Clinical trial results:
A randomised, open-label, multicenter trial to determine safety and efficacy of eculizumab in the prevention of Antibody-Mediated Rejection (AMR) in living donor kidney transplant recipients requiring desensitisation therapy

Summary

EudraCT number	2010-019630-28
Trial protocol	GB DE NO NL ES IT SE
Global end of trial date	13 November 2015

Results information

Result version number	v1 (current)
This version publication date	17 February 2017
First version publication date	17 February 2017

Trial information

Trial identification

Sponsor protocol code	C10-001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01399593
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Alexion Pharmaceuticals Inc
Sponsor organisation address	100 College Street, New Haven, United States, CT 06510
Public contact	European Clinical Trial Information, ALEXION EUROPE SAS, + 33 1 47 10 06 06, clinicaltrials.eu@alexion.com
Scientific contact	European Clinical Trial Information, ALEXION EUROPE SAS, + 33 1 47 10 06 06, clinicaltrials.eu@alexion.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	13 July 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 May 2014
Global end of trial reached?	Yes
Global end of trial date	13 November 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to evaluate the safety and efficacy of eculizumab to prevent AMR in sensitised recipients of living donor kidney transplants requiring desensitisation therapy prior to transplantation. The primary endpoint focused on acute AMR during the first 9 weeks post-transplantation.

Protection of trial subjects:

Vaccination against N. meningitidis at least 14 days prior to study drug initiation and revaccination 30 days later. If not vaccinated 14 days prior, prophylactic antibiotics must have been administered. A booster dose was to be administered 30 days after the initial dose. Pre-transplant infectious disease assessment was performed as part of the screening assessment.

Background therapy:

Patients were to undergo desensitisation therapy according to the practice of the local transplant center prior to transplantation, and this desensitisation practice was to be uniformly applied for all patients at that center throughout the study. The actual length of desensitisation for an individual patient was based on the clinical judgment of the Transplant Center team. Rituximab was prohibited in all patients as part of the pre-transplantation desensitisation therapy due to potential pharmacodynamic interactions.

Evidence for comparator:

The control group was designed to test eculizumab against the best available care (referred to as standard of care, or SOC) consisting of plasmapheresis (PP) and/or intravenous immunoglobulin (IVIg). The best available care consisting of PP and IVIg was chosen because these modalities combined represented the most prevalent therapy reported in the literature and were the best available therapies at the time of this protocol’s inception as per the transplant community.

Actual start date of recruitment	02 November 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	36 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 3
Country: Number of subjects enrolled	Norway: 2
Country: Number of subjects enrolled	Spain: 7
Country: Number of subjects enrolled	Sweden: 5
Country: Number of subjects enrolled	United Kingdom: 15
Country: Number of subjects enrolled	France: 10
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Italy: 6

Country: Number of subjects enrolled	Australia: 5
Country: Number of subjects enrolled	United States: 47
Worldwide total number of subjects	102
EEA total number of subjects	50

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)	96
From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment period lasted from Nov 2011 to Mar 2014. Forty-one sites in Australia, the European Union, and North America participated in this study.

Pre-assignment

Screening details:

Screening lasted approximately 8 wks. Written consent was provided prior to performing any study-required assessments. Patients who met screening criteria were enrolled and underwent desensitisation therapy prior to transplantation, according to local transplant center practice.

Pre-assignment period milestones

Number of subjects started	275[1]
Intermediate milestone: Number of subjects	Passed screening: 137
Intermediate milestone: Number of subjects	Randomised: 104
Number of subjects completed	102

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Physician decision: 13
Reason: Number of subjects	Adverse event, non-fatal: 7
Reason: Number of subjects	Adverse event, serious fatal: 1
Reason: Number of subjects	Enrolment failure: 3
Reason: Number of subjects	Donor or pre-transplantation logistical issues: 62
Reason: Number of subjects	Did not meet inclusion/exclusion criteria: 62
Reason: Number of subjects	Consent withdrawn by subject: 4
Reason: Number of subjects	Failed desensitisation: 18
Reason: Number of subjects	Randomised but not transplanted: 2
Reason: Number of subjects	Passed screening in error: 1

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 275 patients were screened; among them, 102 patients were randomised and transplanted, and received eculizumab or standard of care for up to 9 weeks post-transplantation.

Period 1

Period 1 title	9-wk treatment and 60-day washout (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

This study was an open-label study.

Arms

Are arms mutually exclusive?	Yes

Arm title	Eculizumab treatment group

Arm description:

Patients in the eculizumab treatment group were to receive eculizumab starting approximately 1 hour prior to reperfusion of the allograft and then received a set regimen of dosing for 9 weeks post transplantation, as described in the "Dosage and administration details" section. Data reported are summarised for the "Prevention phase" of the study, i.e., 9-week treatment with eculizumab plus an additional 60-day washout period.

Arm type	Experimental
Investigational medicinal product name	Eculizumab
Investigational medicinal product code	eculizumab
Other name	Soliris
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Eculizumab was administered for 9 weeks according to the following dosing regimen:
Eculizumab 1200 mg prior to allograft transplantation (Day 0, starting approximately one hour prior to kidney allograft reperfusion), eculizumab 900 mg (Days 1, 7, 14, 21, and 28), and eculizumab 1200 mg (Weeks 5, 7 and 9). All doses of eculizumab were administered intravenously, with median infusion time of 39 minutes.

Arm title	SOC treatment group

Arm description:

Patients in the standard of care (SOC) treatment group received prophylactic therapy for acute AMR according to the SOC choice at each participating investigative site, which could have included any combination of PP and IVIg. Patients randomised to SOC who were diagnosed with AMR could have received eculizumab for the treatment of AMR after initially receiving PP and/or IVIg.
Data reported are summarised for the "Prevention phase" of the study, i.e., 9-week treatment plus an additional 60-day washout period. For those patients randomised to the SOC treatment group who were switched to eculizumab for treatment of AMR, from that point forward their data were no longer included in the Prevention Phase.

Arm type	Best available care
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	Eculizumab treatment group	SOC treatment group
Started	51	51
Completed	48	49
Not completed	3	2
Adverse event, serious fatal	1	1
Physician decision	1	-
Adverse event, non-fatal	1	-
Transplantectomy	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Eculizumab treatment group
Reporting group description:	
Patients in the eculizumab treatment group were to receive eculizumab starting approximately 1 hour prior to reperfusion of the allograft and then received a set regimen of dosing for 9 weeks post transplantation, as described in the "Dosage and administration details" section. Data reported are summarised for the "Prevention phase" of the study, i.e., 9-week treatment with eculizumab plus an additional 60-day washout period.	
Reporting group title	SOC treatment group
Reporting group description:	
Patients in the standard of care (SOC) treatment group received prophylactic therapy for acute AMR according to the SOC choice at each participating investigative site, which could have included any combination of PP and IVIg. Patients randomised to SOC who were diagnosed with AMR could have received eculizumab for the treatment of AMR after initially receiving PP and/or IVIg. Data reported are summarised for the "Prevention phase" of the study, i.e., 9-week treatment plus an additional 60-day washout period. For those patients randomised to the SOC treatment group who were switched to eculizumab for treatment of AMR, from that point forward their data were no longer included in the Prevention Phase.	

Reporting group values	Eculizumab treatment group	SOC treatment group	Total
Number of subjects	51	51	102
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	47	49	96
From 65-84 years	4	2	6
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	37	30	67
Male	14	21	35
Race Units: Subjects			
White	37	36	73
Asian	2	3	5
Black or African American	6	6	12
Other	6	6	12
Total DSA Units: MFI			
arithmetic mean	15394.7	17469.8	
standard deviation	± 14163.78	± 12573.44	-
Highest Single DSA Units: MFI			

arithmetic mean	8135	8740.7	
standard deviation	± 4048.08	± 4289.97	-

End points

End points reporting groups

Reporting group title	Eculizumab treatment group

Reporting group description:

Patients in the eculizumab treatment group were to receive eculizumab starting approximately 1 hour prior to reperfusion of the allograft and then received a set regimen of dosing for 9 weeks post transplantation, as described in the "Dosage and administration details" section. Data reported are summarised for the "Prevention phase" of the study, i.e., 9-week treatment with eculizumab plus an additional 60-day washout period.

Reporting group title	SOC treatment group

Reporting group description:

Patients in the standard of care (SOC) treatment group received prophylactic therapy for acute AMR according to the SOC choice at each participating investigative site, which could have included any combination of PP and IVIg. Patients randomised to SOC who were diagnosed with AMR could have received eculizumab for the treatment of AMR after initially receiving PP and/or IVIg.
Data reported are summarised for the "Prevention phase" of the study, i.e., 9-week treatment plus an additional 60-day washout period. For those patients randomised to the SOC treatment group who were switched to eculizumab for treatment of AMR, from that point forward their data were no longer included in the Prevention Phase.

