Clinical trial results:
A Hemoglobin Stabilization and Transfusion Reduction Efficacy and Safety Clinical Investigation, Randomized, Multi-Center, Double-Blind, Placebo-Controlled, Using Eculizumab in Paroxysmal Nocturnal Hemoglobinuria Patients (TRIUMPH)

Summary

EudraCT number	2004-000646-20
Trial protocol	SE IE GB IT
Global end of trial date	27 December 2005

Results information

Result version number	v1 (current)
This version publication date	06 January 2017
First version publication date	06 January 2017

Trial information

Trial identification

Sponsor protocol code	C04-001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00112983
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Alexion Pharmaceuticals Incorporated
Sponsor organisation address	100 College Street , New Haven, CT, United States, 06510
Public contact	European Clinical Trial Information, Alexion Europe SAS, +33 1 47 10 06 06, clinicaltrials.eu@alexion.com
Scientific contact	European Clinical Trial Information, Alexion Europe SAS, +33 1 47 10 06 06, clinicaltrials.eu@alexion.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	24 July 2006
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 December 2005
Global end of trial reached?	Yes
Global end of trial date	27 December 2005
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and efficacy of eculizumab in transfusion-dependent patients with haemolytic paroxysmal haemoglobinuria (PNH).

Protection of trial subjects:

Patients must have been vaccinated for Neisseria meningitidis 14 days prior to randomisation.

Background therapy:

No background therapy used.

Evidence for comparator:

This was a randomised, double-blind, placebo-controlled, multicenter study. The use of a placebo-controlled group was deemed appropriate for this trial because the standard of care applicable at the time of study initiation for PNH (eg, transfusions or other symptomatic treatment measures) was permitted to be used in conjunction with proposed study therapy. Thus, patients were not placed at undue risk and patients may have benefited by increased monitoring of physical signs and symptoms during the study.

Actual start date of recruitment	27 August 2004
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
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: 20
Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Germany: 15
Country: Number of subjects enrolled	Italy: 9
Country: Number of subjects enrolled	United States: 33
Country: Number of subjects enrolled	Ireland: 4
Country: Number of subjects enrolled	Sweden: 2
Country: Number of subjects enrolled	Netherlands: 9
Country: Number of subjects enrolled	Australia: 8
Country: Number of subjects enrolled	Canada: 2
Worldwide total number of subjects	109
EEA total number of subjects	66

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	100
From 65 to 84 years	8
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

A total of 34 clinical sites in the United States, Canada, Australia, Belgium, France, Germany, Ireland, Italy, Netherlands, Sweden, and the United Kingdom participated in this study, and randomly assigned treatment to study patients.

Pre-assignment

Screening details:

Transfusion-dependent haemolytic PNH patients who met all of the selection criteria defined for the screening period, were eligible to enter a 13-wk observation period. 114 patients were screened, 109 patients were enrolled into the observation period, 88 patients were randomized to receive either eculizumab or placebo.

Pre-assignment period milestones

Number of subjects started	109
Number of subjects completed	87

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Did not meet entry criteria for observation period: 1
Reason: Number of subjects	Did not meet entry criteria for treatment phase: 20
Reason: Number of subjects	Randomized in error: 1

Period 1

Period 1 title	Treatment Phase (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Data analyst, Carer, Assessor

Blinding implementation details:

The double-blind was maintained by using identical investigational product kits and labels for investigational product and placebo.

Arms

Are arms mutually exclusive?	Yes
Arm title	eculizumab

Arm description:

Patients randomly assigned to treatment with eculizumab received 600 mg of eculizumab once a week for 4 weeks, followed by 900 mg of eculizumab 1 week later for 1 dose, then 900 mg of eculizumab every 2 weeks for 21 weeks, for a total of 26 weeks of treatment.

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:

600 mg of eculizumab once a week for 4 weeks, followed by 900 mg of eculizumab 1 week later for 1 dose, then 900 mg of eculizumab every 2 weeks for 21 weeks.

Arm title	Placebo

Arm description:

Patients randomly assigned to treatment with placebo received 1 dose of placebo once a week for 5 weeks, then 1 dose every 2 weeks for 21 weeks, for a total of 26 weeks of treatment.

Arm type	Placebo
Investigational medicinal product name	Matching placebo
Investigational medicinal product code	Placebo
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1 dose of placebo once a week for 5 weeks, then 1 dose every 2 weeks for 21 weeks

Number of subjects in period 1[1]	eculizumab	Placebo
Started	43	44
Completed	41	34
Not completed	2	10
Consent withdrawn by subject	1	-
Adverse event, non-fatal	1	-
Lack of efficacy	-	10

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: A total of 114 patients were screened, 109 patients were enrolled in the observation period, and 87 entered treatment phase (treatment period). The baseline period was considered to be at time of entry into the actual treatment period.

Baseline characteristics

Reporting groups	
Reporting group title	eculizumab
Reporting group description:	
Patients randomly assigned to treatment with eculizumab received 600 mg of eculizumab once a week for 4 weeks, followed by 900 mg of eculizumab 1 week later for 1 dose, then 900 mg of eculizumab every 2 weeks for 21 weeks, for a total of 26 weeks of treatment.	
Reporting group title	Placebo
Reporting group description:	
Patients randomly assigned to treatment with placebo received 1 dose of placebo once a week for 5 weeks, then 1 dose every 2 weeks for 21 weeks, for a total of 26 weeks of treatment.	

Reporting group values	eculizumab	Placebo	Total
Number of subjects	43	44	87
Age categorical			
Units: Subjects			
Adults (18-64 years)	37	42	79
From 65-84 years	5	2	7
85 years and over	1	0	1
Age continuous			
Units: years			
arithmetic mean	42.1	38.4	
standard deviation	± 15.47	± 13.38	-
Gender categorical			
Units: Subjects			
Female	23	29	52
Male	20	15	35
Race			
Units: Subjects			
Asian	1	1	2
Unknown or Not Reported	1	1	2
Caucasian	37	41	78
Black	4	0	4
Hispanic	0	1	1
Blood type			
Units: Subjects			
A-	5	1	6
A+	11	20	31
B-	2	0	2
B+	3	5	8
AB+	2	2	4
O-	4	6	10
O+	16	10	26
Weight			
Units: kilogram(s)			
arithmetic mean	74.9	72.8	
standard deviation	± 11.69	± 14.04	-
Height			
Units: centimeters			

arithmetic mean	170.4	169.7	
standard deviation	± 9.37	± 8.89	-
Haemoglobin concentrations prior to transfusion			
Units: gram(s)/decilitre			
median	8.1	7.8	
inter-quartile range (Q1-Q3)	7.3 to 8.5	7.2 to 8.6	-
Haemoglobin concentrations post-transfusion			
Units: gram(s)/decilitre			
median	10.8	9.3	
inter-quartile range (Q1-Q3)	9.6 to 11.1	8.5 to 9.8	-
Number of red blood cells units transfused			
Units: gram(s)/decilitre			
median	18	17	
inter-quartile range (Q1-Q3)	12 to 24	13.5 to 25	-

End points

End points reporting groups

Reporting group title	eculizumab

Reporting group description:

Patients randomly assigned to treatment with eculizumab received 600 mg of eculizumab once a week for 4 weeks, followed by 900 mg of eculizumab 1 week later for 1 dose, then 900 mg of eculizumab every 2 weeks for 21 weeks, for a total of 26 weeks of treatment.

Reporting group title	Placebo

Reporting group description:

Patients randomly assigned to treatment with placebo received 1 dose of placebo once a week for 5 weeks, then 1 dose every 2 weeks for 21 weeks, for a total of 26 weeks of treatment.

Primary: Haemoglobin stabilisation

End point title	Haemoglobin stabilisation

End point description:

Haemoglobin stabilisation and the number of units of packed red blood cells (RBCs) transfused during the treatment phase of the study were defined as co-primary endpoints. For the haemoglobin stabilisation endpoint, patients who dropped out of the study or were transfused above their set points during the treatment phase were treated as not achieving haemoglobin stabilisation.

End point type	Primary

End point timeframe:

Through 26 weeks

End point values	eculizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	44		
Units: Subjects				
Overall (n=87)	21	0		
4 - 14 units (n=30)	12	0		
15 - 25 units (n=35)	5	0		
> 25 units (n=22)	4	0		

Statistical analyses

Statistical analysis title	Statistics for haemoglobin stabilisation

Statistical analysis description:

The analysis was based on the intent-to-treat population.

Comparison groups	eculizumab v Placebo

Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Fisher exact
Parameter estimate	Difference between proportions
Point estimate	0.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.34
upper limit	0.64

Primary: Number of units of packed RBCs transfused

End point title	Number of units of packed RBCs transfused

End point description:

Haemoglobin stabilisation and the number of units of packed red blood cells (RBCs) transfused during the treatment phase of the study were defined as co-primary endpoints.

End point type	Primary

End point timeframe:

Through 26 weeks

End point values	eculizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	44		
Units: number of PRBC units transfused				
arithmetic mean (standard error)				
Overall	3 (± 0.67)	11 (± 0.83)		
4 - 14 units	0.4 (± 0.29)	6.7 (± 0.72)		
15 - 25 units	4.2 (± 1.14)	10.8 (± 1.17)		
> 25 units	4.5 (± 1.59)	17 (± 1.04)		

Statistical analyses

Statistical analysis title	Analysis 1 for number of packed RBC units

Statistical analysis description:

For the number of units of packed RBCs transfused, each patient’s units of packed RBCs transfused after randomization to 26 weeks were calculated. For those patients who discontinued study drug, but remained in the study, their actual transfusion records were used to calculate units; for those patients who have transfusion(s), but dropped out of the study prior to 26 wks, the number of units were prorated.

Comparison groups	eculizumab v Placebo

Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Difference between means
Point estimate	-8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.1
upper limit	-5.9

Secondary: Transfusion Avoidance

End point title	Transfusion Avoidance

End point description:

Proportion of patients achieving transfusion avoidance.

End point type	Secondary

End point timeframe:

Through 26 weeks

End point values	eculizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	44		
Units: subjects				
Overall	22	0		
4 - 14 units	12	0		
15 -25 units	6	0		
> 25 units	4	0		

Statistical analyses

Statistical analysis title	Statistical analysis 1 for transfusion avoidance.

Statistical analysis description:

The analysis of the secondary endpoint of transfusion avoidance was carried out using the 2-sided Fisher exact test. As a sensitivity analysis, those patients who dropped out of the study during the treatment phase prior to having a transfusion were classified as not requiring a transfusion.

Comparison groups	eculizumab v Placebo

Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Fisher exact

Secondary: Haemolysis (as assessed by LDH)

End point title	Haemolysis (as assessed by LDH)

End point description:

A quantitative assessment of chronic haemolysis was obtained by calculating the AUC for LDH from Baseline to Week 26.

End point type	Secondary

End point timeframe:

Through 26 weeks

End point values	eculizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	44		
Units: Decrease of LDH AUC levels				
arithmetic mean (standard error)				
Overall	81141 (± 17626.59)	429874.1 (± 21704.31)		
4 - 14 units	103760.6 (± 49309.63)	391388.7 (± 32020.39)		
15- 25 units	58670.4 (± 3364.68)	444075.6 (± 37304.47)		
> 25 units	85019.5 (± 16790.79)	459115.5 (± 44197.34)		

Statistical analyses

Statistical analysis title	Statistical analysis 1 for AUC for LDH

Statistical analysis description:

The AUC of LDH from baseline to 26 weeks was calculated for each patient. For those patients with missing LDH values, the last observation carry forward method was used to impute missing values.

Comparison groups	eculizumab v Placebo
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Wilcoxon Rank-Sum test

Secondary: Levels of fatigue

End point title	Levels of fatigue

End point description:

The Quality-of-Life (QoL) instrument FACIT-Fatigue scale version 4 was utilised to collect QoL data. The scoring guideline for the FACIT-Fatigue scale version 4 instrument was used to calculate the QoL score; per the corresponding scoring guideline, scores can range from 0 to 52, with higher scores indicating improvement in fatigue. A minimally important difference was defined as a change of 4 or more points at 26 weeks (Visit 18).

End point type	Secondary

End point timeframe:

Through 26 weeks

End point values	eculizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	44		
Units: QoL score				
arithmetic mean (standard error)				
Baseline	36.7 (± 1.6)	34.3 (± 1.88)		
Change from baseline at Wk 3	4.2 (± 1.13)	-1.9 (± 1.9)		
Change from baseline at Wk 12	4.6 (± 1.22)	-3.1 (± 1.52)		
Change from baseline at Wk 20	4.8 (± 1.56)	-2.2 (± 1.91)		
Change from baseline at Wk 26	6.4 (± 1.19)	-4 (± 1.71)		

Statistical analyses

Statistical analysis title	Analysis for the FACIT-Fatigue scale

Statistical analysis description:

The FACIT-Fatigue scale was scored according to published scoring guideline for this instrument. The main hypothesis was that eculizumab would provide a statistically significant increase in patients' scale score compared with placebo.

Comparison groups	eculizumab v Placebo
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.01
Method	Wilcoxon's rank sum test

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Information regarding AEs was collected from the time the patient signed the informed consent form up to 30 days after the last dose of investigational product was administered.

Adverse event reporting additional description:

At every visits, 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/changed concomitant medication regimens. AEs were 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	7

Reporting groups

Reporting group title	eculizumab

Reporting group description:

Patients randomized to this group received 600 mg of eculizumab IV once a week for 4 doses, followed by 900 mg eculizumab IV 1 week later for 1 dose, and 900 mg eculizumab IV every 2 weeks

Reporting group title	Placebo

Reporting group description:

Patients randomized to this group received matching placebo IV once a week for 5 doses, then once every 2 weeks

Serious adverse events	eculizumab	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 43 (9.30%)	9 / 44 (20.45%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemolysis			
subjects affected / exposed	0 / 43 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			

subjects affected / exposed	0 / 43 (0.00%)	2 / 44 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paroxysmal nocturnal haemoglobinuria			
subjects affected / exposed	1 / 43 (2.33%)	3 / 44 (6.82%)	
occurrences causally related to treatment / all	0 / 2	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	1 / 43 (2.33%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	1 / 43 (2.33%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 43 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Central line infection			
subjects affected / exposed	0 / 43 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Folliculitis			

subjects affected / exposed	0 / 43 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal bacteraemia			
subjects affected / exposed	1 / 43 (2.33%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 43 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 43 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	0 / 43 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	eculizumab	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	43 / 43 (100.00%)	40 / 44 (90.91%)	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 43 (2.33%)	3 / 44 (6.82%)	
occurrences (all)	1	5	
Nervous system disorders			
Headache			
subjects affected / exposed	19 / 43 (44.19%)	12 / 44 (27.27%)	
occurrences (all)	27	33	
Dizziness			

subjects affected / exposed	2 / 43 (4.65%)	5 / 44 (11.36%)	
occurrences (all)	2	9	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	5 / 43 (11.63%)	1 / 44 (2.27%)	
occurrences (all)	13	1	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 43 (0.00%)	4 / 44 (9.09%)	
occurrences (all)	0	4	
Paroxysmal nocturnal haemoglobinuria			
subjects affected / exposed	1 / 43 (2.33%)	3 / 44 (6.82%)	
occurrences (all)	1	5	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 43 (2.33%)	3 / 44 (6.82%)	
occurrences (all)	1	4	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	7 / 43 (16.28%)	5 / 44 (11.36%)	
occurrences (all)	8	7	
Diarrhoea			
subjects affected / exposed	4 / 43 (9.30%)	5 / 44 (11.36%)	
occurrences (all)	6	5	
Abdominal pain			
subjects affected / exposed	2 / 43 (4.65%)	5 / 44 (11.36%)	
occurrences (all)	2	6	
Vomiting			
subjects affected / exposed	2 / 43 (4.65%)	5 / 44 (11.36%)	
occurrences (all)	2	6	
Constipation			
subjects affected / exposed	3 / 43 (6.98%)	2 / 44 (4.55%)	
occurrences (all)	3	2	
Reproductive system and breast disorders			

Menorrhagia			
subjects affected / exposed	0 / 43 (0.00%)	3 / 44 (6.82%)	
occurrences (all)	0	3	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	5 / 43 (11.63%)	4 / 44 (9.09%)	
occurrences (all)	6	5	
Pharyngolaryngeal pain			
subjects affected / exposed	3 / 43 (6.98%)	4 / 44 (9.09%)	
occurrences (all)	3	4	
Dyspnoea			
subjects affected / exposed	0 / 43 (0.00%)	3 / 44 (6.82%)	
occurrences (all)	0	3	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	3 / 43 (6.98%)	3 / 44 (6.82%)	
occurrences (all)	3	3	
Rash			
subjects affected / exposed	1 / 43 (2.33%)	3 / 44 (6.82%)	
occurrences (all)	1	3	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 43 (2.33%)	3 / 44 (6.82%)	
occurrences (all)	1	3	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	8 / 43 (18.60%)	4 / 44 (9.09%)	
occurrences (all)	9	7	
Arthralgia			
subjects affected / exposed	3 / 43 (6.98%)	5 / 44 (11.36%)	
occurrences (all)	4	6	
Myalgia			
subjects affected / exposed	3 / 43 (6.98%)	1 / 44 (2.27%)	
occurrences (all)	3	1	
Pain in extremity			

subjects affected / exposed	3 / 43 (6.98%)	1 / 44 (2.27%)	
occurrences (all)	5	1	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	10 / 43 (23.26%)	8 / 44 (18.18%)	
occurrences (all)	11	11	
Upper respiratory tract infection			
subjects affected / exposed	6 / 43 (13.95%)	10 / 44 (22.73%)	
occurrences (all)	6	14	
Sinusitis			
subjects affected / exposed	3 / 43 (6.98%)	3 / 44 (6.82%)	
occurrences (all)	4	3	
Viral infection			
subjects affected / exposed	1 / 43 (2.33%)	5 / 44 (11.36%)	
occurrences (all)	1	5	
Urinary tract infection			
subjects affected / exposed	1 / 43 (2.33%)	4 / 44 (9.09%)	
occurrences (all)	1	5	
Respiratory tract infection			
subjects affected / exposed	3 / 43 (6.98%)	1 / 44 (2.27%)	
occurrences (all)	4	3	
Herpes simplex			
subjects affected / exposed	3 / 43 (6.98%)	0 / 44 (0.00%)	
occurrences (all)	3	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/25833956