



Clinical trial results:

An Open-Label, Multi-Center Clinical Trial Of Eculizumab In Adult Patients With Atypical Hemolytic-Uremic Syndrome

Summary

EudraCT number	2010-020326-18
Trial protocol	GB DE FR BE ES NL IT
Global end of trial date	31 October 2013

Results information

Result version number	v1 (current)
This version publication date	29 July 2016
First version publication date	29 July 2016

Trial information

Trial identification

Sponsor protocol code	C10-004
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01194973
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	11 February 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 October 2013
Global end of trial reached?	Yes
Global end of trial date	31 October 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of eculizumab in adult patients with aHUS to control TMA as characterized by thrombocytopenia, hemolysis and renal impairment.

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: -

Actual start date of recruitment	24 August 2010
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: 2
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	France: 18
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	United States: 8
Worldwide total number of subjects	41
EEA total number of subjects	33

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	38
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 44 patients diagnosed with aHUS signed the informed consent and of these, 41 patients were treated. Three patients were excluded from the study due to failed screening procedure and did not receive eculizumab.

Pre-assignment

Screening details:

Patients had to have signs or symptoms of hemolysis; serum creatinine level \geq ULN and platelet count $<$ LLN.

Pre-assignment period milestones

Number of subjects started	44 ^[1]
Number of subjects completed	41

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Screen failure: 3
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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: Informed consent form was obtained for 44 patients. Of these 44 patients, 41 were treated in the study. The 3 other patients were considered as screen failure.

Period 1

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

Arms

Arm title	eculizumab
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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.

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	41
Completed	38
Not completed	3
Adverse event, non-fatal	1
Pregnancy	1
Lack of efficacy	1

Period 2

Period 2 title	Post Treatment Period (discontinuation)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	eculizumab
Arm description: Patients who discontinue eculizumab treatment at any time during the study will be followed for one year.	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 2 ^[2]	eculizumab
Started	11
Completed	11

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: Patients who discontinued eculizumab treatment at any time were to be followed for one year. It concerned 11 patients: 3 were withdrawn from the study, and 8 completed the study and were not transitioned to commercial eculizumab.

Baseline characteristics

Reporting groups

Reporting group title	eculizumab
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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.

Reporting group values	eculizumab	Total	
Number of subjects	41	41	
Age categorical			
Units: Subjects			
Adults (18-64 years)	38	38	
From 65-84 years	3	3	
Age continuous			
Units: years			
arithmetic mean	40.3		
standard deviation	± 15.33	-	
Gender categorical			
Units: Subjects			
Female	28	28	
Male	13	13	
Race			
Units: Subjects			
Asian	1	1	
American Indian or Alaska Native	0	0	
Black or African American	2	2	
Native Hawaiian or Other Pacific Islander	0	0	
White	38	38	
More than one race	0	0	
Unknown or Not Reported	0	0	
Platelet category			
Units: Subjects			
< 150 x10 ⁹ /L	27	27	
>= 150 x10 ⁹ /L	14	14	
LDH category			
Units: Subjects			
<= ULN	9	9	
> ULN	32	32	
eGFR			
Units: Subjects			
<15 mL/min/1.73*m ²	27	27	
15-29 mL/min/1.73*m ²	6	6	
30-44 mL/min/1.73*m ²	6	6	
45-59 mL/min/1.73*m ²	2	2	
60-89 mL/min/1.73*m ²	0	0	

>=90 mL/min/1.73*m ²	0	0	
CKD			
Units: Subjects			
Stage 0	0	0	
Stage 1	0	0	
Stage 2	0	0	
Stage 3a	2	2	
Stage 3b	6	6	
Stage 4	6	6	
Stage 5	27	27	
Plasma Therapy Duration			
Units: Subjects			
< 2 months	36	36	
>= 2 months	5	5	
Clinical TMA manifestation			
Units: Subjects			
First clinical	30	30	
Multiple	11	11	
Platelet count			
Units: x10 ⁹ /L			
arithmetic mean	119.1		
standard deviation	± 66.09	-	
LDH			
Units: U/L			
arithmetic mean	492.9		
standard deviation	± 500.86	-	
Hemoglobin			
Units: g/L			
arithmetic mean	88.5		
standard deviation	± 16.82	-	
Creatinine			
Units: umol/L			
arithmetic mean	411		
standard deviation	± 264.59	-	

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.	
Reporting group title	eculizumab
Reporting group description:	
Patients who discontinue eculizumab treatment at any time during the study will be followed for one year.	

Primary: Proportion of Patients With Complete TMA Response

End point title	Proportion of Patients With Complete TMA Response ^[1]
End point description:	
Proportion of Patients with Complete TMA response was determined and defined by normalization of hematological parameters (platelet count and LDH) and preservation of renal function (defined as < 25% increase in serum creatinine from baseline) which were sustained for at least two consecutive measurements obtained at least four weeks apart	
End point type	Primary
End point timeframe:	
Through 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 study is a single arm trial and the system did not support statistical analyses for this single arm trial.	

End point values	eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: Percentage of Participants				
number (confidence interval 95%)	73.2 (57.1 to 85.8)			

Statistical analyses

No statistical analyses for this end point

Primary: Proportion of Patients With Modified Complete TMA Response

End point title	Proportion of Patients With Modified Complete TMA Response ^[2]
End point description:	
Proportion of Patients with Modified Complete TMA response through 26 weeks of treatment was determined and defined by normalization of hematological parameters (platelet count and LDH) and improvement in renal function (defined as ≥ 25% reduction from the baseline value in serum creatinine, which were sustained for at least two consecutive measurements obtained at least four weeks apart.	
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 study is a single arm trial and the system did not support statistical analyses for this single arm trial.

End point values	eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: Percentage of Participants				
number (confidence interval 95%)	56.1 (39.7 to 71.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Patients With Complete Hematologic Response

End point title	Proportion of Patients With Complete Hematologic Response
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End point description:

Proportion of Patients with Complete Hematologic response through end of study was determined and defined by normalization of platelet count and LDH sustained for at least two consecutive measurements obtained at least four weeks apart.

End point type	Secondary
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End point timeframe:

Through 26 weeks

End point values	eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: Percentage of Participants				
number (confidence interval 95%)	87.8 (73.8 to 95.9)			

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
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End point description:

Proportion of Patients with Platelet Count Normalization through 26 weeks of treatment was determined and defined as the platelet count observed to be $\geq 150 \times 10^9/L$ on at least 2 consecutive measurements which span a period of at least 4 weeks

End point type	Secondary
End point timeframe:	
Through 26 weeks	

End point values	eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: Percentage of Participants				
number (confidence interval 95%)	97.6 (87.1 to 99.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Patients With Estimated Glomerular Filtration Rate (eGFR) Improvement

End point title	Proportion of Patients With Estimated Glomerular Filtration Rate (eGFR) Improvement
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End point description:

Proportion of Patients with Estimated Glomerular Filtration Rate (eGFR) Improvement was determined and defined as an increase in eGFR by ≥ 15 mL/min/1.73m² from baseline, sustained for at least two consecutive measurements obtained at least four weeks apart.

End point type	Secondary
End point timeframe:	
Through 26 weeks	

End point values	eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: Percentage of Participants				
number (confidence interval 95%)	53.7 (37.4 to 69.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Platelet Count Change From Baseline to 26 Weeks

End point title	Platelet Count Change From Baseline to 26 Weeks
End point description:	

End point type	Secondary
End point timeframe:	
Through 26 weeks	

End point values	eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: 10 ⁹ cells/L				
least squares mean (confidence interval 95%)	117.68 (92.77 to 142.59)			

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:	
Proportion of Patients with Complete TMA response through end of study was determined and defined by normalization of hematological parameters (platelet count and LDH) and preservation of renal function (defined as < 25% increase in serum creatinine from baseline) which were sustained for at least two consecutive measurements obtained at least four weeks apart.	
End point type	Secondary
End point timeframe:	
Through End of Study, Median Exposure 52 Weeks	

End point values	eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: Percentage of Participants				
number (confidence interval 95%)	80.5 (65.1 to 91.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Patients With Modified Complete TMA Response

End point title	Proportion of Patients With Modified Complete TMA Response
End point description:	
Proportion of Patients with Modified Complete TMA response through end of study was determined and defined by normalization of hematological parameters (platelet count and LDH) and improvement in	

renal function (defined as $\geq 25\%$ reduction from the baseline value in serum creatinine, which were sustained for at least two consecutive measurements obtained at least four weeks apart.

End point type	Secondary
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End point timeframe:

Through End of Study, Median Exposure 52 Weeks

End point values	eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: Percentage of Participants				
number (confidence interval 95%)	63.4 (46.9 to 77.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Patients With Complete Hematologic Response

End point title	Proportion of Patients With Complete Hematologic Response
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End point description:

Proportion of Patients with Complete Hematologic response through end of study of treatment was determined and defined by normalization of platelet count and LDH sustained for at least two consecutive measurements obtained at least four weeks apart.

End point type	Secondary
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End point timeframe:

Through End of Study, Median Exposure 52 Weeks

End point values	eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: Percentage of Participants				
number (confidence interval 95%)	97.6 (87.1 to 99.9)			

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
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End point description:

Proportion of Patients with Platelet Count Normalization through end of study of treatment was

determined and defined as the platelet count observed to be $\geq 150 \times 10^9/L$ 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 52 Weeks	

End point values	eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: Percentage of Participants				
number (confidence interval 95%)	100 (91.4 to 100)			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Patients With Estimated Glomerular Filtration Rate (eGFR) Improvement

End point title	Proportion of Patients With Estimated Glomerular Filtration Rate (eGFR) Improvement
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End point description:

Proportion of Patients with Estimated Glomerular Filtration Rate (eGFR) Improvement was determined and defined as an increase in eGFR by $\geq 15 \text{ mL/min/1.73m}^2$ from baseline sustained for at least two consecutive measurements obtained at least four weeks apart

End point type	Secondary
End point timeframe:	
Through End of Study, Median Exposure 52 Weeks	

End point values	eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: Percentage of Participants				
number (confidence interval 95%)	61 (44.5 to 75.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Platelet Count Change From Baseline to 52 Weeks

End point title	Platelet Count Change From Baseline to 52 Weeks
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End point description:

End point type	Secondary
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End point timeframe:

Through 52 Weeks

End point values	eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: 10 ⁹ cells/L				
least squares mean (confidence interval 95%)	102.49 (68.15 to 136.82)			

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 duration of 11.9 months and ranged from 2.9 months to 28.8 months.

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
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	15.1
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Reporting groups

Reporting group title	eculizumab
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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	19 / 41 (46.34%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Shunt malfunction			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypertensive crisis			

subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Venous thrombosis			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Convulsion			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Haemorrhage intracranial			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Paraesthesia			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Posterior reversible encephalopathy syndrome			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Haemolytic uraemic syndrome			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thrombotic microangiopathy			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

General disorders and administration site conditions			
Medical device complication			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Kidney transplant rejection			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 41 (2.44%)		
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	2 / 41 (4.88%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Pulmonary oedema			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			

subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Rash papular			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Skin necrosis			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Renal failure chronic			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Renal impairment			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Renal vessel disorder			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Device related infection				
subjects affected / exposed	1 / 41 (2.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Device related sepsis				
subjects affected / exposed	2 / 41 (4.88%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Genitourinary tract gonococcal infection				
subjects affected / exposed	1 / 41 (2.44%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Meningitis meningococcal				
subjects affected / exposed	1 / 41 (2.44%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Meningococcal sepsis				
subjects affected / exposed	1 / 41 (2.44%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	1 / 41 (2.44%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
subjects affected / exposed	2 / 41 (4.88%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Shunt infection				
subjects affected / exposed	1 / 41 (2.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				

Hyperglycaemia			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypoglycemia			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	eculizumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	41 / 41 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Parathyroid tumour benign			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Haematoma			
subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	3		
Hot flush			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Hypertension			
subjects affected / exposed	5 / 41 (12.20%)		
occurrences (all)	6		
Hypotension			
subjects affected / exposed	7 / 41 (17.07%)		
occurrences (all)	7		
Steal syndrome			

subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Thrombophlebitis			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Venous thrombosis			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	6 / 41 (14.63%)		
occurrences (all)	6		
Calcinosis			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Catheter site discharge			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Catheter site erythema			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Catheter site pruritus			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Chest discomfort			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Chest pain			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Chills			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Device occlusion			

subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	3		
Impaired healing			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Influenza like illness			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Malaise			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Medical device complication			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Oedema			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Oedema peripheral			
subjects affected / exposed	9 / 41 (21.95%)		
occurrences (all)	9		
Pyrexia			
subjects affected / exposed	7 / 41 (17.07%)		
occurrences (all)	7		
Reproductive system and breast disorders			
Amenorrhoea			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Atrophic vulvovaginitis			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Breast cyst			

subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Dysmenorrhoea			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Endometriosis			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Haematospermia			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Metrorrhagia			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	7 / 41 (17.07%)		
occurrences (all)	7		
Dyspnoea			
subjects affected / exposed	5 / 41 (12.20%)		
occurrences (all)	5		
Dyspnoea exertional			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Epistaxis			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Nasal septum deviation			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	3		
Pleural effusion			

subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Productive cough			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Pulmonary congestion			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Pulmonary oedema			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	3		
Rhinitis allergic			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Rhinorrhoea			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Snoring			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Wheezing			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Psychiatric disorders			
Agitation			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Anxiety			
subjects affected / exposed	4 / 41 (9.76%)		
occurrences (all)	4		
Depressed mood			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Depression			
subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	3		

Insomnia			
subjects affected / exposed	5 / 41 (12.20%)		
occurrences (all)	5		
Nightmare			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Investigations			
Blood pressure increased			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Cardiac murmur			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Eosinophil count increased			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Free haemoglobin present			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Liver function test abnormal			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Platelet count decreased			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Urine protein/creatinine ratio increased			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Weight decreased			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
White blood cell count increased			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			

Arteriovenous fistula site complication			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Contusion			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Foot fracture			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Infusion related reaction			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Procedural complication			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Shunt malfunction			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Skeletal injury			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Upper limb fracture			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Wound			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Cardiomyopathy			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Palpitations			

subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Tachycardia			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Nervous system disorders			
Amnesia			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Dizziness			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Headache			
subjects affected / exposed	15 / 41 (36.59%)		
occurrences (all)	15		
Loss of consciousness			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Migraine			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Paraesthesia			
subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	3		
Polyneuropathy			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Presyncope			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Sciatica			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Syncope			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		

Tremor subjects affected / exposed occurrences (all)	1 / 41 (2.44%) 1		
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	7 / 41 (17.07%) 7		
Eosinophilia subjects affected / exposed occurrences (all)	1 / 41 (2.44%) 1		
Iron deficiency anaemia subjects affected / exposed occurrences (all)	1 / 41 (2.44%) 1		
Leukopenia subjects affected / exposed occurrences (all)	1 / 41 (2.44%) 5		
Lymphopenia subjects affected / exposed occurrences (all)	3 / 41 (7.32%) 3		
Neutropenia subjects affected / exposed occurrences (all)	2 / 41 (4.88%) 2		
Spontaneous haematoma subjects affected / exposed occurrences (all)	1 / 41 (2.44%) 1		
Thrombocytopenia subjects affected / exposed occurrences (all)	2 / 41 (4.88%) 2		
Ear and labyrinth disorders			
Ear pain subjects affected / exposed occurrences (all)	1 / 41 (2.44%) 1		
Tinnitus subjects affected / exposed occurrences (all)	1 / 41 (2.44%) 1		
Tympanic membrane perforation			

subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Vertigo			
subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	3		
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Conjunctivitis			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Eye inflammation			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Lacrimation increased			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Retinopathy hypertensive			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Uveitis			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Vision blurred			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	4		
Constipation			

subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	3		
Diarrhoea			
subjects affected / exposed	13 / 41 (31.71%)		
occurrences (all)	14		
Dry mouth			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Dyspepsia			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Dysphagia			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Enteritis			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Gastrointestinal disorder			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Gastrointestinal pain			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Gingival hypertrophy			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Mouth ulceration			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	5 / 41 (12.20%)		
occurrences (all)	5		
Odynophagia			

subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Stomatitis			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	6 / 41 (14.63%)		
occurrences (all)	6		
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Cholelithiasis			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Cholestasis			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Hepatocellular injury			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	5 / 41 (12.20%)		
occurrences (all)	5		
Dermatitis			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Eczema			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Intertrigo			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Night sweats			

subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Petechiae			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Photosensitivity reaction			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	4 / 41 (9.76%)		
occurrences (all)	4		
Purpura			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Rash			
subjects affected / exposed	4 / 41 (9.76%)		
occurrences (all)	4		
Rash erythematous			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Rash pruritic			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Skin discolouration			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Urticaria			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Renal and urinary disorders			
Anuria			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Dysuria			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		

Haematuria			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Proteinuria			
subjects affected / exposed	5 / 41 (12.20%)		
occurrences (all)	5		
Renal failure acute			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	2		
Renal failure chronic			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	3		
Renal impairment			
subjects affected / exposed	6 / 41 (14.63%)		
occurrences (all)	7		
Renal vessel disorder			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Tubulointerstitial nephritis			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Urine abnormality			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Vesicoureteric reflux			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Endocrine disorders			
Hyperparathyroidism			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	8 / 41 (19.51%)		
occurrences (all)	8		
Bone pain			

subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Back pain			
subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	3		
Chondrocalcinosis			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Haemarthrosis			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Joint effusion			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Joint stiffness			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Muscle spasms			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Musculoskeletal pain			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Myalgia			
subjects affected / exposed	4 / 41 (9.76%)		
occurrences (all)	4		
Neck pain			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Osteopenia			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Rhabdomyolysis			

subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Infections and infestations			
Asymptomatic bacteriuria			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Bacterial infection			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Bacteriuria			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
BK virus infection			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Bronchitis			
subjects affected / exposed	5 / 41 (12.20%)		
occurrences (all)	5		
Bronchitis viral			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Catheter site infection			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Cystitis			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Dental gangrene			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Device related infection			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	2		
Device related sepsis			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	3		

Ear infection			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Erysipelas			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Folliculitis			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Gastroenteritis			
subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	3		
Genital infection fungal			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Herpes zoster			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Infection			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Influenza			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Laryngitis			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Lung infection			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Lymphangitis			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	8 / 41 (19.51%)		
occurrences (all)	8		

Onychomycosis			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Oral fungal infection			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Oral herpes			
subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	3		
Otitis media			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Pharyngitis			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Pulmonary sepsis			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Pyelonephritis			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	2		
Respiratory tract infection			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Rhinitis			
subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	3		
Sinusitis			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Staphylococcal infection			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Tinea pedis			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		

Upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 41 (2.44%) 1		
Urinary tract infection subjects affected / exposed occurrences (all)	7 / 41 (17.07%) 7		
Vaginitis bacterial subjects affected / exposed occurrences (all)	1 / 41 (2.44%) 1		
Viral infection subjects affected / exposed occurrences (all)	2 / 41 (4.88%) 2		
Metabolism and nutrition disorders			
Acidosis subjects affected / exposed occurrences (all)	2 / 41 (4.88%) 2		
Decreased appetite subjects affected / exposed occurrences (all)	1 / 41 (2.44%) 1		
Dehydration subjects affected / exposed occurrences (all)	1 / 41 (2.44%) 1		
Electrolyte imbalance subjects affected / exposed occurrences (all)	1 / 41 (2.44%) 1		
Hypercalcaemia subjects affected / exposed occurrences (all)	1 / 41 (2.44%) 1		
Hypercreatininaemia subjects affected / exposed occurrences (all)	2 / 41 (4.88%) 2		
Hyperkalaemia subjects affected / exposed occurrences (all)	4 / 41 (9.76%) 4		
Hyperphosphataemia			

subjects affected / exposed	5 / 41 (12.20%)		
occurrences (all)	5		
Hyperuricaemia			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Hypervolaemia			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Hypocalcaemia			
subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	3		
Hypoglycaemia			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Hypokalaemia			
subjects affected / exposed	4 / 41 (9.76%)		
occurrences (all)	4		
Hypomagnesaemia			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Hypophosphataemia			
subjects affected / exposed	4 / 41 (9.76%)		
occurrences (all)	4		
Iron deficiency			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Metabolic acidosis			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Overweight			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Vitamin D deficiency			

subjects affected / exposed	4 / 41 (9.76%)		
occurrences (all)	4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 December 2010	Global modification to clinical study protocol to implement, in particular, a Data Monitoring Committee
07 June 2011	Global modification to the clinical study protocol to increase the number of patients to be enrolled in the clinical study.

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/25833956>