.77)			
4-8 hours, n=6	60033.3 (± 13577.43)			
24 hours, n=6	50933.3 (± 12681.11)			
168 hours, n=5	28260.0 (± 9643.29)			
Day 30, n=6	17366.7 (± 6809.60)			
Day 90, n=7	5047.0 (± 2914.37)			
6 months, n=7	1083.4 (± 720.18)			
12 months, n=6	19.2 (± 99999)			

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-operative, 0.75 hours, 4-8 hours, 24 hours, 168 hours, Day 30, Day 90, 6 months and 12 months after kidney reperfusion. Log-transformed geometric mean and 95% confidence interval have been presented.

End point type	Secondary

End point timeframe:

Pre-operative, 0.75 hours, 4-8 hours, 24 hours, 168 hours, Day 30, Day 90, 6 months and 12 months after kidney reperfusion

End point values	GSK1070806 3 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	7[16]			
Units: Log (nanograms per milliliter)				
geometric mean (confidence interval 95%)	36315.1 (10237.6 to 128818.4)			

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 the last measurable concentration (AUC[0-t]) and AUC from time 0 to infinite time (AUC[0-inf]) of GSK1070806

End point title	Area under the plasma concentration time curve (AUC) from time 0 to the last measurable concentration (AUC[0-t]) and AUC from time 0 to infinite time (AUC[0-inf]) of GSK1070806

End point description:

Blood samples were to be collected to evaluate PK of GSK1070806 at Pre-operative, 0.75 hours, 4-8 hours, 24 hours, 168 hours, Day 30, Day 90, 6 months and 12 months after kidney reperfusion. Log-transformed geometric mean and 95% confidence interval have been presented.

End point type	Secondary

End point timeframe:

Pre-operative, 0.75 hours, 4-8 hours, 24 hours, 168 hours, Day 30, Day 90, 6 months and 12 months after kidney reperfusion

End point values	GSK1070806 3 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	7[17]			
Units: Log (Hour*nanograms per milliliter)				
geometric mean (confidence interval 95%)				
AUC (0-t), n=7	26131338.2 (8927844.0 to 76485076.9)			
AUC (0-inf), n=6	41032450.7 (28127219.0 to 59858815.6)			

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) at Baseline and change from Baseline over time post-transplant

End point title	Serum levels of free, total, and GSK1070806 bound Interleukin 18 (IL-18) at Baseline and change from Baseline 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. Change from Baseline was post Baseline value minus Baseline value. Data will be posted by June 2019.

End point type	Secondary

End point timeframe:

Baseline and at 0.75 hours, 4-8 hours, Day 1, Day 2, Day 30, Day 90, 6 and 12 months post reperfusion

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 was not collected as the immunogenicity samples were not collected for this terminated indication since healthy volunteers showed low titers and Type 2 Diabetics showed no titers per Investigator's Brochure.

End point type	Secondary

End point timeframe:

0.75 hour and 4-8 hour on Day 0, Day 1, Day 2, Day 30, Day 90, 6 months and 12 months post reperfusion

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 titer was to be assessed using a validated ECL immunoassay. Data was not collected as the immunogenicity samples were not collected for this terminated indication since healthy volunteers showed low titers and Type 2 Diabetics showed no titers per Investigator's Brochure.

End point type	Secondary

End point timeframe:

0.75 hour and 4-8 hour on Day 0, Day 1, Day 2, Day 30, Day 90, 6 months and 12 months post reperfusion

End point values	GSK1070806 3 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[20]			
Units: Picograms 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	0 / 2		
deaths causally related to treatment / all	0 / 0		
Cardiac failure			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
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		
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		
Gastrointestinal disorders			
Small intestinal obstruction			
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		

End stage renal disease			
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		
Visceral leishmaniasis			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
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		
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		

Transplant rejection			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Wheezing			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Product issues			
Product contamination			
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		
Candida test positive			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Body temperature decreased			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Haemoglobin increased			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		

Blood glucose increased			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Cytomegalovirus test positive			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Weight increased			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Wound evisceration			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Wound dehiscence			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Arteriovenous fistula site complication			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Post procedural discharge			
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	5 / 7 (71.43%)		
occurrences (all)	5		
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 occurrences (all)	2 / 7 (28.57%) 2		
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all)	4 / 7 (57.14%) 4		
Nausea subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2		
Abdominal pain subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 2		
Diarrhoea subjects affected / exposed occurrences (all)	3 / 7 (42.86%) 3		
Frequent bowel movements subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Dyspepsia subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Inguinal hernia subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Lip swelling subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Vomiting subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Skin and subcutaneous tissue disorders Decubitus ulcer subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Pruritus			

subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Urticaria			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Renal and urinary disorders			
Renal disorder			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Urinary retention			
subjects affected / exposed	2 / 7 (28.57%)		
occurrences (all)	4		
Ureteric stenosis			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Renal impairment			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	2 / 7 (28.57%)		
occurrences (all)	4		
Escherichia urinary tract infection			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Lower respiratory tract infection			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	2		
Influenza			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Postoperative wound infection			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Pyelonephritis acute			

subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Bacterial disease carrier			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Nail infection			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Pharyngotonsillitis			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Purulent discharge			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Urinary tract infection enterococcal			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	2		
Diabetes mellitus			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Fluid overload			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Hyperkalaemia			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Hypomagnesaemia			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Hypoglycaemia			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		

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