Primary: Treatment failure rate

End point title	Treatment failure rate

End point description:

The primary efficacy endpoint was treatment failure rate, a composite endpoint defined as the occurrence of 1) biopsy-proven acute AMR, 2) graft loss, 3) patient death, or 4) loss to follow-up measured through 9 weeks post-transplantation.

End point type	Primary

End point timeframe:

9 weeks post-transplantation

End point values	Eculizumab treatment group	SOC treatment group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	51		
Units: Number of patients				
Treatment failure rate	5	7		
Acute AMR	5	5		
Graft loss	0	3		
Death	1	1		
Loss to follow-up	0	2		

Statistical analyses

Statistical analysis title	Statistical analysis 1 for treatment failure rate

Statistical analysis description:

The analysis was based on full analysis set and analysed by randomised treatment.

Comparison groups	SOC treatment group v Eculizumab treatment group
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.76
Method	Fisher exact
Parameter estimate	Proportion difference
Point estimate	-3.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.9
upper limit	16.3

Notes:

[1] - The primary efficacy variable was a binary outcome variable where patients meeting the composite endpoint of the occurrence of 1) biopsy-proven acute AMR, 2) graft loss, 3) patient death, or 4) loss to follow-up definition at Week 9 post-transplantation were considered treatment failures and all others were considered treatment successes.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Safety was evaluated for all patients through their duration in the study by randomised treatment and, separately, by actual treatment received.

Adverse event reporting additional description:

Serious and non-serious adverse events are summarised for the "Prevention Phase" (i.e., first 9 wks of prophylactic treatment post-transplantation and an additional 60 days for washout). Data from the Prevention Phase are considered as the most relevant given that it includes only data from patients under treatment for the prevention of acute AMR.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	SOC treatment group

Reporting group description:

If patient were switched to eculizumab for the treatment of acute AMR, from that point forward their data were no longer included in the Prevention Phase.

Reporting group title	Eculizumab treatment group

Reporting group description:

All patients randomised to receive eculizumab during the Prevention Phase.

Serious adverse events	SOC treatment group	Eculizumab treatment group	
Total subjects affected by serious adverse events			
subjects affected / exposed	38 / 51 (74.51%)	36 / 51 (70.59%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events	1	1	
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemic shock			

subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphocele			
subjects affected / exposed	5 / 51 (9.80%)	3 / 51 (5.88%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Superior vena cava occlusion			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	0 / 51 (0.00%)	2 / 51 (3.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Nephrostomy			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Hypothermia			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired healing			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Influenza like illness			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Kidney transplant rejection			
subjects affected / exposed	18 / 51 (35.29%)	14 / 51 (27.45%)	
occurrences causally related to treatment / all	0 / 20	1 / 15	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug hypersensitivity			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Social circumstances			
Convalescent			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			

subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Anti-glomerular basement membrane antibody			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Antibody test positive			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatinine increased			
subjects affected / exposed	0 / 51 (0.00%)	3 / 51 (5.88%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug level increased	Additional description: High Level of Tacrolimus		
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Complications of transplanted kidney			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delayed graft function			
subjects affected / exposed	1 / 51 (1.96%)	2 / 51 (3.92%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft thrombosis			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Incisional hernia			
subjects affected / exposed	0 / 51 (0.00%)	2 / 51 (3.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haematoma			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			
subjects affected / exposed	1 / 51 (1.96%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural pain			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound dehiscence			
subjects affected / exposed	2 / 51 (3.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nervous system disorders			

Cerebellar haemorrhage			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	2 / 51 (3.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 51 (1.96%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coagulopathy			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Abdominal wall haematoma			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	2 / 51 (3.92%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine perforation			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	1 / 51 (1.96%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis relapsing			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			

subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 51 (3.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Focal segmental glomerulosclerosis			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	2 / 51 (3.92%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrectasia			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrotic syndrome			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal injury			

subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteric dilatation			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral stenosis			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary incontinence			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal haemorrhage			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myalgia			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
BK virus infection			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Abdominal sepsis	Additional description: Fatality occurred in one patient who experienced both one serious adverse event of abdominal sepsis on Day 16 and one serious adverse event of bacterial sepsis on Day 36.		
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Bacteraemia			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial sepsis	Additional description: Fatality occurred in one patient who experienced both one serious adverse event of abdominal sepsis on Day 16 and one serious adverse event of bacterial sepsis on Day 36.		
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Bronchitis			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related sepsis			
subjects affected / exposed	1 / 51 (1.96%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia bacteraemia			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia urinary tract infection			
subjects affected / exposed	1 / 51 (1.96%)	3 / 51 (5.88%)	
occurrences causally related to treatment / all	0 / 1	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Haemophilus infection			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metapneumovirus infection			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 51 (0.00%)	3 / 51 (5.88%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	1 / 51 (1.96%)	2 / 51 (3.92%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			

subjects affected / exposed	1 / 51 (1.96%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection enterococcal			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection pseudomonal			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection staphylococcal			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic acidosis			

subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	SOC treatment group	Eculizumab treatment group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	47 / 51 (92.16%)	51 / 51 (100.00%)	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 51 (1.96%)	3 / 51 (5.88%)	
occurrences (all)	2	3	
Haematoma			
subjects affected / exposed	3 / 51 (5.88%)	1 / 51 (1.96%)	
occurrences (all)	3	1	
Hypertension			
subjects affected / exposed	11 / 51 (21.57%)	11 / 51 (21.57%)	
occurrences (all)	12	13	
Hypotension			
subjects affected / exposed	9 / 51 (17.65%)	6 / 51 (11.76%)	
occurrences (all)	11	7	
Lymphocele			
subjects affected / exposed	2 / 51 (3.92%)	3 / 51 (5.88%)	
occurrences (all)	4	3	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	7 / 51 (13.73%)	7 / 51 (13.73%)	
occurrences (all)	9	7	
Chest pain			

subjects affected / exposed	1 / 51 (1.96%)	5 / 51 (9.80%)	
occurrences (all)	1	5	
Oedema			
subjects affected / exposed	4 / 51 (7.84%)	5 / 51 (9.80%)	
occurrences (all)	4	5	
Chills			
subjects affected / exposed	3 / 51 (5.88%)	1 / 51 (1.96%)	
occurrences (all)	4	1	
Oedema peripheral			
subjects affected / exposed	13 / 51 (25.49%)	9 / 51 (17.65%)	
occurrences (all)	15	13	
Pain			
subjects affected / exposed	5 / 51 (9.80%)	3 / 51 (5.88%)	
occurrences (all)	7	5	
Pyrexia			
subjects affected / exposed	11 / 51 (21.57%)	9 / 51 (17.65%)	
occurrences (all)	12	12	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	3 / 51 (5.88%)	5 / 51 (9.80%)	
occurrences (all)	3	5	
Kidney transplant rejection			
subjects affected / exposed	7 / 51 (13.73%)	11 / 51 (21.57%)	
occurrences (all)	7	12	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	4 / 51 (7.84%)	3 / 51 (5.88%)	
occurrences (all)	4	3	
Pulmonary oedema			
subjects affected / exposed	3 / 51 (5.88%)	0 / 51 (0.00%)	
occurrences (all)	3	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 51 (1.96%)	7 / 51 (13.73%)	
occurrences (all)	1	8	
Insomnia			

subjects affected / exposed	7 / 51 (13.73%)	4 / 51 (7.84%)	
occurrences (all)	7	4	
Investigations			
Antibody test positive			
subjects affected / exposed	0 / 51 (0.00%)	3 / 51 (5.88%)	
occurrences (all)	0	3	
Blood creatinine increased			
subjects affected / exposed	10 / 51 (19.61%)	8 / 51 (15.69%)	
occurrences (all)	10	10	
Liver function test abnormal			
subjects affected / exposed	3 / 51 (5.88%)	6 / 51 (11.76%)	
occurrences (all)	3	6	
Injury, poisoning and procedural complications			
Incision site pain			
subjects affected / exposed	6 / 51 (11.76%)	8 / 51 (15.69%)	
occurrences (all)	6	10	
Perinephric collection			
subjects affected / exposed	1 / 51 (1.96%)	3 / 51 (5.88%)	
occurrences (all)	1	3	
Procedural haemorrhage			
subjects affected / exposed	1 / 51 (1.96%)	3 / 51 (5.88%)	
occurrences (all)	1	3	
Procedural pain			
subjects affected / exposed	8 / 51 (15.69%)	7 / 51 (13.73%)	
occurrences (all)	9	10	
Wound secretion			
subjects affected / exposed	4 / 51 (7.84%)	0 / 51 (0.00%)	
occurrences (all)	4	0	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	7 / 51 (13.73%)	5 / 51 (9.80%)	
occurrences (all)	7	6	
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 51 (7.84%)	6 / 51 (11.76%)	
occurrences (all)	4	7	

Headache			
subjects affected / exposed	2 / 51 (3.92%)	9 / 51 (17.65%)	
occurrences (all)	3	12	
Tremor			
subjects affected / exposed	8 / 51 (15.69%)	11 / 51 (21.57%)	
occurrences (all)	11	12	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	24 / 51 (47.06%)	14 / 51 (27.45%)	
occurrences (all)	31	20	
Leukopenia			
subjects affected / exposed	17 / 51 (33.33%)	12 / 51 (23.53%)	
occurrences (all)	17	14	
Thrombocytopenia			
subjects affected / exposed	6 / 51 (11.76%)	2 / 51 (3.92%)	
occurrences (all)	7	2	
Hypofibrinogenaemia			
subjects affected / exposed	3 / 51 (5.88%)	0 / 51 (0.00%)	
occurrences (all)	3	0	
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 51 (0.00%)	3 / 51 (5.88%)	
occurrences (all)	0	3	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	6 / 51 (11.76%)	3 / 51 (5.88%)	
occurrences (all)	7	3	
Constipation			
subjects affected / exposed	13 / 51 (25.49%)	12 / 51 (23.53%)	
occurrences (all)	13	12	
Diarrhoea			
subjects affected / exposed	15 / 51 (29.41%)	17 / 51 (33.33%)	
occurrences (all)	19	24	
Nausea			
subjects affected / exposed	14 / 51 (27.45%)	22 / 51 (43.14%)	
occurrences (all)	17	25	
Vomiting			

subjects affected / exposed	5 / 51 (9.80%)	10 / 51 (19.61%)	
occurrences (all)	5	10	
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 51 (5.88%)	1 / 51 (1.96%)	
occurrences (all)	3	1	
Flatulence			
subjects affected / exposed	3 / 51 (5.88%)	4 / 51 (7.84%)	
occurrences (all)	3	4	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	3 / 51 (5.88%)	1 / 51 (1.96%)	
occurrences (all)	3	1	
Pruritus			
subjects affected / exposed	9 / 51 (17.65%)	8 / 51 (15.69%)	
occurrences (all)	10	8	
Rash			
subjects affected / exposed	0 / 51 (0.00%)	3 / 51 (5.88%)	
occurrences (all)	0	3	
Renal and urinary disorders			
Anuria			
subjects affected / exposed	3 / 51 (5.88%)	0 / 51 (0.00%)	
occurrences (all)	3	0	
Bladder spasm			
subjects affected / exposed	2 / 51 (3.92%)	3 / 51 (5.88%)	
occurrences (all)	2	3	
Dysuria			
subjects affected / exposed	4 / 51 (7.84%)	2 / 51 (3.92%)	
occurrences (all)	4	2	
Haematuria			
subjects affected / exposed	8 / 51 (15.69%)	5 / 51 (9.80%)	
occurrences (all)	8	5	
Oliguria			
subjects affected / exposed	4 / 51 (7.84%)	0 / 51 (0.00%)	
occurrences (all)	4	0	
Polyuria			

subjects affected / exposed	4 / 51 (7.84%)	4 / 51 (7.84%)	
occurrences (all)	4	4	
Proteinuria			
subjects affected / exposed	1 / 51 (1.96%)	4 / 51 (7.84%)	
occurrences (all)	1	4	
Renal impairment			
subjects affected / exposed	1 / 51 (1.96%)	3 / 51 (5.88%)	
occurrences (all)	1	3	
Renal tubular necrosis			
subjects affected / exposed	3 / 51 (5.88%)	2 / 51 (3.92%)	
occurrences (all)	3	2	
Urinary retention			
subjects affected / exposed	3 / 51 (5.88%)	1 / 51 (1.96%)	
occurrences (all)	3	1	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	8 / 51 (15.69%)	5 / 51 (9.80%)	
occurrences (all)	8	7	
Muscular weakness			
subjects affected / exposed	3 / 51 (5.88%)	0 / 51 (0.00%)	
occurrences (all)	3	0	
Musculoskeletal pain			
subjects affected / exposed	2 / 51 (3.92%)	5 / 51 (9.80%)	
occurrences (all)	2	6	
Infections and infestations			
BK virus infection			
subjects affected / exposed	2 / 51 (3.92%)	8 / 51 (15.69%)	
occurrences (all)	2	9	
Oral candidiasis			
subjects affected / exposed	1 / 51 (1.96%)	4 / 51 (7.84%)	
occurrences (all)	1	4	
Upper respiratory tract infection			
subjects affected / exposed	2 / 51 (3.92%)	7 / 51 (13.73%)	
occurrences (all)	2	7	
Urinary tract infection			

subjects affected / exposed	12 / 51 (23.53%)	19 / 51 (37.25%)	
occurrences (all)	15	27	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 51 (1.96%)	5 / 51 (9.80%)	
occurrences (all)	1	5	
Diabetes mellitus			
subjects affected / exposed	7 / 51 (13.73%)	4 / 51 (7.84%)	
occurrences (all)	7	4	
Fluid overload			
subjects affected / exposed	5 / 51 (9.80%)	2 / 51 (3.92%)	
occurrences (all)	5	2	
Hyperglycaemia			
subjects affected / exposed	11 / 51 (21.57%)	13 / 51 (25.49%)	
occurrences (all)	11	14	
Hyperkalaemia			
subjects affected / exposed	12 / 51 (23.53%)	7 / 51 (13.73%)	
occurrences (all)	14	7	
Hyperlipidaemia			
subjects affected / exposed	0 / 51 (0.00%)	4 / 51 (7.84%)	
occurrences (all)	0	4	
Hyperphosphataemia			
subjects affected / exposed	3 / 51 (5.88%)	3 / 51 (5.88%)	
occurrences (all)	3	3	
Hypocalcaemia			
subjects affected / exposed	10 / 51 (19.61%)	14 / 51 (27.45%)	
occurrences (all)	11	15	
Hypokalaemia			
subjects affected / exposed	8 / 51 (15.69%)	10 / 51 (19.61%)	
occurrences (all)	8	11	
Hypomagnesaemia			
subjects affected / exposed	10 / 51 (19.61%)	12 / 51 (23.53%)	
occurrences (all)	10	13	
Hyponatraemia			
subjects affected / exposed	2 / 51 (3.92%)	3 / 51 (5.88%)	
occurrences (all)	2	3	

Hypophosphataemia			
subjects affected / exposed	9 / 51 (17.65%)	16 / 51 (31.37%)	
occurrences (all)	9	16	
Metabolic acidosis			
subjects affected / exposed	4 / 51 (7.84%)	8 / 51 (15.69%)	
occurrences (all)	4	8	
Vitamin D deficiency			
subjects affected / exposed	4 / 51 (7.84%)	5 / 51 (9.80%)	
occurrences (all)	4	5	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 June 2011	Changes implemented as part of a first global amendment included: - To specify that randomisation was to be stratified by the pre-transplant desensitisation protocol used - To specify that all patients must have been re-vaccinated according to current medical guidelines for vaccination use - To clarify the use of other therapies in the eculizumab treatment arm - To add a secondary endpoint "Treatment failure rate defined as the occurrence of 1) biopsy-proven AMR, 2) graft loss, 3) patient death, or 4) loss to follow-up at Month 12 post-transplantation
04 November 2011	Changes implemented as part of a second global amendment included: - To update the enrollment and randomisation screening/enrollment - To update the diagnosis and main criteria for inclusion/exclusion criteria - To specify a maximum of 9 weeks of eculizumab treatment for AMR
04 May 2012	Changes implemented as part of the third global amendment included: - To update B and T flow crossmatch levels - To explain the length of time between signing of the informed consent and transplantation (desensitisation) - To explain the timing for patients to receive meningococcal vaccination - To add a section describing eculizumab dosing after treatment with FFP
11 February 2013	Purpose of fourth global protocol amendment was to: - Update the enrollment criteria. - Revise the cross-match requirements for patient eligibility and desensitization. - Clarify current procedures and explain the reason for the added procedures. - Increased the number of planned patients from 80 to 90, requiring an increase in the number of screened patients from 100 to 130 based on revised statistical analysis

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
13 November 2015	The primary composite endpoint, defined as the occurrence of biopsy-proven AMR, graft loss, patient death, or loss to follow-up at Week 9 post-transplantation, did not reach statistical significance. While the primary composite endpoint rate in the eculizumab treatment group was as expected from earlier studies with eculizumab, the rate in the standard of care treatment group (control group) was lower than was expected, based on natural history studies reported in the literature. Given this, the trial was terminated and no analyses of other efficacy endpoints have been performed. No safety signal has been reported to the Sponsor by the independent data monitoring committee.	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Data interpretation confounded by open-label study with potential reporting bias, unequal exposure to randomised prevention therapy between groups, some patients in SOC arm received eculizumab for treatment of AMR, all patients immunosuppressed.

Notes: