



Clinical trial results:

A Randomized, Double-Blind, Placebo-Controlled, Cross-Over, Multi-Center Study of Eculizumab in Patients with Generalized Myasthenia Gravis (gMG) Who Have Moderate to Severe Muscle Weakness Despite Treatment with Immunosuppressants.

Summary

EudraCT number	2009-014669-13
Trial protocol	GB
Global end of trial date	16 March 2011

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	C08-001
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
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	16 March 2011
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	16 March 2011
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to determine whether eculizumab is safe and effective in the treatment of patients with generalized myasthenia gravis despite treatment with various immunosuppressants, such as prednisone, methotrexate, Cellcept, cyclosporine, and cyclophosphamide, that are currently available.

Protection of trial subjects:

Patients must have been vaccinated for N meningitides 14 days prior to randomization at Visit 1 or during the observation period, as determined by the principal investigator's discretion.

Background therapy:

Patients may continue on their MG medications, IST and/or cholinesterase inhibitor but must be on a stable dose prior and during the study.

Evidence for comparator:

This was a Randomized, Double-Blind, Placebo-Controlled, Cross-Over, Multi-Center Study of Eculizumab in Patients with Generalized Myasthenia Gravis (gMG) who have Moderate to Severe Muscle Weakness Despite Treatment with Immunosuppressants. All patients received the treatment.

Actual start date of recruitment	01 October 2008
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 13
Country: Number of subjects enrolled	United Kingdom: 1
Worldwide total number of subjects	14
EEA total number of subjects	1

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)	11
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Patients received standard of care during the Screening Period. Patients were randomized to a treatment sequence to receive eculizumab in Period 1 followed by placebo in Period 2 or placebo in Period 1 followed by eculizumab in Period 2. Patients were permitted to continue on background immunosuppressive therapy throughout the study.

Period 1

Period 1 title	Treatment Period 1
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:

Patients were centrally randomized via Almac Clinical Service's secure web-based randomization application, WebEZ. The randomization code was maintained by Almac Clinical Services.

Arms

Are arms mutually exclusive?	Yes
Arm title	Eculizumab period 1

Arm description:

Patients received eculizumab 600 mg via IV infusion over approximately 35 minutes once a week (every 7 ± 2 days) for 4 weeks followed by 900 mg eculizumab via IV infusion over approximately 35 minutes every two weeks (every 14 ± 2 days) for 7 doses.

Arm type	Experimental
Investigational medicinal product name	eculizumab
Investigational medicinal product code	
Other name	soliris
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1 dose of 600mg weekly for 4 weeks, 900 mg for the fifth week. And 900 mg every two weeks for 6 doses

Arm title	Placebo period 1
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Arm description:

Patients received placebo via IV infusion... more over approximately 35 minutes once a week (every 7 ± 2 days) for 4 weeks followed by matching placebo via IV infusion over approximately 35 minutes every two weeks (every 14 ± 2 days) for 7 doses.

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 weekly for 4 weeks than 1 dose for the fifth week and 1 doses every two weeks for 6 doses

Number of subjects in period 1	Eculizumab period 1	Placebo period 1
Started	7	7
Completed	7	7

Period 2

Period 2 title	Treatment Period 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Eculizumab period 2

Arm description:

All these patients received placebo during period 1

During Period 2:

Patients received ecuzumab 600 mg via IV infusion over approximately 35 minutes once a week (every 7 ± 2 days) for 4 weeks followed by 900 mg ecuzumab via IV infusion over approximately 35 minutes every two weeks (every 14 ± 2 days) for 7 doses.

Arm type	Experimental
Investigational medicinal product name	eculizumab
Investigational medicinal product code	
Other name	soliris
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1 dose of 600mg weekly for 4 weeks, 900 mg for the fifth week. And 900 mg every two week for 6 doses

Arm title	Placebo period 2
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Arm description:

All these patients received ecuzumab during period 1

During period 2:

Patients received placebo via IV infusion... more over approximately 35 minutes once a week (every 7 ± 2 days) for 4 weeks followed by matching placebo via IV infusion over approximately 35 minutes every two weeks (every 14 ± 2 days) for 7 doses.

Arm type	Placebo
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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 weekly for 4 weeks than 1 dose for the fifth week and 1 doses every two weeks for 6 doses

Number of subjects in period 2^[1]	Ecuzumab period 2	Placebo period 2
Started	6	6
Completed	6	5
Not completed	0	1
Lack of efficacy	-	1

Notes:

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

Justification: 1 patient discontinued during the placebo sequence of treatment due to lack of efficacy

Baseline characteristics

Reporting groups

Reporting group title	Treatment Period 1
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Reporting group description: -

Reporting group values	Treatment Period 1	Total	
Number of subjects	14	14	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	11	11	
From 65-84 years	3	3	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	49		
standard deviation	± 14	-	
Gender categorical			
Units: Subjects			
Female	8	8	
Male	6	6	
Race			
Units: Subjects			
Caucasian	11	11	
Hispanic	2	2	
Black	1	1	
Myasthenia Gravis Fondation of America (MGFA) classification at screening			
Units: Subjects			
IIa	2	2	
IIb	2	2	
IIIa	8	8	
IVa	2	2	

End points

End points reporting groups

Reporting group title	Eculizumab period 1
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Reporting group description:

Patients received eculizumab 600 mg via IV infusion over approximately 35 minutes once a week (every 7 ± 2 days) for 4 weeks followed by 900 mg eculizumab via IV infusion over approximately 35 minutes every two weeks (every 14 ± 2 days) for 7 doses.

Reporting group title	Placebo period 1
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Reporting group description:

Patients received placebo via IV infusion... more over approximately 35 minutes once a week (every 7 ± 2 days) for 4 weeks followed by matching placebo via IV infusion over approximately 35 minutes every two weeks (every 14 ± 2 days) for 7 doses.

Reporting group title	Eculizumab period 2
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Reporting group description:

All these patients received placebo during period 1

During Period 2:

Patients received eculizumab 600 mg via IV infusion over approximately 35 minutes once a week (every 7 ± 2 days) for 4 weeks followed by 900 mg eculizumab via IV infusion over approximately 35 minutes every two weeks (every 14 ± 2 days) for 7 doses.

Reporting group title	Placebo period 2
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Reporting group description:

All these patients received eculizumab during period 1

During period 2:

Patients received placebo via IV infusion... more over approximately 35 minutes once a week (every 7 ± 2 days) for 4 weeks followed by matching placebo via IV infusion over approximately 35 minutes every two weeks (every 14 ± 2 days) for 7 doses.

Subject analysis set title	Eculizumab Both Period
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Subject analysis set type	Full analysis
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Subject analysis set description:

Eculizumab

Eculizumab: eculizumab 600 mg IV weekly for 4 doses followed by eculizumab 900 mg IV every two weeks for 7 doses

Subject analysis set title	Placebo Both Period
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Subject analysis set type	Full analysis
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Subject analysis set description:

Placebo

Placebo: Placebo IV weekly for 4 doses then every two weeks for 7 doses

Primary: Quantitative Myasthenia Gravis (QMG): The Primary Efficacy Endpoint in This Study Was the Percentage of Patients With a 3-point Reduction From Baseline in the QMG Total Score for Disease Severity.

End point title	Quantitative Myasthenia Gravis (QMG): The Primary Efficacy Endpoint in This Study Was the Percentage of Patients With a 3-point Reduction From Baseline in the QMG Total Score for Disease Severity. ^[1]
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End point description:

The QMG scoring system is considered to be an objective evaluation of muscle strength based on quantitative testing of sentinel muscle groups. The MGFA task force has recommended that the QMG score be used in prospective studies of therapy for MG.

End point type	Primary
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End point timeframe:

16 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: No statistical analysis provided for Quantitative Myasthenia Gravis (QMG): The Primary Efficacy Endpoint in This Study Was the Percentage of Patients With a 3-point Reduction From Baseline in the QMG Total Score for Disease Severity.

End point values	Eculizumab period 1	Placebo period 1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	7		
Units: percentage of patients				
number (not applicable)	86	57		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in QMG Total Score

End point title	Mean Change From Baseline in QMG Total Score
End point description:	
The QMG scoring system is considered to be an objective evaluation of muscle strength based on quantitative testing of sentinel muscle groups. The Myasthenia Gravis Foundation of America task force has recommended that the QMG score be used in prospective studies of therapy for MG. The QMG scoring system consists of 13 items. Each item is graded 0 to 3, with 3 being the most severe. The range of total QMG score is 0-39.	
End point type	Secondary
End point timeframe:	
16 weeks	

End point values	Eculizumab period 1	Placebo period 1	Eculizumab Both Period	Placebo Both Period
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	7	7	7 ^[2]	7 ^[3]
Units: unit on a scale				
arithmetic mean (standard deviation)	-7.43 (± 5.563)	-2.71 (± 4.855)	-7.92 (± 5.054)	-3.67 (± 4.008)

Notes:

[2] - There are 12 subjects in this group (Eculizumab period 1+ Eculizumab period 2)

[3] - There are 12 subjects in this group (Eculizumab period 1+ Eculizumab period 2)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Eculizumab Both Period v Placebo Both Period

Number of subjects included in analysis	14
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.0144 ^[4]
Method	paired t-test
Parameter estimate	Mean difference (net)
Point estimate	-4.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.45
upper limit	-1.05

Notes:

[4] - No multiple comparisons or multiplicity adjustments were conducted.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Eculizumab period 1 v Placebo period 1
Number of subjects included in analysis	14
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.117 ^[5]
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	-4.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.8
upper limit	1.37

Notes:

[5] - No multiple comparisons or multiplicity adjustments were conducted

Secondary: Change From Baseline in the MGFA Post-Intervention Status (PIS)

End point title	Change From Baseline in the MGFA Post-Intervention Status (PIS)
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End point description:

The MGFA PIS is designed to assess the clinical state of MG patients at any time after treatment of MG is initiated. Change in status categories of Improved, Unchanged, Worse, Exacerbation, and Died of MG was to be assessed and recorded at every visit from Visits 3 to 24 (Weeks 1 to 16). Minimal manifestations were to be assessed at these visits.

End point type	Secondary
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End point timeframe:

16 weeks

End point values	Ecuzumab period 1	Placebo period 1	Ecuzumab period 2	Placebo period 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	7	6	6
Units: subject				
Improved	5	6	6	2
Unchanged	2	1	0	4
Worse	0	0	0	0
Exacerbation	0	0	0	0
Died of MG	0	0	0	0

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Ecuzumab period 1 v Placebo period 1
Number of subjects included in analysis	14
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 1 ^[6]
Method	Chi-squared
Confidence interval	

Notes:

[6] - No multiple comparisons or multiplicity adjustments were conducted.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Ecuzumab period 2 v Placebo period 2
Number of subjects included in analysis	12
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.0606 ^[7]
Method	Chi-squared

Notes:

[7] - No multiple comparisons or multiplicity adjustments were conducted.

Secondary: Change From Baseline in the MG-Activity of Daily Living Profile (MG-ADL)

End point title	Change From Baseline in the MG-Activity of Daily Living Profile (MG-ADL)
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End point description:

The MG-ADL is an 8-point questionnaire that focuses on relevant symptoms and functional performance of activities of daily living (ADL) in MG patients. The 8 items of the MG-ADL were derived from symptom-based components of the original 13-item QMG to assess disability secondary to ocular (2 items), bulbar (3 items), respiratory (1 item), and gross motor or limb (2 items) impairment related to effects from MG. In this functional status instrument, each response is graded 0 (normal) to 3 (most severe). The range of total MG-ADL score is 0 – 24. MG-ADL was to be performed at every study visit. The recall period for MG-ADL was since the preceding study visit (1 or 2 weeks).

End point type	Secondary
End point timeframe:	
16 weeks	

End point values	Ecuzumab period 1	Placebo period 1	Ecuzumab Both Period	Placebo Both Period
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	7	7	7 ^[8]	7 ^[9]
Units: unit on a scale				
arithmetic mean (standard deviation)	4.29 (± 1.799)	7.86 (± 3.716)	5.42 (± 3.315)	7 (± 3.464)

Notes:

[8] - There are 12 subjects in this group (Ecuzumab period 1+ Ecuzumab period 2)

[9] - There are 12 subjects in this group (Ecuzumab period 1+ Ecuzumab period 2)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo Both Period v Ecuzumab Both Period
Number of subjects included in analysis	14
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.1873 ^[10]
Method	paired t-test
Parameter estimate	Mean difference (net)
Point estimate	-1.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.08
upper limit	0.91

Notes:

[10] - No multiple comparisons or multiplicity adjustments were conducted.

Statistical analysis title	Statistical analysis 2
Comparison groups	Placebo period 1 v Ecuzumab period 1
Number of subjects included in analysis	14
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.041 ^[11]
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	-3.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.97
upper limit	-0.17

Notes:

[11] - No multiple comparisons or multiplicity adjustments were conducted.

Secondary: Change From Baseline in the QoL Instrument, SF-36.

End point title	Change From Baseline in the QoL Instrument, SF-36.
End point description:	
The SF-36 is a multi-purpose, short-form health survey with 36 questions. It yields an 8-scale profile of functional health and well-being scores (physical functioning, role-physical, bodily pain, general health, mental health, role-emotional, social functioning and vitality) as well as psychometrically-based physical and mental health summary measures. It is a generic measure, as opposed to one that targets a specific age, disease or treatment group. The lower the score the more disability; the higher the score the less disability. Norm-based scoring involving a linear T-score transformation method was used so that scores for each of the health domain scales and component summary measures have a mean of 50 and a standard deviation of 10 based on the 1998 US general population. Thus, scores above and below 50 are above and below the average, respectively, in the 1998 US general.	
End point type	Secondary
End point timeframe:	
16 weeks	

End point values	Ecuzumab period 1	Placebo period 1	Ecuzumab Both Period	Placebo Both Period
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	7	7	7 ^[12]	7 ^[13]
Units: unit on a scale				
arithmetic mean (standard deviation)				
Physical Functioning (Last Visit)	56.43 (± 29.255)	64.29 (± 24.054)	57.92 (± 26.921)	57.08 (± 27.507)
Role Physical (Last Visit)	61.61 (± 38.6)	68.75 (± 25.769)	64.06 (± 31.771)	60.94 (± 27.324)
Bodily Pain (Last Visit)	60 (± 24.235)	74.86 (± 20.651)	66.75 (± 22.511)	76.17 (± 15.689)
General Health (Last Visit)	47.86 (± 16.994)	40.43 (± 23.201)	44.67 (± 16.267)	37.5 (± 19.365)
Vitality (Last Visit)	50 (± 23.936)	52.68 (± 15.67)	53.13 (± 19.31)	48.96 (± 18.238)
Social Functioning (Last Visit)	66.07 (± 25.733)	82.14 (± 17.466)	66.67 (± 24.034)	78.13 (± 17.778)
Role Emotional (Last Visit)	77.38 (± 36.233)	71.43 (± 29.603)	70.83 (± 34.542)	82.64 (± 25.981)
Mental Health (Last Visit)	76.43 (± 17.728)	58.57 (± 25.284)	69.17 (± 20.542)	68.75 (± 23.27)
Physical Component Score (Last Visit)	38.73 (± 10.235)	44.97 (± 7.721)	41.4 (± 8.591)	40.32 (± 10.025)
Mental Component Score (Last Visit)	49.5 (± 12.066)	43.95 (± 12.53)	46.11 (± 12.596)	49.03 (± 11.476)

Notes:

[12] - There are 12 subjects in this group (Ecuzumab period 1+ Ecuzumab period 2)

[13] - There are 12 subjects in this group (Ecuzumab period 1+ Ecuzumab period 2)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
No multiple comparisons or multiplicity adjustments were conducted.	
Comparison groups	Placebo Both Period v Ecuzumab Both Period

Number of subjects included in analysis	14
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.919
Method	paired t-test
Parameter estimate	Mean difference (net)
Point estimate	0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.94
upper limit	18.6

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo period 1 v Eculizumab period 1
Number of subjects included in analysis	14
Analysis specification	Post-hoc
Analysis type	superiority ^[14]
P-value	= 0.5931
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	-7.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	-39.05
upper limit	23.33

Notes:

[14] - Physical Functioning

Statistical analysis title	Statistical Analysis 3
Statistical analysis description:	
Role Physical	
Comparison groups	Eculizumab Both Period v Placebo Both Period
Number of subjects included in analysis	14
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.7319 ^[15]
Method	paired t-test
Parameter estimate	Mean difference (net)
Point estimate	3.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.64
upper limit	22.89

Notes:

[15] - No multiple comparisons or multiplicity adjustments were conducted.

Statistical analysis title	Statistical Analysis 4
Statistical analysis description:	
Role Physical	
Comparison groups	Ecuzumab period 1 v Placebo period 1
Number of subjects included in analysis	14
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.691 ^[16]
Method	t-test, 2-sided
Parameter estimate	Median difference (net)
Point estimate	-7.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-45.36
upper limit	31.08

Notes:

[16] - No multiple comparisons or multiplicity adjustments were conducted.

Statistical analysis title	Statistical Analysis 5
Statistical analysis description:	
Bodily Pain	
Comparison groups	Ecuzumab Both Period v Placebo Both Period
Number of subjects included in analysis	14
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.1311 ^[17]
Method	paired t-test
Parameter estimate	Median difference (net)
Point estimate	-9.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.18
upper limit	3.34

Notes:

[17] - No multiple comparisons or multiplicity adjustments were conducted.

Statistical analysis title	Statistical Analysis 6
Statistical analysis description:	
Bodily Pain	
Comparison groups	Ecuzumab period 1 v Placebo period 1

Number of subjects included in analysis	14
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.2406 ^[18]
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	-14.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	-41.08
upper limit	11.36

Notes:

[18] - No multiple comparisons or multiplicity adjustments were conducted.

Statistical analysis title	Statistical Analysis 7
Statistical analysis description:	
General Health	
Comparison groups	Ecuzumab Both Period v Placebo Both Period
Number of subjects included in analysis	14
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.0578 ^[19]
Method	paired t-test
Parameter estimate	Mean difference (net)
Point estimate	7.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.29
upper limit	14.62

Notes:

[19] - No multiple comparisons or multiplicity adjustments were conducted.

Statistical analysis title	Statistical Analysis 8
Statistical analysis description:	
General Health	
Comparison groups	Ecuzumab period 1 v Placebo period 1
Number of subjects included in analysis	14
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.5073 ^[20]
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	7.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.26
upper limit	31.11

Notes:

[20] - No multiple comparisons or multiplicity adjustments were conducted.

Statistical analysis title	Statistical Analysis 9
Statistical analysis description:	
Vitality	
Comparison groups	Eculizumab Both Period v Placebo Both Period
Number of subjects included in analysis	14
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.2474 ^[21]
Method	paired t-test
Parameter estimate	Median difference (net)
Point estimate	4.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.39
upper limit	11.72

Notes:

[21] - No multiple comparisons or multiplicity adjustments were conducted.

Statistical analysis title	Statistical Analysis 10
Statistical analysis description:	
Vitality	
Comparison groups	Eculizumab period 1 v Placebo period 1
Number of subjects included in analysis	14
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.8085 ^[22]
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	-2.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	-26.24
upper limit	20.88

Notes:

[22] - No multiple comparisons or multiplicity adjustments were conducted.

Statistical analysis title	Statistical Analysis 11
Statistical analysis description:	
Social Functioning	
Comparison groups	Eculizumab Both Period v Placebo Both Period

Number of subjects included in analysis	14
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.0716 ^[23]
Method	paired t-test
Parameter estimate	Mean difference (net)
Point estimate	-11.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.13
upper limit	1.21

Notes:

[23] - No multiple comparisons or multiplicity adjustments were conducted.

Statistical analysis title	Statistical Analysis 12
Statistical analysis description:	
Social Functioning	
Comparison groups	Placebo period 1 v Eculizumab period 1
Number of subjects included in analysis	14
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.1966 ^[24]
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	-16.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-41.86
upper limit	9.54

Notes:

[24] - No multiple comparisons or multiplicity adjustments were conducted.

Statistical analysis title	Statistical Analysis 13
Statistical analysis description:	
Role Emotional	
Comparison groups	Eculizumab Both Period v Placebo Both Period
Number of subjects included in analysis	14
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.1701 ^[25]
Method	paired t-test
Parameter estimate	Mean difference (net)
Point estimate	-11.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	-29.6
upper limit	5.99

Notes:

[25] - No multiple comparisons or multiplicity adjustments were conducted.

Statistical analysis title	Statistical Analysis 14
Statistical analysis description:	
Role emotional	
Comparison groups	Eculizumab period 1 v Placebo period 1
Number of subjects included in analysis	14
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.7422 [26]
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	5.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	-32.58
upper limit	44.48

Notes:

[26] - No multiple comparison or multiplicity adjustments were conducted.

Statistical analysis title	Statistical Analysis 15
Statistical analysis description:	
Mental Health	
Comparison groups	Eculizumab Both Period v Placebo Both Period
Number of subjects included in analysis	14
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.9007 [27]
Method	paired t-test
Parameter estimate	Mean difference (net)
Point estimate	0.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.83
upper limit	7.67

Notes:

[27] - No multiple comparisons or multiplicity adjustments were conducted.

Statistical analysis title	Statistical Analysis 16
Statistical analysis description:	
Mental Health	
Comparison groups	Placebo period 1 v Eculizumab period 1

Number of subjects included in analysis	14
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.1519 ^[28]
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	17.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.57
upper limit	43.29

Notes:

[28] - No multiple comparisons or multiplicity adjustments were conducted.

Statistical analysis title	Statistical Analysis 17
Statistical analysis description:	
Physical Component Score	
Comparison groups	Ecuzumab Both Period v Placebo Both Period
Number of subjects included in analysis	14
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.6807 ^[29]
Method	paired t-test
Parameter estimate	Mean difference (net)
Point estimate	1.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.57
upper limit	6.72

Notes:

[29] - No multiple comparisons or multiplicity adjustments were conducted.

Statistical analysis title	Statistical Analysis 18
Statistical analysis description:	
Physical Component Score	
Comparison groups	Ecuzumab period 1 v Placebo period 1
Number of subjects included in analysis	14
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.2226 ^[30]
Method	t-test, 2-sided
Parameter estimate	Median difference (net)
Point estimate	-6.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.79
upper limit	4.32

Notes:

[30] - No multiple comparisons or multiplicity adjustments were conducted.

Statistical analysis title	Statistical Analysis 19
Statistical analysis description:	
Mental Component Score	
Comparison groups	Placebo Both Period v Eculizumab Both Period
Number of subjects included in analysis	14
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.1505 ^[31]
Method	paired t-test
Parameter estimate	Mean difference (net)
Point estimate	-2.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.1
upper limit	1.26

Notes:

[31] - No multiple comparisons or multiplicity adjustments were conducted.

Statistical analysis title	Statistical Analysis 20
Statistical analysis description:	
Mental Component Score	
Comparison groups	Eculizumab period 1 v Placebo period 1
Number of subjects included in analysis	14
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.4151 ^[32]
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	5.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.77
upper limit	19.87

Notes:

[32] - No multiple comparisons or multiplicity adjustments were conducted.

Secondary: Change From Baseline in Respiratory Function Tests to Characterize the Degree of Involvement of Respiratory Muscles

End point title	Change From Baseline in Respiratory Function Tests to Characterize the Degree of Involvement of Respiratory Muscles
End point description:	
Change from Baseline in Forced Vital Capacity	
End point type	Secondary
End point timeframe:	
16 weeks	

End point values	Eculizumab period 1	Placebo period 1	Eculizumab Both Period	Placebo Both Period
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	7	7	7 ^[33]	7 ^[34]
Units: percentage of predicted				
arithmetic mean (standard deviation)				
Change From Baseline in Respiratory Function Tests	76.43 (± 15.328)	87 (± 23.544)	80 (± 14.894)	76.75 (± 23.152)

Notes:

[33] - There are 12 subjects in this group (Eculizumab period 1+ Eculizumab period 2)

[34] - There are 12 subjects in this group (Eculizumab period 1+ Eculizumab period 2)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Forced Vital Capacity	
Comparison groups	Eculizumab Both Period v Placebo Both Period
Number of subjects included in analysis	14
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.3377 ^[35]
Method	paired t-test
Parameter estimate	Mean difference (net)
Point estimate	3.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.94
upper limit	10.44

Notes:

[35] - No multiple comparisons or multiplicity adjustments were conducted.

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
No multiple comparisons or multiplicity adjustments were conducted.	
Comparison groups	Eculizumab period 1 v Placebo period 1
Number of subjects included in analysis	14
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.3391 ^[36]
Method	t-test, 2-sided
Parameter estimate	Median difference (net)
Point estimate	-10.57

Confidence interval	
level	95 %
sides	2-sided
lower limit	-33.71
upper limit	12.56

Notes:

[36] - No multiple comparisons or multiplicity adjustments were conducted.

Statistical analysis title	Statistical Analysis 3
Statistical analysis description: Negative Inspiratory Force	
Comparison groups	Ecuzumab Both Period v Placebo Both Period
Number of subjects included in analysis	14
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 1
Method	paired t-test
Parameter estimate	Mean difference (net)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.35
upper limit	4.35

Statistical analysis title	Statistical Analysis 4
Statistical analysis description: Negative Inspiratory Force	
Comparison groups	Ecuzumab period 1 v Placebo period 1
Number of subjects included in analysis	14
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.2292 ^[37]
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	-6.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.87
upper limit	4.73

Notes:

[37] - No multiple comparisons or multiplicity adjustments were conducted.

Secondary: Change From Baseline in Respiratory Function Tests to Characterize the Degree of Involvement of Respiratory Muscles

End point title	Change From Baseline in Respiratory Function Tests to Characterize the Degree of Involvement of Respiratory Muscles
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End point description:	
Change from Baseline in Forced Vital Capacity	
End point type	Secondary
End point timeframe:	
16 weeks	

End point values	Eculizumab period 1	Placebo period 1	Eculizumab Both Period	Placebo Both Period
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	7	7	7 ^[38]	7 ^[39]
Units: Percentage of Predicted				
arithmetic mean (standard deviation)				
Change from Baseline in Respiratory Function Test	76.43 (± 15.328)	87 (± 23.544)	80 (± 14.894)	76.75 (± 23.152)

Notes:

[38] - There are 12 subjects in this group (Eculizumab period 1+ Eculizumab period 2)

[39] - There are 12 subjects in this group (Eculizumab period 1+ Eculizumab period 2)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Forced Vital Capacity	
Comparison groups	Eculizumab Both Period v Placebo Both Period
Number of subjects included in analysis	14
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.3377 ^[40]
Method	paired t-test
Parameter estimate	Mean difference (net)
Point estimate	3.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.94
upper limit	10.44

Notes:

[40] - No multiple comparisons or multiplicity adjustments were conducted.

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Forced Vital Capacity	
Comparison groups	Eculizumab period 1 v Placebo period 1

Number of subjects included in analysis	14
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.3391 ^[41]
Method	t-test, 2-sided
Parameter estimate	Median difference (net)
Point estimate	-10.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-33.71
upper limit	12.56

Notes:

[41] - No multiple comparisons or multiplicity adjustments were conducted.

Statistical analysis title	Statistical Analysis 3
Statistical analysis description: Negative Inspiratory Force	
Comparison groups	Ecuzumab Both Period v Placebo Both Period
Number of subjects included in analysis	14
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 1 ^[42]
Method	paired t-test
Parameter estimate	Mean difference (net)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.35
upper limit	4.35

Notes:

[42] - No multiple comparisons or multiplicity adjustments were conducted.

Statistical analysis title	Statistical Analysis 4
Statistical analysis description: Negative Inspiratory Force	
Comparison groups	Ecuzumab period 1 v Placebo period 1
Number of subjects included in analysis	14
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.2292 ^[43]
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-6.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.87
upper limit	4.73

Notes:

[43] - No multiple comparisons or multiplicity adjustments were conducted.

Secondary: Change From Baseline in Respiratory Function Tests to Characterize the Degree of Involvement of Respiratory Muscles

End point title	Change From Baseline in Respiratory Function Tests to Characterize the Degree of Involvement of Respiratory Muscles
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End point description:

Change from Baseline in Negative Inspiratory Force. NIF is a measurement of respiratory muscle strength and ventilator reserve. NIF is represented by centimeters of water pressure (cmH₂O). A normal NIF measurement is negative 60 cmH₂O, or as 100% predicted value.

End point type	Secondary
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End point timeframe:

16 weeks

End point values	Eculizumab period 1	Placebo period 1	Eculizumab Both Period	Placebo Both Period
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	7	7	7 ^[44]	7 ^[45]
Units: Percentage of Predicted				
arithmetic mean (standard deviation)				
Change From Baseline in Respiratory Function Tests	92.43 (± 13.464)	99 (± 2.646)	93.5 (± 12.087)	93.5 (± 12.042)

Notes:

[44] - There are 12 subjects in this group (Eculizumab period 1+ Eculizumab period 2)

[45] - There are 12 subjects in this group (Eculizumab period 1+ Eculizumab period 2)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to the End of Treatment (16 Weeks) in the Two Most Affected QMG Items for Disease Severity (Individual Test Item: Double Vision)

End point title	Change From Baseline to the End of Treatment (16 Weeks) in the Two Most Affected QMG Items for Disease Severity (Individual Test Item: Double Vision)
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End point description:

The QMG scoring system is considered to be an objective evaluation of muscle strength based on quantitative testing of sentinel muscle groups. The MGFA task force has recommended that the QMG score be used in prospective studies of therapy for MG.

End point type	Secondary
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End point timeframe:

16 weeks

End point values	Eculizumab period 1	Placebo period 1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7 ^[46]	7 ^[47]		
Units: Unit on a scale				
arithmetic mean (standard deviation)				
Change From Baseline to the End of Treatment	-0.71 (± 1.113)	-0.29 (± 0.488)		

Notes:

[46] - Eculizumab

[47] - Placebo

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to the End of Treatment (16 Weeks) in the Two Most Affected QMG Items for Disease Severity (Individual Test Item: Ptosis)

End point title	Change From Baseline to the End of Treatment (16 Weeks) in the Two Most Affected QMG Items for Disease Severity (Individual Test Item: Ptosis)
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End point description:

The QMG scoring system is considered to be an objective evaluation of muscle strength based on quantitative testing of sentinel muscle groups. The MGFA task force has recommended that the QMG score be used in prospective studies of therapy for MG.

End point type	Secondary
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End point timeframe:

16 weeks

End point values	Eculizumab period 1	Placebo period 1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4 ^[48]	4 ^[49]		
Units: Unit on a scale				
arithmetic mean (standard deviation)				
Change From Baseline to the End of Treatment	-1 (± 1.155)	-0.5 (± 1)		

Notes:

[48] - Eculizumab

[49] - Placebo

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

46 weeks (Screening Period [up to 4 weeks], Treatment Period 1 [16 weeks], Washout Period [5 weeks], Treatment Period 2 [16 weeks], Follow-up Period [5 weeks]) for adverse events (AEs); 42 weeks for treatment emergent AEs (TEAEs).

Adverse event reporting additional description:

TEAEs were collected at every visit and follow-up

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	11.0
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Reporting groups

Reporting group title	Placebo
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Reporting group description:

Placebo

Placebo: Placebo IV weekly for 4 doses then every two weeks for 7 doses

Events that occurred during the Washout Period were attributed to treatment assignment during Treatment Period 1.

Reporting group title	Eculizumab
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Reporting group description:

Eculizumab

Eculizumab: eculizumab 600 mg IV weekly for 4 doses followed by eculizumab 900 mg IV every two weeks for 7 doses

Events that occurred during the Washout Period were attributed to treatment assignment during Treatment Period 1.

Serious adverse events	Placebo	Eculizumab	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 13 (7.69%)	1 / 13 (7.69%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Nervous system disorders			
Myasthenia Gravis A †			
subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myasthenia Gravis Crisis A †			
subjects affected / exposed	1 / 13 (7.69%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	Eculizumab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 13 (84.62%)	13 / 13 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acrochordon A †			
subjects affected / exposed	1 / 13 (7.69%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Haematoma A †			
subjects affected / exposed	1 / 13 (7.69%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Application Site Pruritus A †			
subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Chest Discomfort A †			
subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Chest Pain A †			
subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Cyst A †			
subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Fatigue A †			
subjects affected / exposed	1 / 13 (7.69%)	2 / 13 (15.38%)	
occurrences (all)	1	2	
Influenza Like Illness A †			
subjects affected / exposed	1 / 13 (7.69%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Pain A †			
subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Pyrexia A †			

subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Vessel Puncture Site Haematoma A †			
subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Hepatic Steatosis A †			
subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Erectile Dysfunction A †			
subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Menstrual Disorder A †			
subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Polymenorrhoea A †			
subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough A †			
subjects affected / exposed	0 / 13 (0.00%)	3 / 13 (23.08%)	
occurrences (all)	0	4	
Dysphonia A †			
subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Dyspnoea A †			
subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	2	
Hyperventilation A †			
subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Pharyngolaryngeal Pain A †			
subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Respiratory Tract Congestion A †			

subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 13 (7.69%) 1	
Psychiatric disorders Insomnia A † subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 13 (7.69%) 1	
Investigations Heart Rate Increased A † subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 13 (7.69%) 1	
Lymphocyte Count Decreased A † subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 13 (7.69%) 1	
Weight Decreased A † subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 13 (7.69%) 1	
Weight Increased A † subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 13 (7.69%) 1	
White Blood Cell Count Decreased A † subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 2	0 / 13 (0.00%) 0	
Injury, poisoning and procedural complications Contusion A † subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 3	2 / 13 (15.38%) 2	
Limb Injury A † subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 13 (7.69%) 1	
Muscle Strain A † subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 13 (7.69%) 1	
Procedural Nausea A † subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 13 (0.00%) 0	
Scratch A †			

subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 13 (7.69%) 1	
Tendon Rupture A † subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 13 (7.69%) 1	
Tooth Fracture A † subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 13 (0.00%) 0	
Wound A † subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 13 (7.69%) 1	
Nervous system disorders			
Carpal Tunnel Syndrome A † subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 13 (0.00%) 0	
Cholinergic Syndrome A † subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 13 (7.69%) 1	
Dizziness A † subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	2 / 13 (15.38%) 2	
Headache A † subjects affected / exposed occurrences (all)	4 / 13 (30.77%) 9	3 / 13 (23.08%) 14	
Memory Impairment A † subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 13 (0.00%) 0	
Paraesthesia A † subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 13 (7.69%) 1	
Presyncope A † subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 13 (7.69%) 1	
Sensory Disturbance A † subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 13 (7.69%) 2	

Sinus Headache A † subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 13 (7.69%) 2	
Blood and lymphatic system disorders			
Haematochezia A † subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 13 (7.69%) 1	
Leukopenia A † subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 13 (0.00%) 0	
Lip Dry A † subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 13 (7.69%) 1	
Nausea A † subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 4	4 / 13 (30.77%) 9	
Eye disorders			
Diplopia A † subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 13 (7.69%) 1	
Eye Discharge A † subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 13 (7.69%) 1	
Lacrimation Increased A † subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 13 (7.69%) 1	
Ocular Hyperaemia A † subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 13 (7.69%) 1	
Gastrointestinal disorders			
Abdominal Discomfort A † subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 13 (0.00%) 0	
Abdominal Pain A † subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 13 (7.69%) 1	
Abdominal Pain Upper A †			

subjects affected / exposed	1 / 13 (7.69%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Constipation A †			
subjects affected / exposed	0 / 13 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	2	
Dental Caries A †			
subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	2	
Diarrhoea A †			
subjects affected / exposed	1 / 13 (7.69%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Dyspepsia A †			
subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	2	
Oesophageal Food Impaction A †			
subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Salivary Gland Enlargement A †			
subjects affected / exposed	1 / 13 (7.69%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Vomiting A †			
subjects affected / exposed	1 / 13 (7.69%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Skin and subcutaneous tissue disorders			
Dermatitis Allergic A †			
subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Eczema A †			
subjects affected / exposed	1 / 13 (7.69%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Erythema A †			
subjects affected / exposed	1 / 13 (7.69%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Hyperhidrosis A †			
subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	

Pruritus Generalised A † subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 13 (0.00%) 0	
Rash A † subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 13 (7.69%) 1	
Skin Lesion A † subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 13 (7.69%) 1	
Renal and urinary disorders Haematuria A † subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 13 (7.69%) 1	
Nephrolithiasis A † subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 13 (7.69%) 1	
Musculoskeletal and connective tissue disorders Arthralgia A † subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	1 / 13 (7.69%) 1	
Back Pain A † subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 3	4 / 13 (30.77%) 5	
Bone Pain A † subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 13 (7.69%) 1	
Muscle Spasms A † subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	2 / 13 (15.38%) 3	
Musculoskeletal Pain A † subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 13 (7.69%) 1	
Musculoskeletal Stiffness A † subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 13 (0.00%) 0	
Myalgia A †			

subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 5	3 / 13 (23.08%) 3	
Neck Pain A † subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	3 / 13 (23.08%) 3	
Pain In Extremity A † subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 13 (0.00%) 0	
Infections and infestations			
Bronchitis A † subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 13 (0.00%) 0	
Cellulitis A † subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 13 (0.00%) 0	
Fungal Infection A † subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 13 (7.69%) 1	
Gastroenteritis Viral A † subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	1 / 13 (7.69%) 1	
Influenza A † subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	2 / 13 (15.38%) 2	
Nasopharyngitis A † subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 3	3 / 13 (23.08%) 3	
Onychomycosis A † subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 13 (7.69%) 1	
Oral Infection A † subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 13 (7.69%) 2	
Rhinitis A † subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 13 (0.00%) 0	

Sinusitis A † subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 13 (7.69%) 2	
Upper Respiratory Tract Infection A † subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	1 / 13 (7.69%) 1	
Viral Infection A † subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 2	2 / 13 (15.38%) 2	
Viral Upper Respiratory Tract Infection A † subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 13 (0.00%) 0	
Metabolism and nutrition disorders Type 2 Diabetes Mellitus A † subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 13 (7.69%) 2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 March 2009	Amendment 2 (US only) To address the recruitment concerns, this amendment will remove the inclusion criterion #3 "Duration of MG symptoms less than or equal to 10 years" and modify exclusion criterion #3 to specify a patient with MG status that, in the opinion of the Investigator, has reached a "burned out" stage will be excluded. This change will allow the recruitment of patients who have a likelihood of response to therapy based on their disease severity and MG treatment history.
07 May 2009	Amendment 2 (Canada Only) To address the recruitment concerns, this amendment will remove the inclusion criterion #3 "Duration ofMG symptoms less than or equal to 10 years" and modify exclusion criterion #3 to specify a patient with MG status that, in the opinion of the Investigator, has reached a "burned out" stage will be excluded. This change will allow the recruitment of patients who have a likelihood of response to therapy based on their disease severity and MG treatment history.
17 November 2009	Amendment 4 (UK Only) The purpose of this Amendment is to specify that women of childbearing potential must use adequate contraception methods during the study and for 5 months after treatment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Small sample size limited ability to detect intercohort differences. Carryover effect from Treatment Period (TP) 1 warrants cautious interpretation of TP 2 data.

Study terminated early; 13 patients received eculizumab or placebo in TP2.

Notes: