Clinical trial results:
An open label, multi-center trial of eculizumab in patients with Shiga-toxin producing Escherichia Coli Hemolytic-Uremic Syndrome (STEC-HUS)

Summary

EudraCT number	2011-002691-17
Trial protocol	DE
Global end of trial date	20 April 2012

Results information

Result version number	v1 (current)
This version publication date	24 July 2016
First version publication date	24 July 2016

Trial information

Trial identification

Sponsor protocol code	C11-001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01410916
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Alexion Pharmaceuticals Incorporated
Sponsor organisation address	352 Knotter Drive, Cheshire, CT, United States, 06410
Public contact	European Clinical Trial Information, Alexion Europe SAS, +33 1 47 10 06 06, clinicaltrials.eu@alxn.com
Scientific contact	European Clinical Trial Information, Alexion Europe SAS, +33 1 47 10 06 06, clinicaltrials.eu@alxn.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000876-PIP02-11
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	21 May 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 April 2012
Global end of trial reached?	Yes
Global end of trial date	20 April 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Safety and efficacy of eculizumab treatment in patients with STEC-HUS

Protection of trial subjects:

Vaccination against N. meningitidis at least 14 days prior to study drug initiation or prophylactic antibiotics protection

Background therapy: -

Evidence for comparator:

None

Actual start date of recruitment	22 July 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	2 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 198
Worldwide total number of subjects	198
EEA total number of subjects	198

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)	2
Adolescents (12-17 years)	7
Adults (18-64 years)	163
From 65 to 84 years	25
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

196 patients were retrospectively enrolled after signing ICF. All received commercially available eculizumab prior to enrollment and at least 1 dose of eculizumab as investigational product following study entry. Two patients were enrolled prospectively. This represents the IIT/safety population.

Pre-assignment

Screening details:

At screening, the following to be collected: medical history, demographics, historical data review, administration/confirmation of N. meningiditis vaccination and prophylactic antibiotics; neurology assessments, clinical laboratories, safety, seizure assessment, disease-specific information.

Pre-assignment period milestones

Number of subjects started	198
Number of subjects completed	198

Period 1

Period 1 title	Treatment Period (28 weeks) (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	eculizumab

Arm description:

A total of 196 patients were retrospectively enrolled after signing ICF. All received commercially available eculizumab prior to enrollment and at least 1 dose of eculizumab as investigational product following study entry. Two patients were enrolled prospectively. This represents the IIT/safety population.

Fixed dosing of eculizumab based on body weight cohorts were administered. Adjustment of dose to accommodate patient growth was possible.

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 to be administered intravenously (IV) according to the regimens described below:
- If weight ≥ 40 kg: Induction: 900 mg weekly x 4; Maintenance: 1200 mg Wk5; then 1200 mg every 2 weeks
- If weight 30 - < 40 kg: Induction: 600 mg weekly x 2; Maintenance: 900 mg Wk3; then 900 mg every 2 weeks
- If weight 20 - < 30 kg: Induction: 600 mg weekly x 2 ; Maintenance: 600 mg Wk3; then 600 mg every 2 weeks
- If weight 10 - < 20 kg: Induction: 600 mg weekly x 1; Maintenance: 300 mg Wk2; then 300 mg every 2 weeks
- If weight 5 - < 10 kg: Induction: 300 mg weekly x 1; Maintenance: 300 mg Wk2; then 300 mg every 3 weeks

Induction: 300 mg weekly x 1
Maintenance: 300 mg Wk2; then 300 mg every 2 weeks

Number of subjects in period 1	eculizumab
Started	198
Completed	184
Not completed	14
Patient condition improvement	2
Adverse Event	2
Lost to follow-up	7
Patient/parent decision	3

Baseline characteristics

Reporting groups	
Reporting group title	eculizumab

Reporting group description:

A total of 196 patients were retrospectively enrolled after signing ICF. All received commercially available eculizumab prior to enrollment and at least 1 dose of eculizumab as investigational product following study entry. Two patients were enrolled prospectively. This represents the IIT/safety population.

Fixed dosing of eculizumab based on body weight cohorts were administered. Adjustment of dose to accommodate patient growth was possible.

