

## **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	
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### **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)	-
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Notes:

Sponsors	
Alexion Pharmaceuticals Incorporated	
100 College Street , New Haven, CT, United States, 06510	
European Clinical Trial Information, Alexion Europe SAS, +33 1 47 10 06 06, clinicaltrials.eu@alexion.com	
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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 placebocontrolled 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

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

Treatment Phase (overall period)
Yes
Randomised - controlled
Double blind
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
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#### 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	
-		1	
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	IPlacebo
Reporting group title	II Ideebo

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			
Age continuous			
Age continuous Units: years arithmetic mean	42.1	38.4	
Units: years	42.1 ± 15.47	38.4 <del>± 13.38</del>	
Units: years arithmetic mean		1.12	

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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**

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Reporting group title	Jeculizumad

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.

Placebo Reporting group title

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
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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:		
	number of units of packed red blood cells (RBCs) transfused during 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
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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.
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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
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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 chroBaseline to Week 26.	onic haemolysis was obtained by calculating the AUC for LDH from	
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:		
	eks was calculated for each patient. For those patients with 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 title	Alialysis 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.)

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 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%)	l I
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	· 		i i
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		,	' ' 
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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	
	_	J	
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	
Cood. Circo (any	O	3	
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	
Comphination			
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	
	O	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)			
occurrences (an)	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)	é	)Tj 0 <u>p</u> _ET 1 0 0 1	0 0 cm 1 w 0 J ]5] 00 J ]	0 d 533 643 m
eccurrences (all)				
subjects affected / exposed	3 / 43 (6.98%)	3 / 44 (6.82%)		
occurrences (all)		3		

### 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