Clinical trial results:
AN OPEN-LABEL, MULTI-CENTER CONTROLLED CLINICAL TRIAL OF ECULIZUMAB IN ADULT PATIENTS WITH PLASMA THERAPY-RESISTANT ATYPICAL HEMOLYTIC-UREMIC SYNDROME (AHUS)

Summary

EudraCT number	2008-006952-23
Trial protocol	DE NL SE AT FR ES GB IT
Global end of trial date	17 October 2011

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	C08-002A

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00844545
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)	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	01 July 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 October 2011
Global end of trial reached?	Yes
Global end of trial date	17 October 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the effect of eculizumab to reduce TMA as measured by platelet count change from baseline (BL) during the Treatment Period (26 weeks) in patients with plasma therapy (PT)-resistant aHUS (protocol defined), including assessment of the proportion of patients who achieved Platelet Count Normalization from baseline through 26 weeks. Platelet Count Normalization was defined as the platelet count observed to be ≥150 x 10^9/L on at least two consecutive measurements which span a period of at least four weeks.

Protection of trial subjects:

Patients must have been vaccinated at least 14 days prior to receiving the first dose of eculizumab, or be vaccinated and receive treatment with appropriate antibiotics until 14 days after the vaccination.

Background therapy:

No background therapy was used in this trial.

Evidence for comparator:

Each patient served as his/her own control.

Actual start date of recruitment	24 July 2009
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	Austria: 1
Country: Number of subjects enrolled	France: 6
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	United States: 7
Worldwide total number of subjects	17
EEA total number of subjects	10

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)	1
Adults (18-64 years)	15
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Results from Study C08-002A were combined with results from another study, Study C08-002B. Study C08-002A (2008-006952-23) was conducted in adults (n=16) and Study C08-002B (2008-006953-41) was conducted in adolescents (n=1). Combined results from these 2 studies are reported here.

Pre-assignment

Screening details:

Patients had to exhibit a decrease in platelet count despite at least 4 Plasma Therapy (PT) treatments in the 1 week immediately prior to screening. Patients who met the eligibility criteria during screening were enrolled into the Treatment Period which commenced with the first eculizumab dose.

Pre-assignment period milestones

Number of subjects started	17
Number of subjects completed	17

Period 1

Period 1 title	Treatment Period (26 Weeks)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Eculizumab

Arm description:

All patients received open-label eculizumab administered intravenously on the following dose schedule: Induction dose - 900 mg per week for four weeks and a dose of 1200 mg one week later; Maintenance dose – 1200 mg every two weeks. Patients who received plasma exchange or infusion during the eculizumab treatment period received a supplemental dose of 600 mg within one hour before plasma infusion or within one hour after the completion of each plasma exchange.

The intent-to-treat (ITT) population was defined as all patients who received any amount of eculizumab, and were considered evaluable for safety and efficacy analyses. For both the efficacy and safety analyses, all 17 patients who were treated with study drug were included in the ITT population.

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:

Induction dose - 900 mg per week for four weeks and a dose of 1200 mg one week later.
Maintenance dose – 1200 mg every two weeks.

Patients who received plasma exchange or infusion during the eculizumab treatment period received a supplemental dose of 600 mg within one hour before plasma infusion or within one hour after the completion of each plasma exchange.

Number of subjects in period 1	Eculizumab
Started	17
Completed	15
Not completed	2
Adverse event, non-fatal	1
Protocol deviation	1

Period 2

Period 2 title	Extension Treatment Period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Eculizumab

Arm description:

Long-term follow-up of patients receiving eculizumab

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:

Induction dose - 900 mg per week for four weeks and a dose of 1200 mg one week later.
Maintenance dose – 1200 mg every two weeks.

Patients who received plasma exchange or infusion during the eculizumab treatment period received a supplemental dose of 600 mg within one hour before plasma infusion or within one hour after the completion of each plasma exchange.

Number of subjects in period 2[1]	Eculizumab
Started	13
Completed	11
Not completed	2
Adverse event, non-fatal	2

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: This extension treatment period is open to patients willing to continue to receive eculizumab until the product is registered and available. 13 patients out of the 17 that were enrolled

entered this extension treatment period.

Period 3	
Period 3 title	Post Treatment Period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Post-treatment arm

Arm description:

Patients who discontinued eculizumab treatment at any time during the study were followed for 8 weeks after discontinuing eculizumab treatment.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 3[2]	Post-treatment arm
Started	6
Completed	5
Not completed	1
Consent withdrawn by subject	1

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: This period is open only to patients who discontinued eculizumab at any time during the study. 6 patients out of the 17 patients who received eculizumab discontinued treatment and entered this post-treatment period.

Baseline characteristics

Reporting groups	
Reporting group title	Eculizumab

Reporting group description:

All patients received open-label eculizumab administered intravenously on the following dose schedule: Induction dose - 900 mg per week for four weeks and a dose of 1200 mg one week later; Maintenance dose – 1200 mg every two weeks. Patients who received plasma exchange or infusion during the eculizumab treatment period received a supplemental dose of 600 mg within one hour before plasma infusion or within one hour after the completion of each plasma exchange.

The intent-to-treat (ITT) population was defined as all patients who received any amount of eculizumab, and were considered evaluable for safety and efficacy analyses. For both the efficacy and safety analyses, all 17 patients who were treated with study drug were included in the ITT population.

Reporting group values	Eculizumab	Total	
Number of subjects	17	17	
Age categorical Units: Subjects			
Adolescents (12-17 years)	1	1	
Adults (18-64 years)	15	15	
From 65-84 years	1	1	
Age continuous Units: years			
arithmetic mean	31.8		
standard deviation	± 13.32	-	
Gender categorical Units: Subjects			
Female	12	12	
Male	5	5	
Race Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	1	1	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	1	1	
White	15	15	
More than one race	0	0	
Unknown or Not Reported	0	0	
Platelet Category Units: Subjects			
< 150 x10^9/L	15	15	
>= 150 x10^9/L	2	2	
LDH category Units: Subjects			
> ULN	10	10	
<= ULN	7	7	
eGFR category Units: Subjects			
< 15	7	7	

15 ≤ 30	5	5	
30 ≤ 45	4	4	
45 ≤ 60	1	1	
CKD Units: Subjects			
Stage 3a	1	1	
Stage 3b	4	4	
Stage 4	5	5	
Stage 5	7	7	
Platelet count Units: x10^9/L			
arithmetic mean	109.03		
standard deviation	± 32.07	-	
LDH Units: U/L			
arithmetic mean	322.5		
standard deviation	± 138.15	-	
Creatinine Units: micromole(s)/litre			
arithmetic mean	351.5		
standard deviation	± 214.92	-	
eGFR Units: mL/min/1.73*m^2			
arithmetic mean	22.9		
standard deviation	± 14.54	-	

End points

End points reporting groups

Reporting group title	Eculizumab

Reporting group description:

All patients received open-label eculizumab administered intravenously on the following dose schedule: Induction dose - 900 mg per week for four weeks and a dose of 1200 mg one week later; Maintenance dose – 1200 mg every two weeks. Patients who received plasma exchange or infusion during the eculizumab treatment period received a supplemental dose of 600 mg within one hour before plasma infusion or within one hour after the completion of each plasma exchange.

The intent-to-treat (ITT) population was defined as all patients who received any amount of eculizumab, and were considered evaluable for safety and efficacy analyses. For both the efficacy and safety analyses, all 17 patients who were treated with study drug were included in the ITT population.

Reporting group title	Eculizumab

Reporting group description:

Long-term follow-up of patients receiving eculizumab

Reporting group title	Post-treatment arm

Reporting group description:

Patients who discontinued eculizumab treatment at any time during the study were followed for 8 weeks after discontinuing eculizumab treatment.

Primary: Platelet Count Change From Baseline to 26 Weeks

End point title	Platelet Count Change From Baseline to 26 Weeks[1]

End point description:

End point type	Primary

End point timeframe:

From Baseline to 26 weeks

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: This trial is a single arm trial and the system dose not support statistical analyses for single arm trial.

End point values	Eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: 10^9 cells/L				
least squares mean (confidence interval 95%)	65.18 (37.01 to 93.36)			

Statistical analyses

No statistical analyses for this end point

Primary: Proportion of Patients With Platelet Count Normalization

End point title	Proportion of Patients With Platelet Count Normalization[2]

End point description:

The primary objective of the study (per protocol) was to assess the effect of eculizumab to reduce TMA as measured by platelet count change from baseline (BL) during the Treatment Period (26 weeks) in patients with plasma therapy (PT)-resistant aHUS (protocol defined), including assessment of the proportion of patients who achieved Platelet Count Normalization from baseline through 26 weeks. Platelet Count Normalization was defined as the platelet count observed to be ≥150 x 10^9/L on at least two consecutive measurements which span a period of at least four weeks.

End point type	Primary

End point timeframe:

Through 26 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: This trial is a single arm trial and the system dose not support statistical analyses for single arm trial.

End point values	Eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: Percentage of Participants				
number (confidence interval 95%)	82 (57 to 96)			

Statistical analyses

No statistical analyses for this end point

Primary: Proportion of Patients With Hematologic Normalization

End point title	Proportion of Patients With Hematologic Normalization[3]

End point description:

Hematologic Normalization was defined as normalization of both platelet count and lactic dehydrogenase (LDH) sustained for at least two consecutive measurements which spanned a period of at least four weeks.

End point type	Primary

End point timeframe:

Through 26 weeks

Notes:

[3] - 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: This trial is a single arm trial and the system dose not support statistical analyses for single arm trial.

End point values	Eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: Percentage of Participants				
number (confidence interval 95%)	76 (50 to 93)			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Patients With Complete TMA Response

End point title	Proportion of Patients With Complete TMA Response

End point description:

The proportion of patients who achieved a Complete TMA Response from baseline through 26 weeks of treatment with eculizumab was determined. Complete TMA Response was defined as Hematologic Normalization plus improvement in renal function (defined as ≥ 25% reduction from baseline in serum creatinine), which was sustained for two consecutive measurements over a period of at least four weeks.

End point type	Secondary

End point timeframe:

Through 26 weeks

End point values	Eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: Percentage of Participants				
number (confidence interval 95%)	65 (38 to 86)			

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 (# PE/PI and # Dialysis Events/Patient/Day) in the eculizumab treatment period (from baseline through 26 weeks) for PE/PI and (from the fifteenth day following the first eculizumab dose through 26 weeks) for new dialysis events was compared with the TMA Intervention Rate during the pre-eculizumab treatment period.

End point type	Secondary

End point timeframe:

Through 26 weeks

End point values	Eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: # events/patient/day				
arithmetic mean (standard deviation)	0.04 (± 0.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Platelet Count Change From Baseline to 156 Weeks

End point title	Platelet Count Change From Baseline to 156 Weeks

End point description:

End point type	Secondary

End point timeframe:

From Baseline to 156 Weeks

End point values	Eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: 10^9 cells/L				
least squares mean (confidence interval 95%)	111.62 (98.12 to 125.13)			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Patients With Platelet Count Normalization

End point title	Proportion of Patients With Platelet Count Normalization

End point description:

Platelet Count Normalization was defined as the platelet count observed to be ≥150 x 10^9/L on at least two consecutive measurements which span a period of at least four weeks.

End point type	Secondary

End point timeframe:

Through End of Study, Median Exposure 100.29 Weeks

End point values	Eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: Percentage of Participants				
number (confidence interval 95%)	88 (64 to 99)			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Patients With Hematologic Normalization

End point title	Proportion of Patients With Hematologic Normalization

End point description:

End point type	Secondary

End point timeframe:

Through End of Study, Median Exposure 100.29 Weeks

End point values	Eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: Percentage of Participants				
number (confidence interval 95%)	88 (64 to 99)			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Patients With Complete TMA Response

End point title	Proportion of Patients With Complete TMA Response

End point description:

The proportion of patients who achieved a Complete TMA Response from baseline through end of the study was determined. Complete TMA Response was defined as Hematologic Normalization plus improvement in renal function (defined as ≥25% reduction from baseline in serum creatinine), which was sustained for two consecutive measurements over a period of at least four weeks.

End point type	Secondary

End point timeframe:

Through End of Study, Median Exposure 100.29 Weeks

End point values	Eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: Percentage of Participants				
number (confidence interval 95%)	76 (50 to 93)			

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 (# PE/PI and # Dialysis Events/Patient/Day) in the eculizumab treatment period (from baseline through end of the study) for PE/PI and (from the fifteenth day following the first eculizumab dose through end of the study) for new dialysis events was compared with the TMA Intervention Rate during the pre-eculizumab treatment period.

End point type	Secondary

End point timeframe:

Through End of Study, Median Exposure 100.29 Weeks

End point values	Eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: # events/patient/day				
arithmetic mean (standard deviation)	0.04 (± 0.11)			

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK) and Pharmacodynamics (PD); Minimum and Maximum Blood Concentration

End point title	Pharmacokinetics (PK) and Pharmacodynamics (PD); Minimum and Maximum Blood Concentration

End point description:

PK parameters Cmin and Cmax were estimated using a population PK model developed from the observed PK concentration data.

End point type	Secondary

End point timeframe:

Induction Phase for 4 weeks followed by Maintenance Phase starting on Week 5 through 26 weeks or longer

End point values	Eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: microgram(s)/millilitre				
arithmetic mean (standard deviation)				
max concentration during induction period	145.16 (± 26.56)			
min concentration during induction period	93.66 (± 22.1)			
max concentration during maintenance	345.14 (± 89.74)			
min concentration during maintenance	151.8 (± 68.16)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Through end of study; Exposure to eculizumab in this study extended for a median of 100 weeks and ranged from two weeks to 186 weeks.

Adverse event reporting additional description:

At every visit, patients were asked a standard non-leading question to elicit any changes in their medical well-being including inquiry about any hospitalization, accidents, and new or changed concomitant medication regimens. AEs were also documented from any data collected (e.g. laboratory values, physical examination findings, ECG changes, etc.).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.1

Reporting groups

Reporting group title	Eculizumab

Reporting group description:

All patients received open-label eculizumab administered intravenously on the following dose schedule: Induction dose - 900 mg per week for four weeks and a dose of 1200 mg one week later; Maintenance dose – 1200 mg every two weeks. Patients who received plasma exchange or infusion during the eculizumab treatment period received a supplemental dose of 600 mg within one hour before plasma infusion or within one hour after the completion of each plasma exchange.

Serious adverse events	Eculizumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 17 (100.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Vascular disorders			
Accelerated hypertension			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Embolism venous			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypertension			
subjects affected / exposed	3 / 17 (17.65%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		

Malignant hypertension			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Transplant rejection			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Alcohol withdrawal syndrome			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Respiratory fume inhalation disorder			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Pericardial effusion				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Convulsion				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Headache				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Posterior reversible encephalopathy syndrome				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anaemia				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haemolytic anaemia				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haemolytic uraemic syndrome				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Leukopenia				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Pancytopenia			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastritis			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ileus			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Oesophagitis			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pancreatitis acute			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal failure acute			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal impairment			
subjects affected / exposed	3 / 17 (17.65%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Systemic lupus erythematosus			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Asymptomatic bacteriuria			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchitis			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Escherichia sepsis			

subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Upper respiratory tract infection			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Varicella			
subjects affected / exposed	1 / 17 (5.88%)		
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	Eculizumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 17 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Vascular disorders			
Haematoma			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Hypertension			

subjects affected / exposed	7 / 17 (41.18%)		
occurrences (all)	8		
Hypotension			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Orthostatic hypotension			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Poor venous access			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Thrombophlebitis superficial			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Surgical and medical procedures			
Tooth extraction			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	3 / 17 (17.65%)		
occurrences (all)	3		
Chest discomfort			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Chest pain			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Cyst			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Face oedema			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Fatigue			

subjects affected / exposed	3 / 17 (17.65%)		
occurrences (all)	3		
Influenza like illness			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Oedema			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Oedema peripheral			
subjects affected / exposed	5 / 17 (29.41%)		
occurrences (all)	5		
Pain			
subjects affected / exposed	3 / 17 (17.65%)		
occurrences (all)	3		
Pyrexia			
subjects affected / exposed	3 / 17 (17.65%)		
occurrences (all)	4		
Tenderness			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Thirst			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Seasonal allergy			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Reproductive system and breast disorders			
Adenomyosis			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	2		
Breast calcifications			

subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Cervical dysplasia			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Menorrhagia			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Metrorrhagia			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	2		
Ovarian cyst			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Uterine malposition			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Vulvovaginal discomfort			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 17 (23.53%)		
occurrences (all)	4		
Dyspnoea			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Dyspnoea exertional			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Emphysema			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Epistaxis			

subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Nasal congestion			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Nasal septum deviation			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Pleural effusion			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Productive cough			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Rhinorrhoea			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Sinus congestion			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Upper-airway cough syndrome			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Psychiatric disorders			
Alcoholism			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Anxiety			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Depression			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		

Dysthymic disorder subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Insomnia subjects affected / exposed occurrences (all)	4 / 17 (23.53%) 4		
Nervousness subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Sleep disorder subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Investigations Antibiotic resistant Staphylococcus test positive subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Blood lactate dehydrogenase increased subjects affected / exposed occurrences (all)	2 / 17 (11.76%) 2		
Carbon dioxide abnormal subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Haematocrit decreased subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Haemoglobin decreased subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Haptoglobin decreased subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Reticulocyte count increased subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Vitamin D decreased			

subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Weight decreased			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Arteriovenous fistula aneurysm			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Contusion			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Excoriation			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Eye injury			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Incision site oedema			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Laceration			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Muscle rupture			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Vascular graft complication			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Cardiac disorders			
Bradycardia			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Pericardial effusion			

subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Nervous system disorders			
Ageusia			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Dizziness			
subjects affected / exposed	3 / 17 (17.65%)		
occurrences (all)	3		
Headache			
subjects affected / exposed	7 / 17 (41.18%)		
occurrences (all)	7		
Lethargy			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Loss of consciousness			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Migraine			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Paraesthesia			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Presyncope			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Sinus headache			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Syncope			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		

Tremor			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	6 / 17 (35.29%)		
occurrences (all)	6		
Iron deficiency anaemia			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Leukopenia			
subjects affected / exposed	3 / 17 (17.65%)		
occurrences (all)	4		
Lymphopenia			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Neutropenia			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Thrombocytopenia			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Cerumen impaction			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Vertigo			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Eye disorders			
Cataract			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Conjunctival haemorrhage			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Conjunctival hyperaemia			

subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Conjunctivitis			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Eye pain			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Photophobia			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	2		
Abdominal pain upper			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Dental caries			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Diarrhoea			
subjects affected / exposed	8 / 17 (47.06%)		
occurrences (all)	8		
Food poisoning			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Gastritis			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Gastrointestinal pain			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Glossodynia			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		

Haemorrhoids			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Impaired gastric emptying			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	5 / 17 (29.41%)		
occurrences (all)	5		
Oral pain			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Rectal haemorrhage			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Toothache			
subjects affected / exposed	3 / 17 (17.65%)		
occurrences (all)	3		
Vomiting			
subjects affected / exposed	8 / 17 (47.06%)		
occurrences (all)	8		
Hepatobiliary disorders			
Cholestasis			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Hepatocellular injury			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Dermatitis contact			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Dry skin			

subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Erythema			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Increased tendency to bruise			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Rash			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Skin depigmentation			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Skin disorder			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Skin irritation			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Skin lesion			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Urticaria			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Haematuria			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	2		

Nephropathy toxic subjects affected / exposed occurrences (all) Pollakiuria subjects affected / exposed occurrences (all) Proteinuria subjects affected / exposed occurrences (all) Renal failure acute subjects affected / exposed occurrences (all) Renal impairment subjects affected / exposed occurrences (all) Renal pain subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1 1 / 17 (5.88%) 1 2 / 17 (11.76%) 2 1 / 17 (5.88%) 1 2 / 17 (11.76%) 5 1 / 17 (5.88%) 1		
Endocrine disorders Cushingoid subjects affected / exposed occurrences (all) Hyperparathyroidism secondary subjects affected / exposed occurrences (all) Hypothalamo-pituitary disorder subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1 1 / 17 (5.88%) 1 1 / 17 (5.88%) 1		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Bone pain	1 / 17 (5.88%) 1 3 / 17 (17.65%) 3		

subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Flank pain			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Intervertebral disc degeneration			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Joint swelling			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Muscle spasms			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Myalgia			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Neck pain			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Osteopenia			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Systemic lupus erythematosus			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Tendonitis			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Infections and infestations			
Abscess			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		

Bronchitis				
subjects affected / exposed	4 / 17 (23.53%)			
occurrences (all)	4			
Campylobacter infection				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Cystitis				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Ear infection				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Fungal infection				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Gastroenteritis				
subjects affected / exposed	3 / 17 (17.65%)			
occurrences (all)	3			
Genital herpes				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Haemophilus infection				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Herpes zoster				
subjects affected / exposed	2 / 17 (11.76%)			
occurrences (all)	2			
Impetigo				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Influenza				
subjects affected / exposed	2 / 17 (11.76%)			
occurrences (all)	2			
Lower respiratory tract infection				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			

Nasopharyngitis				
subjects affected / exposed	3 / 17 (17.65%)			
occurrences (all)	3			
Onychomycosis				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Papilloma viral infection				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Pharyngitis				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Pharyngitis streptococcal				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Rhinitis				
subjects affected / exposed	3 / 17 (17.65%)			
occurrences (all)	3			
Sinusitis				
subjects affected / exposed	2 / 17 (11.76%)			
occurrences (all)	2			
Staphylococcal infection				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Tonsillitis				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Tooth abscess				
subjects affected / exposed	2 / 17 (11.76%)			
occurrences (all)	2			
Tooth infection				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Tracheobronchitis				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			

Upper respiratory tract infection subjects affected / exposed occurrences (all)	4 / 17 (23.53%) 5		
Urinary tract infection subjects affected / exposed occurrences (all)	6 / 17 (35.29%) 6		
Urinary tract infection bacterial subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Metabolism and nutrition disorders Acidosis subjects affected / exposed occurrences (all)	2 / 17 (11.76%) 2		
Dehydration subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Dyslipidaemia subjects affected / exposed occurrences (all)	2 / 17 (11.76%) 2		
Fluid overload subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Fluid retention subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Hyperkalaemia subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Hyperphosphataemia subjects affected / exposed occurrences (all)	2 / 17 (11.76%) 2		
Hyperlipidaemia subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Hypocalcaemia			

subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Hypokalaemia			
subjects affected / exposed	3 / 17 (17.65%)		
occurrences (all)	3		
Hypomagnesaemia			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Iron deficiency			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Metabolic acidosis			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Obesity			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Vitamin D deficiency			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 September 2009	Protocol version 2.0
26 August 2010	Protocol version 3.0

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/23738544