Reporting group values	eculizumab	Total	
Number of subjects	198	198	
Age categorical Units: Subjects			
Pediatric patients (< 18)	9	9	
Adults (18 ≤ 45)	112	112	
Adults (45 ≤ 65)	51	51	
≥ 65	26	26	
Age continuous Units: years			
arithmetic mean	42.1		
standard deviation	± 17.06	-	
Gender categorical Units: Subjects			
Female	142	142	
Male	56	56	
Race Units: Subjects			
White	198	198	
PE/PI at Baseline Units: Subjects			
Yes	181	181	
No	17	17	
Ever on PE/PI Units: Subjects			
Yes	186	186	
No	12	12	
Ventilator use at Baseline Units: Subjects			
Yes	47	47	
No	151	151	
Baseline Seizure Status			
Seizure status is presented in patients with brain involvement at baseline. Reporting group (IIT/Safety population): Data available for 166 subjects			
Units: Subjects			
Yes	43	43	
No	123	123	
Not brain involvement	32	32	

Therapeutic Coma at Baseline			
Reporting group (IIT/Safety population): Data available for 166 subjects.			
Units: Subjects			
Yes	35	35	
No	131	131	
Not brain involvement	32	32	
Hospitalization at Baseline Units: Subjects			
Yes	197	197	
No	1	1	
WBC category Units: Subjects			
> 20 x 10^9/L	33	33	
≤ 20 x 10^9/L	165	165	
Kidney involvement at Baseline Units: Subjects			
Kidney involvement	190	190	
No kidney involvement	8	8	
Brain involvement at Baseline Units: Subjects			
Brain involvement	166	166	
No brain involvement	32	32	
Thrombosis at Baseline Units: Subjects			
Thrombosis	0	0	
No thrombosis	198	198	
Brain and kidney involvement at Baseline Units: Subjects			
Brain and kidney involvement	158	158	
No brain and kidney involvement	40	40	
No organ involvement at Baseline Units: Subjects			
No organ involvement	0	0	
Any organ involvement	198	198	
Dialysis prior to treatment Units: Number of days			
arithmetic mean	5		
standard deviation	± 11.27	-	
PE/PI prior to treatment Units: Number of Days			
arithmetic mean	4.3		
standard deviation	± 2.3	-	
Duration from Onset of PE/PI to initiation of eculizumab at baseline Units: days			
arithmetic mean	6.7		
standard deviation	± 9.06	-	
Duration from onset of diarrhea to onset of PE/PI at baseline Units: days			
arithmetic mean	7		

standard deviation	± 2.54	-	
Duration from onset of diarrhea to initiation of eculizumab at baseline			
Units: days			
arithmetic mean	12.7		
standard deviation	± 9.36	-	
Modified Rankin Score at Baseline			
Units: Modified Rankin Score			
arithmetic mean	3.7		
standard deviation	± 1.18	-	
Baseline Creatinine			
Units: micromole(s)/litre			
arithmetic mean	217.3		
standard deviation	± 102.57	-	
Baseline eGFR			
eGFR are presented for patients with kidney involvement who were not on dialysis at baseline.			
Units: mL/min/1.73m^2			
arithmetic mean	34		
standard deviation	± 16.29	-	
Baseline haemoglobin			
Units: gram(s)/litre			
arithmetic mean	84.5		
standard deviation	± 15.94	-	
Baseline Lactate Dehydrogenase			
Units: U/L			
arithmetic mean	844.4		
standard deviation	± 459.84	-	
Baseline Platelets			
Units: 10^9/L			
arithmetic mean	78.2		
standard deviation	± 65.33	-	
Baseline White Blood Cells			
Units: 10^9/L			
arithmetic mean	14		
standard deviation	± 6.86	-	

End points

End points reporting groups

Reporting group title	eculizumab

Reporting group description:

A total of 196 patients were retrospectively enrolled after signing ICF. All received commercially available eculizumab prior to enrollment and at least 1 dose of eculizumab as investigational product following study entry. Two patients were enrolled prospectively. This represents the IIT/safety population.

Fixed dosing of eculizumab based on body weight cohorts were administered. Adjustment of dose to accommodate patient growth was possible.

Primary: Improvement in systemic TMA and vital organ at Wk 8

End point title	Improvement in systemic TMA and vital organ at Wk 8[1]

End point description:

It consists of complete and partial responders, as defined below:

- Complete Responder: (i) Hematologic Normalization (platelet count ≥150 x 10^9/L at any 2 consecutive measures); (ii) Clinically important improvement in all of the affected major vital organs: brain, kidney, thrombosis when abnormal at baseline and with baseline abnormality plausibly related to EHEC event; and (iii) no clinically important worsening in Brain, Kidney, Thrombosis.

- Partial Responder: (i) Hematologic Improvement (>25% increase in platelet count at any 2 consecutive measures) or Hematologic Normalization; (ii) Clinically important improvement in none, one, or more affected major organs: brain, kidney and thrombosis when abnormal at baseline and when baseline abnormality plausibly related to the STEC event; and (iii) no clinically important worsening in Brain, Kidney, Thrombosis.

End point type	Primary

End point timeframe:

Through Week 8

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: The system does not support statistical analyses for a single arm trial.

End point values	eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	198			
Units: Percentage of patients				
number (confidence interval 95%)				
Complete response	80.3 (74.1 to 85.6)			
Partial response	94.4 (90.3 to 97.2)			

Statistical analyses

No statistical analyses for this end point

Primary: Improvement in systemic TMA and vital organ at Wk 28

End point title	Improvement in systemic TMA and vital organ at Wk 28[2]

End point description:

Evidence for sustained response to eculizumab continuing after the end of the dosing period was evaluated by the global assessment of efficacy defined as response rate (CR+PR) at Week 28.

End point type	Primary

End point timeframe:

28 weeks

Notes:

[2] - 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: The system does not support statistical analyses for a single arm trial.

End point values	eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	198			
Units: Percentage of patients				
number (confidence interval 95%)				
Complete response	88.9 (83.7 to 92.9)			
Partial response	94.4 (90.3 to 97.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: New Ventilator Requirement

End point title	New Ventilator Requirement

End point description:

End point type	Secondary

End point timeframe:

Week 8 and week 28

End point values	eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	198			
Units: percent				
number (confidence interval 95%)				
Week 8	6.1 (3.2 to 10.3)			
Week 28	6.1 (3.2 to 10.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: New Dialysis After Day 14 of eculizumab treatment

End point title	New Dialysis After Day 14 of eculizumab treatment

End point description:

End point type	Secondary

End point timeframe:

Week 8 and week 28

End point values	eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	53			
Units: Percentage of patients				
number (confidence interval 95%)				
Week 8	0 (0 to 6.7)			
Week 28	0 (0 to 6.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Hematological Normalization and No New Organ Involvement

End point title	Hematological Normalization and No New Organ Involvement

End point description:

End point type	Secondary

End point timeframe:

Week 8 and week 28

End point values	eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	198			
Units: Percentage of patients				
number (confidence interval 95%)				
Week 8	91.4 (86.6 to 94.9)			
Week 28	92.9 (88.4 to 96.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Hematological Normalization

End point title	Hematological Normalization

End point description:

Platelet ≥ 150x10^9/L for any two measures (all patients)

End point type	Secondary

End point timeframe:

Week 8 and week 28

End point values	eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	198			
Units: Percentage of patients				
number (confidence interval 95%)				
Week 8	97 (93.5 to 98.9)			
Week 28	98.5 (95.6 to 99.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Hematological Normalization

End point title	Hematological Normalization

End point description:

Platelet ≥ 150x10^9/L for any two measures (patients with platelets <150 x 10^9/L at Baseline)

End point type	Secondary

End point timeframe:

At week 8 and 28

End point values	eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	174			
Units: Percentage of patients				
number (confidence interval 95%)				
Week 8	96.6 (92.6 to 98.7)			
Week 28	98.3 (95 to 99.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Global Assessement of Neurological Function : Clinically Important Improvement

End point title	Global Assessement of Neurological Function : Clinically Important Improvement

End point description:

Clinically important improvement is assessed in patients with the associated organ involvement at baseline.
Results in the PP population were found to be similar to those of the ITT population, so only the ITT results are shown for all secondary endpoint assessments.

End point type	Secondary

End point timeframe:

At week 8, week 16 and week 28

End point values	eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	152			
Units: Percentage of patients				
number (confidence interval 95%)				
Week 8	88.8 (82.7 to 93.3)			
Week 16	94.7 (89.9 to 97.7)			
Week 28	96.1 (91.6 to 98.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Global Assessment of Neurological Function : Clinically Important Worsening

End point title	Global Assessment of Neurological Function : Clinically Important Worsening

End point description:

Results in the PP population were found to be similar to those of the ITT population, so only the ITT results are shown for all secondary endpoint assessments.
Clinically important worsening is assessed in all patients.

End point type	Secondary

End point timeframe:

At week 8, week 16 and week 28

End point values	eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	193			
Units: Percentage of patients				
number (confidence interval 95%)				
Week 8	2.1 (0.6 to 5.2)			
Week 16	2.1 (0.6 to 5.2)			
Week 28	2.1 (0.6 to 5.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Global Assessment of Renal Function : Clinically Important Improvement

End point title	Global Assessment of Renal Function : Clinically Important Improvement

End point description:

Clinically important improvement is assessed in patients with the associated organ involvement at baseline.

End point type	Secondary

End point timeframe:

At week 8, week 16 and week 28

End point values	eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	182			
Units: Percentage of patients				
number (confidence interval 95%)				
Week 8	96.2 (92.2 to 98.4)			
Week 16	98.4 (95.3 to 99.7)			
Week 28	98.9 (96.1 to 99.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Global Assessment of Renal Function : Clinically Important Worsening

End point title	Global Assessment of Renal Function : Clinically Important Worsening

End point description:

Clinically important worsening is assessed in all patients.
In the ITT population, 137 patients could not be assessed for clinically important worsening in renal function as they were on dialysis at baseline.

End point type	Secondary

End point timeframe:

At week 8, week 16 and week 28

End point values	eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	61			
Units: Percentage of patients				
number (confidence interval 95%)				
Week 8	4.9 (1 to 13.7)			
Week 16	4.9 (1 to 13.7)			
Week 28	4.9 (1 to 13.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: TMA event-free statut for > 6 weeks

End point title	TMA event-free statut for > 6 weeks

End point description:

TMA event-free status for >6 weeks: defined as no plasma therapy, no ≥25% decrease in platelet count, and no new dialysis.
The cumulative incidence was estimated using the cumulative distribution function (CDF).

End point type	Secondary

End point timeframe:

Up to Week 28

End point values	eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	198			
Units: Percentage of patients				
number (not applicable)				
No TMA	99.5			
Censored	0.5			

Statistical analyses

No statistical analyses for this end point

Secondary: TMA intervention rate

End point title	TMA intervention rate

End point description:

TMA intervention rate defined as the number of PE/PI interventions plus the number of dialysis events per patient per day. The TMA intervention rate was calculated pretreatment and post-treatment.
Pre-treatment is from the onset of diarrhea to just prior to the first dose of eculizumab (day -1).
Post-treatment is from the first dose of eculizumab (Day 0) to the end of study follow up (or discontinuation day for discontinued patients).
P-value is calculated using a two-sided Wilcoxon signed rank test.

End point type	Secondary

End point timeframe:

Up to 28 weeks

End point values	eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	198			
Units: Percentage of patients				
arithmetic mean (standard deviation)				
Pretreatment TMA intervention rate	0.5192 (± 0.2906)			
Post-treatment TMA intervention rate	0.0549 (± 0.0784)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Improvement in systemic TMA and vital organ at Wk 8 for Patients Dosed Beyond 8 Weeks

End point title	Improvement in systemic TMA and vital organ at Wk 8 for Patients Dosed Beyond 8 Weeks

End point description:

Global assessment of efficacy (CR + PR) at Week 8 for patients who were dosed beyond Week 8
This analysis is a sub-group analysis (Intent-to-Treat Population)

End point type	Other pre-specified

End point timeframe:

8 weeks

End point values	eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	27			
Units: Percentage of patients				
number (confidence interval 95%)				
Complete response	74.1 (53.7 to 88.9)			
Partial response	85.2 (66.3 to 95.8)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Through end of study

Adverse event reporting additional description:

All AEs that occurred after the patient had given consent must have been reported and followed to satisfactory resolution or until the Principal Investigator deems the event to be chronic or the patient to be stable.
In the non SAE section below, non SAE and SAE are reported.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.0

Reporting groups

Reporting group title	eculizumab

Reporting group description:

A total of 196 patients were retrospectively enrolled after signing ICF. All received commercially available eculizumab prior to enrollment and at least 1 dose of eculizumab as investigational product following study entry. Two patients were enrolled prospectively. This represents the IIT/safety population.

Fixed dosing of eculizumab based on body weight cohorts were administered. Adjustment of dose to accommodate patient growth was possible.

Serious adverse events	eculizumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	66 / 198 (33.33%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Prostate cancer			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Haematoma			

subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Haemorrhage				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypertensive crisis				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Venous thrombosis				
subjects affected / exposed	3 / 198 (1.52%)			
occurrences causally related to treatment / all	3 / 3			
deaths causally related to treatment / all	0 / 0			
Pregnancy, puerperium and perinatal conditions				
Amniotic cavity disorder				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Complication of pregnancy				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Pyrexia				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Anaphylactic reaction				

subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Cervical dysplasia			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	3 / 198 (1.52%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			
subjects affected / exposed	2 / 198 (1.01%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary oedema			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	4 / 198 (2.02%)		
occurrences causally related to treatment / all	4 / 4		
deaths causally related to treatment / all	0 / 0		

Psychiatric disorders			
Transient psychosis			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Blood creatinine increased			
subjects affected / exposed	2 / 198 (1.01%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Ejection fraction decreased			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Platelet count decreased			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Post procedural haemorrhage			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Shunt occlusion			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Suture rupture			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Left ventricular failure			

subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Myocardial ischaemia				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tachyarrhythmia				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Aphasia				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Brain oedema				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebral infarction				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Convulsion				
subjects affected / exposed	24 / 198 (12.12%)			
occurrences causally related to treatment / all	2 / 30			
deaths causally related to treatment / all	0 / 0			
Dysaesthesia				

subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Epilepsy				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Haemorrhagic stroke				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hemianopia				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hemiparesis				
subjects affected / exposed	2 / 198 (1.01%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Neurological symptom				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Partial seizures				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anaemia				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haemolytic uraemic syndrome				

subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Heparin-induced thrombocytopenia				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Optic nerve disorder				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal adhesions				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Colonic stenosis				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal haemorrhage				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Haemorrhoidal haemorrhage				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ileus				

subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatitis				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Subileus				
subjects affected / exposed	2 / 198 (1.01%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholangitis				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cholecystitis acute				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cholelithiasis				
subjects affected / exposed	2 / 198 (1.01%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Liver disorder				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				

Angioedema				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Dermatitis allergic				
subjects affected / exposed	2 / 198 (1.01%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Urethral prolapse				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Device related infection				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haematoma infection				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infection				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	10 / 198 (5.05%)			
occurrences causally related to treatment / all	7 / 10			
deaths causally related to treatment / all	0 / 0			
Pneumonia herpes viral				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			

Pseudomonas infection			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	2 / 198 (1.01%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Staphylococcal sepsis			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Type 1 diabetes mellitus			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	eculizumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	196 / 198 (98.99%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	74 / 198 (37.37%)		
occurrences (all)	81		

Hypotension			
subjects affected / exposed	12 / 198 (6.06%)		
occurrences (all)	12		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	12 / 198 (6.06%)		
occurrences (all)	12		
Chest pain			
subjects affected / exposed	10 / 198 (5.05%)		
occurrences (all)	10		
Fatigue			
subjects affected / exposed	30 / 198 (15.15%)		
occurrences (all)	32		
Oedema			
subjects affected / exposed	29 / 198 (14.65%)		
occurrences (all)	30		
Oedema peripheral			
subjects affected / exposed	64 / 198 (32.32%)		
occurrences (all)	80		
Pyrexia			
subjects affected / exposed	25 / 198 (12.63%)		
occurrences (all)	28		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	19 / 198 (9.60%)		
occurrences (all)	21		
Dyspnoea			
subjects affected / exposed	32 / 198 (16.16%)		
occurrences (all)	34		
Pleural effusion			
subjects affected / exposed	48 / 198 (24.24%)		
occurrences (all)	51		
Alopecia			
subjects affected / exposed	69 / 198 (34.85%)		
occurrences (all)	69		
Psychiatric disorders			

Agitation subjects affected / exposed occurrences (all)	19 / 198 (9.60%) 19		
Anxiety subjects affected / exposed occurrences (all)	11 / 198 (5.56%) 12		
Depression subjects affected / exposed occurrences (all)	11 / 198 (5.56%) 11		
Disorientation subjects affected / exposed occurrences (all)	15 / 198 (7.58%) 16		
Restlessness subjects affected / exposed occurrences (all)	12 / 198 (6.06%) 12		
Sleep disorder subjects affected / exposed occurrences (all)	17 / 198 (8.59%) 18		
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all)	11 / 198 (5.56%) 11		
Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all)	12 / 198 (6.06%) 12		
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all)	13 / 198 (6.57%) 13		
Nervous system disorders Aphasia subjects affected / exposed occurrences (all)	21 / 198 (10.61%) 24		
Convulsion subjects affected / exposed occurrences (all)	28 / 198 (14.14%) 35		

Disturbance in attention			
subjects affected / exposed	11 / 198 (5.56%)		
occurrences (all)	12		
Dizziness			
subjects affected / exposed	18 / 198 (9.09%)		
occurrences (all)	20		
Headache			
subjects affected / exposed	95 / 198 (47.98%)		
occurrences (all)	102		
Myoclonus			
subjects affected / exposed	11 / 198 (5.56%)		
occurrences (all)	11		
Paraesthesia			
subjects affected / exposed	10 / 198 (5.05%)		
occurrences (all)	10		
Tremor			
subjects affected / exposed	28 / 198 (14.14%)		
occurrences (all)	29		
Insomnia			
subjects affected / exposed	20 / 198 (10.10%)		
occurrences (all)	21		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	13 / 198 (6.57%)		
occurrences (all)	13		
Leukopenia			
subjects affected / exposed	13 / 198 (6.57%)		
occurrences (all)	13		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	22 / 198 (11.11%)		
occurrences (all)	24		
Eye disorders			
Diplopia			
subjects affected / exposed	10 / 198 (5.05%)		
occurrences (all)	10		
Vision blurred			

subjects affected / exposed	12 / 198 (6.06%)		
occurrences (all)	12		
Visual impairment			
subjects affected / exposed	10 / 198 (5.05%)		
occurrences (all)	10		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	26 / 198 (13.13%)		
occurrences (all)	27		
Abdominal pain upper			
subjects affected / exposed	14 / 198 (7.07%)		
occurrences (all)	14		
Ascites			
subjects affected / exposed	15 / 198 (7.58%)		
occurrences (all)	15		
Constipation			
subjects affected / exposed	20 / 198 (10.10%)		
occurrences (all)	20		
Diarrhoea			
subjects affected / exposed	21 / 198 (10.61%)		
occurrences (all)	23		
Flatulence			
subjects affected / exposed	13 / 198 (6.57%)		
occurrences (all)	13		
Nausea			
subjects affected / exposed	61 / 198 (30.81%)		
occurrences (all)	66		
Vomiting			
subjects affected / exposed	44 / 198 (22.22%)		
occurrences (all)	46		
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	10 / 198 (5.05%)		
occurrences (all)	10		
Renal and urinary disorders			

Nocturia			
subjects affected / exposed	17 / 198 (8.59%)		
occurrences (all)	17		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	22 / 198 (11.11%)		
occurrences (all)	26		
Back pain			
subjects affected / exposed	21 / 198 (10.61%)		
occurrences (all)	22		
Myalgia			
subjects affected / exposed	14 / 198 (7.07%)		
occurrences (all)	19		
Pain in extremity			
subjects affected / exposed	10 / 198 (5.05%)		
occurrences (all)	10		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	31 / 198 (15.66%)		
occurrences (all)	33		
Pneumonia			
subjects affected / exposed	19 / 198 (9.60%)		
occurrences (all)	21		
Urinary tract infection			
subjects affected / exposed	22 / 198 (11.11%)		
occurrences (all)	23		
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	11 / 198 (5.56%)		
occurrences (all)	11		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported