Clinical trial results:
PROSPECTIVE, DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED PHASE III STUDY EVALUATING EFFICACY AND SAFETY OF OCTAGAM 10% IN PATIENTS WITH DERMATOMYOSITIS

Summary

EudraCT number	2016-002902-37
Trial protocol	CZ DE HU NL RO
Global end of trial date	05 November 2019

Results information

Result version number	v1 (current)
This version publication date	20 November 2020
First version publication date	20 November 2020

Trial information

Trial identification

Sponsor protocol code	GAM10-08

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02728752
WHO universal trial number (UTN)	-
Other trial identifiers	IND: 16925

Notes:

Sponsors

Sponsor organisation name	Octapharma Pharmazeutika Produktionsges.m.b.H.
Sponsor organisation address	Oberlaaer Strasse 235, Vienna, Austria, 1100
Public contact	Global Clinical Project Manager, Octapharma Pharmazeutika Produktionsges.m.b.H., 0043 1 61032 1168, clinical.department@octapharma.com
Scientific contact	Global Clinical Project Manager, Octapharma Pharmazeutika Produktionsges.m.b.H., 0043 1 61032 1168, clinical.department@octapharma.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	03 July 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 November 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To provide confirmatory data on the beneficial effect of 2.0 g/kg of Octagam 10% given every 4 weeks compared with placebo in subjects with active DM based on the percentage of responders at Week 16.

Protection of trial subjects:

This trial was conducted in accordance to the principles of ICH- GCP, ensuring that the rights, safety and well-being of patients are protected and in consistency with the Declaration of Helsinki and national regulatory requirements. Inclusion and exclusion criteria were carefully defined in order to protect subjects from contraindications, interactions with other medication and risk factors associated with the investigational medicinal product. Study safety was assessed such as monitoring of AEs and SAEs, monitoring of safety lab results, concomitant medication and vital signs.

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	27 February 2017
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	Netherlands: 1
Country: Number of subjects enrolled	Poland: 4
Country: Number of subjects enrolled	Czech Republic: 12
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Hungary: 15
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	Romania: 2
Country: Number of subjects enrolled	Russian Federation: 21
Country: Number of subjects enrolled	Ukraine: 8
Country: Number of subjects enrolled	United States: 27
Worldwide total number of subjects	95
EEA total number of subjects	38

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)	75
From 65 to 84 years	20
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Patients with a diagnosis of definite or probable Dermatomyositis according to the Bohan and Peter criteria were were screened according to predefined in- and exclusion criteria.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Subjects received 4 infusions of placebo every 4 weeks during the blinded First Period (up to week 16). If confirmed deterioration (deterioration at 2 consecutive visits) during the First Period, subjects switched to Octagam 10%. After response assessment at Week 16, all subjects with no confirmed deterioration and subjects switched to Octagam 10% due to confirmed deterioration but without further confirmed deterioration during the First Period continued to receive 2.0 g/kg of Octagam 10% every 4 weeks during the subsequent 6-months open-label Extension Period. At Week 28, subjects who were stable on 2.0 g/kg Octagam 10% could be switched to 1.0 g/kg Octagam 10%, at the discretion of the investigator. Subjects randomized to placebo and switched to Octagam 10% due to confirmed deterioration, who deteriorated also during Octagam 10% treatment at 2 consecutive visits were droped-out after response assessment at Week 16 and did not enter the Extension Period.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received 4 infusions of placebo every 4 weeks during the blinded First Period (up to week 16). If confirmed deterioration (deterioration at 2 consecutive visits) during the First Period, subjects switched to Octagam 10%.

Arm title	Octagam 10%

Arm description:

Subjects received 4 infusions of 2.0 g/kg Octagam 10% every 4 weeks during the blinded First Period (16 weeks). If confirmed deterioration (deterioration at 2 consecutive visits) during the First Period, subjects switched to the alternate treatment. After response assessment at Week 16, all subjects with no confirmed deterioration during the First Period continued receiving 2.0 g/kg of Octagam 10% every 4 weeks during the subsequent 6-months open-label Extension Period. At Week 28, subjects who were stable on 2.0 g/kg Octagam 10% could be switched to 1.0 g/kg Octagam 10%, at the discretion of the investigator. Subjects randomized to Octagam and switched to the alternate treatment due to confirmed deterioration were droped-out after response assessment at Week 16 and did not enter the Extension Period.

Arm type	Experimental

Investigational medicinal product name	Octagam 10%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received 4 infusions of 2.0 g/kg Octagam 10% every 4 weeks during the blinded First Period (16 weeks). If confirmed deterioration (deterioration at 2 consecutive visits) during the First Period, subjects switched to the alternate treatment. After response assessment at Week 16, all subjects with no confirmed deterioration during the First Period continued receiving 2.0 g/kg of Octagam 10% every 4 weeks during the subsequent 6-months open-label Extension Period. At Week 28, subjects who were stable on 2.0 g/kg Octagam 10% could be switched to 1.0 g/kg Octagam 10%, at the discretion of the investigator. Subjects randomized to Octagam and switched to the alternate treatment due to confirmed deterioration were droped-out after response assessment at Week 16 and did not enter the Extension Period.

Number of subjects in period 1	Placebo	Octagam 10%
Started	48	47
Completed	35	34
Not completed	13	13
Patient decision	4	4
Adverse event, non-fatal	7	5
other reason	2	3
Administrative reason	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo

Reporting group description:

Subjects received 4 infusions of placebo every 4 weeks during the blinded First Period (up to week 16). If confirmed deterioration (deterioration at 2 consecutive visits) during the First Period, subjects switched to Octagam 10%. After response assessment at Week 16, all subjects with no confirmed deterioration and subjects switched to Octagam 10% due to confirmed deterioration but without further confirmed deterioration during the First Period continued to receive 2.0 g/kg of Octagam 10% every 4 weeks during the subsequent 6-months open-label Extension Period. At Week 28, subjects who were stable on 2.0 g/kg Octagam 10% could be switched to 1.0 g/kg Octagam 10%, at the discretion of the investigator. Subjects randomized to placebo and switched to Octagam 10% due to confirmed deterioration, who deteriorated also during Octagam 10% treatment at 2 consecutive visits were droped-out after response assessment at Week 16 and did not enter the Extension Period.

Reporting group title	Octagam 10%

Reporting group description:

Subjects received 4 infusions of 2.0 g/kg Octagam 10% every 4 weeks during the blinded First Period (16 weeks). If confirmed deterioration (deterioration at 2 consecutive visits) during the First Period, subjects switched to the alternate treatment. After response assessment at Week 16, all subjects with no confirmed deterioration during the First Period continued receiving 2.0 g/kg of Octagam 10% every 4 weeks during the subsequent 6-months open-label Extension Period. At Week 28, subjects who were stable on 2.0 g/kg Octagam 10% could be switched to 1.0 g/kg Octagam 10%, at the discretion of the investigator. Subjects randomized to Octagam and switched to the alternate treatment due to confirmed deterioration were droped-out after response assessment at Week 16 and did not enter the Extension Period.

Reporting group values	Placebo	Octagam 10%	Total
Number of subjects	48	47	95
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	51.35	54.04	
full range (min-max)	22 to 79	22 to 77	-
Gender categorical Units: Subjects			
Female	35	36	71
Male	13	11	24

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

Subjects received 4 infusions of placebo every 4 weeks during the blinded First Period (up to week 16). If confirmed deterioration (deterioration at 2 consecutive visits) during the First Period, subjects switched to Octagam 10%. After response assessment at Week 16, all subjects with no confirmed deterioration and subjects switched to Octagam 10% due to confirmed deterioration but without further confirmed deterioration during the First Period continued to receive 2.0 g/kg of Octagam 10% every 4 weeks during the subsequent 6-months open-label Extension Period. At Week 28, subjects who were stable on 2.0 g/kg Octagam 10% could be switched to 1.0 g/kg Octagam 10%, at the discretion of the investigator. Subjects randomized to placebo and switched to Octagam 10% due to confirmed deterioration, who deteriorated also during Octagam 10% treatment at 2 consecutive visits were droped-out after response assessment at Week 16 and did not enter the Extension Period.

Reporting group title	Octagam 10%

Reporting group description:

Subjects received 4 infusions of 2.0 g/kg Octagam 10% every 4 weeks during the blinded First Period (16 weeks). If confirmed deterioration (deterioration at 2 consecutive visits) during the First Period, subjects switched to the alternate treatment. After response assessment at Week 16, all subjects with no confirmed deterioration during the First Period continued receiving 2.0 g/kg of Octagam 10% every 4 weeks during the subsequent 6-months open-label Extension Period. At Week 28, subjects who were stable on 2.0 g/kg Octagam 10% could be switched to 1.0 g/kg Octagam 10%, at the discretion of the investigator. Subjects randomized to Octagam and switched to the alternate treatment due to confirmed deterioration were droped-out after response assessment at Week 16 and did not enter the Extension Period.

Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

The full analysis set (FAS) is defined according to the intention-to-treat principle and consists of all randomized subjects. It is expected that the FAS will coincide with the safety set.

Subject analysis set title	Safety Analysis Set
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety analysis set (SAF) consists of all subjects who received at least part of one infusion of Octagam or placebo.

Subject analysis set title	Time to Minimal Improvement Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

Time to Minimal Improvement - From Start of First Treatment in Overall Period

Subject analysis set title	Time to Minimal Improvement Octagam 10%
Subject analysis set type	Full analysis

Subject analysis set description:

Time to Minimal Improvement - From Start of First Treatment in Overall Period

Subject analysis set title	Time to Moderate Improvement Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

Time to Moderate Improvement - From Start of First Treatment in Overall Period

Subject analysis set title	Time to Moderate Improvement Octagam 10%
Subject analysis set type	Full analysis

Subject analysis set description:

Time to Moderate Improvement - From Start of First Treatment in Overall Period

Subject analysis set title	Time to Major Improvement Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

Time to Major Improvement - From Start of First Treatment in Overall Period

Subject analysis set title	Time to Major Improvement Octagam 10%
Subject analysis set type	Full analysis

Subject analysis set description:

Time to Major Improvement - From Start of First Treatment in Overall Period

Primary: Number of Patients Who Had an Increase of ≥20 Points on the Total Improvement Score (TIS)

End point title	Number of Patients Who Had an Increase of ≥20 Points on the Total Improvement Score (TIS)

End point description:

Proportion of responders in the 2.0 g/kg Octagam 10% and placebo arms at Week 16 relative to baseline (Week 0). A responder being defined as a patient with an increase of ≥20 points on the Total Improvement Score (TIS, a scale from 0 to 100; 20-39 points being minimal improvement, 40-59 points being moderate improvement, and ≥60 points being major improvement
Full Analysis Set : Octagam (N=47) Placebo (N=48)

End point type	Primary

End point timeframe:

At week 16

End point values	Placebo	Octagam 10%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	47		
Units: Patients				
number (not applicable)				
Number of patients (%)	21 43.75	37 78.72		

Statistical analyses

Statistical analysis title	Proportion of Responders

Statistical analysis description:

The primary endpoint measure 'response' was assessed at Week 16 based on the TIS score. The proportion of responders within both treatment groups was compared by the Cochran-Mantel-Haenszel test, stratified by GDA at baseline (randomization stratum), using a two-sided alpha level of 0.05. The primary analysis was to be considered a
success if the proportion of responders was significantly higher in the octagam 10% group compared to the placebo group.

Comparison groups	Placebo v Octagam 10%
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0008
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Response Rate
Point estimate	34.97

Confidence interval	
level	95 %
sides	2-sided
lower limit	16.7
upper limit	53.24

Secondary: Proportion of TIS Responders by Improvement Category at Week 16

End point title	Proportion of TIS Responders by Improvement Category at Week 16

End point description:

The TIS (Total Improvement Score) is a scale from 0 to 100 that allows for the discrimination between minimal, moderate and major responders depending on their improvement in the combined 6 CSM: ≥20 to 39 points being minimal improvement, ≥40 to 59 points being moderate improvement, and ≥60 points being major improvement.
Full Analysis Set : Octagam (N=47) Placebo (N=48)

End point type	Secondary

End point timeframe:

16 weeks

End point values	Placebo	Octagam 10%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	47		
Units: patients				
number (not applicable)				
Primary	21	37		
Primary (%)	43.75	78.72		
At least moderate improvement	11	32		
At least moderate improvement (%)	22.92	68.09		
At least major improvement	4	15		
At least major improvement (%)	8.33	31.91		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of TIS Responders by Improvement Category at Week 40

End point title	Proportion of TIS Responders by Improvement Category at Week 40

End point description:

The TIS (Total Improvement Score) is a scale from 0 to 100 that allows for the discrimination between minimal, moderate and major responders depending on their improvement in the combined 6 CSM: ≥20 to 39 points being minimal improvement, ≥40 to 59 points being moderate improvement, and ≥60 points being major improvement.
Forty-five patients in the octagam 10% group and 46 patients in the placebo group completed the First Period and entered the 24-week Extension Period during which all patients received open-label octagam 10% treatment.
Full Analysis Set : Octagam (N=47) Placebo (N=48)

End point type	Secondary
End point timeframe: 40 weeks	

End point values	Placebo	Octagam 10%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	45		
Units: Patients				
number (not applicable)				
At least minimal improvement	32	32		
At least minimal improvement (%)	69.57	71.11		
At least moderate improvement	28	26		
At least moderate improvement (%)	60.87	57.78		
At least major improvement	14	17		
At least major improvement (%)	30.43	37.78		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline (Week 0) to End of First Period (Week 16) in the Modified Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI)

End point title	Mean Change From Baseline (Week 0) to End of First Period (Week 16) in the Modified Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI)

End point description:

The modified CDASI has 3 activity measures (erythema, scale, and erosion/ulceration) and 2 damage measures (poikiloderma and calcinosis) which are assessed over 15 body areas. In addition, Gottron's papules on the hands are evaluated both for activity and damage. Lastly, the activity of periungual changes and alopecia is assessed.
Full Analysis Set : Octagam (N=47) Placebo (N=48)

End point type	Secondary
End point timeframe: First 16 weeks	

End point values	Placebo	Octagam 10%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	45		
Units: Score				
arithmetic mean (standard deviation)				
Total Activity Score	-1.16 (± 7.000)	-9.36 (± 10.542)		

Total Damage Score	-0.02 (± 0.771)	-0.67 (± 1.871)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From End of First Period (Week 16) to End of Extension Period (Week 40) in the Modified Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI)

End point title	Mean Change From End of First Period (Week 16) to End of Extension Period (Week 40) in the Modified Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI)

End point description:

The modified CDASI has 3 activity measures (erythema, scale, and erosion/ulceration) and 2 damage measures (poikiloderma and calcinosis) which are assessed over 15 body areas. In addition, Gottron's papules on the hands are evaluated both for activity and damage. Lastly, the activity of periungual changes and alopecia is assessed.
Full Analysis Set : Octagam (N=47) Placebo (N=48) Different numbers of patients analyzed in each group due to patient discontinuation

End point type	Secondary

End point timeframe:

From week 16 to Week 40

End point values	Placebo	Octagam 10%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	34		
Units: Score				
arithmetic mean (standard deviation)				
Total Activity Score	-8.52 (± 11.344)	-1.79 (± 4.169)		
Total Damage Score	-0.24 (± 0.969)	0.26 (± 2.220)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline (Week 0) to End of First Period (Week 16) in: SF-36v2 Health Survey

End point title	Mean Change From Baseline (Week 0) to End of First Period (Week 16) in: SF-36v2 Health Survey

End point description:

The SF-36 is a multi-purpose, short-form health survey with only 36 questions. It yields an 8-scale profile of functional health and well-being scores as well as psychometrically-based physical and mental health summary measures and a preference-based health utility index.
Different numbers of patients analyzed in each group due to patient discontinuation.

Full Analysis Set : Octagam (N=47) Placebo (N=48) Different numbers of patients analyzed in each group due to patient discontinuation

End point type	Secondary

End point timeframe:

From start of the trial till Week 16

End point values	Placebo	Octagam 10%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	43		
Units: Score				
arithmetic mean (standard deviation)				
Physical Functioning	2.27 (± 4.598)	7.06 (± 8.220)		
Role Physical	1.88 (± 8.154)	4.49 (± 8.444)		
Bodily Pain	1.29 (± 8.089)	5.29 (± 9.632)		
General Health	3.20 (± 6.732)	5.46 (± 6.431)		
Vitality	4.22 (± 7.540)	6.63 (± 9.458)		
Social Functioning	2.56 (± 7.686)	4.66 (± 10.401)		
Role Emotional	0.65 (± 9.157)	3.24 (± 8.162)		
Mental Health	1.89 (± 7.340)	3.95 (± 7.024)		
Physical Health Score	2.39 (± 5.945)	6.27 (± 8.720)		
Mental Health Score	1.95 (± 7.580)	3.36 (± 7.399)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline (Week 0) to Extension Period (Week 40) in: SF-36v2 Health Survey

End point title	Mean Change From Baseline (Week 0) to Extension Period (Week 40) in: SF-36v2 Health Survey

End point description:

The SF-36 is a multi-purpose, short-form health survey with only 36 questions. It yields an 8-scale profile of functional health and well-being scores as well as psychometrically-based physical and mental health summary measures and a preference-based health utility index.
Full Analysis Set : Octagam (N=47) Placebo (N=48) Different numbers of patients analyzed in each group due to patient discontinuation

End point type	Secondary

End point timeframe:

From start of the trial till Week 40

End point values	Placebo	Octagam 10%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	34		
Units: Score				
arithmetic mean (standard deviation)				
Physical Functioning	6.65 (± 8.258)	8.77 (± 10.930)		
Role Physical	6.80 (± 9.945)	8.32 (± 10.870)		
Bodily Pain	6.09 (± 11.597)	6.22 (± 12.895)		
General Health	6.74 (± 6.808)	6.42 (± 10.170)		
Vitality	9.25 (± 9.742)	8.65 (± 11.385)		
Social Functioning	8.31 (± 11.272)	7.82 (± 12.537)		
Role Emotional	5.07 (± 11.118)	3.17 (± 12.580)		
Mental Health	7.92 (± 10.202)	6.31 (± 8.974)		
Physical Health Score	6.31 (± 8.598)	8.41 (± 11.858)		
Mental Health Score	7.39 (± 10.154)	4.83 (± 9.631)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline (Week 0) to End of First Period (Week 16) in Physician's Global Disease Activity

End point title	Mean Change From Baseline (Week 0) to End of First Period (Week 16) in Physician's Global Disease Activity

End point description:

10 cm VAS assessing global disease activity from "No evidence of disease activity" to "Extremely active or severe disease activity"; Disease Activity being defined as potentially reversible pathology or physiology resulting from the myositis). Assessment completed by physician. 0 is lowest score and 10 is highest score. Higher score associated with worse outcome.
Full Analysis Set : Octagam (N=47) Placebo (N=48) Different numbers of patients analyzed in each group due to patient discontinuation

End point type	Secondary

End point timeframe:

From start of the trial till Week 16

End point values	Placebo	Octagam 10%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	45		
Units: Score				
arithmetic mean (standard deviation)	-0.60 (± 1.815)	-2.39 (± 1.987)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline (Week 0) to Extension Period (Week 40) in Physician's Global Disease Activity

End point title	Mean Change From Baseline (Week 0) to Extension Period (Week 40) in Physician's Global Disease Activity

End point description:

10 cm VAS assessing global disease activity from "No evidence of disease activity" to "Extremely active or severe disease activity"; Disease Activity being defined as potentially reversible pathology or physiology resulting from the myositis). Assessment completed by physician. 0 is lowest score and 10 is highest score. Higher score associated with worse outcome.
Full Analysis Set : Octagam (N=47) Placebo (N=48) Different numbers of patients analyzed in each group due to patient discontinuation

End point type	Secondary

End point timeframe:

From start of the trial till Week 40

End point values	Placebo	Octagam 10%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	34		
Units: Score				
arithmetic mean (standard deviation)	-2.93 (± 1.888)	-3.06 (± 1.817)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline (Week 0) to End of First Period (Week 16) in: Patient Global Disease Activity

End point title	Mean Change From Baseline (Week 0) to End of First Period (Week 16) in: Patient Global Disease Activity

End point description:

Patient's Global Disease Activity (10cm VAS assessing the overall activity of the patient's disease today from "No evidence of disease activity" to "Extremely active or severe disease activity", Disease Activity being active inflammation in the patient's muscles, skin, joints, intestines, heart, lungs or other parts of the body, which can improve when treated with medicines). 0 is lowest score and 10 is highest score. Higher score associated with worse outcome.
Full Analysis Set : Octagam (N=47) Placebo (N=48) Different numbers of patients analyzed in each

group due to patient discontinuation

End point type	Secondary

End point timeframe:

From start of the trial till Week 16

End point values	Placebo	Octagam 10%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	45		
Units: Score				
arithmetic mean (standard deviation)	-1.11 (± 2.094)	-2.19 (± 2.276)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline (Week 0) to Extension Period (Week 40) in: Patient Global Disease Activity

End point title	Mean Change From Baseline (Week 0) to Extension Period (Week 40) in: Patient Global Disease Activity

End point description:

Patient’s Global Disease Activity (10cm VAS assessing the overall activity of the patient’s disease today from “No evidence of disease activity” to “Extremely active or severe disease activity”, Disease Activity being active inflammation in the patient’s muscles, skin, joints, intestines, heart, lungs or other parts of the body, which can improve when treated with medicines). 0 is lowest score and 10 is highest score. Higher score associated with worse outcome.
Full Analysis Set : Octagam (N=47) Placebo (N=48) Different numbers of patients analyzed in each group due to patient discontinuation

End point type	Secondary

End point timeframe:

From start of the trial till Week 40.

End point values	Placebo	Octagam 10%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	33		
Units: Score				
arithmetic mean (standard deviation)	-2.77 (± 2.133)	-2.71 (± 2.651)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline (Week 0) to End of First Period (Week 16) in: MMT-8

End point title	Mean Change From Baseline (Week 0) to End of First Period (Week 16) in: MMT-8

End point description:

Manual Muscle Testing - MMT-8; a set of 8 designated muscles tested bilaterally [potential score 0 – 150]. Higher score associated with better outcome.
Full Analysis Set : Octagam (N=47) Placebo (N=48) Different numbers of patients analyzed in each group due to patient discontinuation

End point type	Secondary

End point timeframe:

From start of the trial till Week 16

End point values	Placebo	Octagam 10%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	45		
Units: Score				
arithmetic mean (standard deviation)	3.21 (± 9.390)	14.38 (± 14.581)		

Statistical analyses

No statistical analyses for this end point

Secondary: Measure Title Mean Change From Baseline (Week 0) to Extension Period (Week 40) in: MMT-8

End point title	Measure Title Mean Change From Baseline (Week 0) to Extension Period (Week 40) in: MMT-8

End point description:

Manual Muscle Testing - MMT-8; a set of 8 designated muscles tested bilaterally [potential score 0 – 150]. Higher score associated with better outcome.
Full Analysis Set : Octagam (N=47) Placebo (N=48) Different numbers of patients analyzed in each group due to patient discontinuation

End point type	Secondary

End point timeframe:

Time Frame From start of the trial till Week 40

End point values	Placebo	Octagam 10%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	33		
Units: Score				
arithmetic mean (standard deviation)	12.00 (± 7.491)	20.09 (± 14.486)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline (Week 0) to End of First Period (Week 16) in: Health Assessment Questionnaire

End point title	Mean Change From Baseline (Week 0) to End of First Period (Week 16) in: Health Assessment Questionnaire

End point description:

Health Assessment Questionnaire (HAQ); a generic rather than a disease-specific instrument; comprised of 8 sections: dressing, arising, eating, walking, hygiene, reach, grip, and activities. There are 2 or 3 questions for each section. Scoring within each section is from 0 [without any difficulty] to 3 [unable to do]. For each section the score given to that section is the worst score within the section. The 8 scores of the 8 sections are summed and divided by 8). Assessment completed by patients. Lowest score 0 highest score 24. Higher score associated with worse outcome.
Full Analysis Set : Octagam (N=47) Placebo (N=48) Different numbers of patients analyzed in each group due to patient discontinuation

End point type	Secondary

End point timeframe:

From start of the trial till Week 16

End point values	Placebo	Octagam 10%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	45		
Units: Score				
arithmetic mean (standard deviation)	-0.16 (± 0.366)	-0.56 (± 0.590)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline (Week 0) to Extension Period (Week 40) in: Health Assessment Questionnaire

End point title	Mean Change From Baseline (Week 0) to Extension Period (Week 40) in: Health Assessment Questionnaire

End point description:

Health Assessment Questionnaire (HAQ); a generic rather than a disease-specific instrument; comprised of 8 sections: dressing, arising, eating, walking, hygiene, reach, grip, and activities. There are 2 or 3 questions for each section. Scoring within each section is from 0 [without any difficulty] to 3 [unable to do]. For each section the score given to that section is the worst score within the section. The 8 scores of the 8 sections are summed and divided by 8). Assessment completed by patients. Lowest score 0 highest score 24. Higher score associated with worse outcome.
Full Analysis Set : Octagam (N=47) Placebo (N=48) Different numbers of patients analyzed in each group due to patient discontinuation

End point type	Secondary

End point timeframe:

From start of the trial till Week 40

End point values	Placebo	Octagam 10%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	33		
Units: Score				
arithmetic mean (standard deviation)	-0.54 (± 0.524)	-0.66 (± 0.805)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline (Week 0) to End of First Period (Week 16) in Enzymes (Alanine Aminotransferase)

End point title	Mean Change From Baseline (Week 0) to End of First Period (Week 16) in Enzymes (Alanine Aminotransferase)

End point description:

Full Analysis Set : Octagam (N=47) Placebo (N=48) Different numbers of patients analyzed in each group due to patient discontinuation

End point type	Secondary

End point timeframe:

From start of the trial till Week 16

End point values	Placebo	Octagam 10%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	42		
Units: U/L				
arithmetic mean (standard deviation)	-4.47 (± 29.796)	-8.52 (± 18.474)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline (Week 0) to Extension Period (Week 40) in Enzymes (Alanine Aminotransferase)

End point title	Mean Change From Baseline (Week 0) to Extension Period (Week 40) in Enzymes (Alanine Aminotransferase)

End point description:

Full Analysis Set : Octagam (N=47) Placebo (N=48) Different numbers of patients analyzed in each group due to patient discontinuation.

End point type	Secondary

End point timeframe:

From start of the trial till Week 40

End point values	Placebo	Octagam 10%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	33		
Units: U/L				
arithmetic mean (standard deviation)	-4.06 (± 14.787)	-7.15 (± 18.480)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline (Week 0) to End of First Period (Week 16) in Enzymes (Aspartate Aminotransferase)

End point title	Mean Change From Baseline (Week 0) to End of First Period (Week 16) in Enzymes (Aspartate Aminotransferase)

End point description:

Full Analysis Set : Octagam (N=47) Placebo (N=48) Different numbers of patients analyzed in each group due to patient discontinuation.

End point type	Secondary

End point timeframe:

From start of the trial till Week 40

End point values	Placebo	Octagam 10%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	44		
Units: U/L				
arithmetic mean (standard deviation)	-3.07 (± 31.317)	-7.82 (± 26.139)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline (Week 0) to Extension Period (Week 40) in Enzymes (Aspartate Aminotransferase)

End point title	Mean Change From Baseline (Week 0) to Extension Period (Week 40) in Enzymes (Aspartate Aminotransferase)

End point description:

Full Analysis Set : Octagam (N=47) Placebo (N=48) Different numbers of patients analyzed in each group due to patient discontinuation.

End point type	Secondary

End point timeframe:

From start of the trial till Week 40

End point values	Placebo	Octagam 10%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	34		
Units: U/L				
arithmetic mean (standard deviation)	-2.20 (± 16.421)	-7.76 (± 26.431)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline (Week 0) to End of First Period (Week 16) in Enzymes (Lactate Dehydrogenase)

End point title	Mean Change From Baseline (Week 0) to End of First Period (Week 16) in Enzymes (Lactate Dehydrogenase)

End point description:

Full Analysis Set : Octagam (N=47) Placebo (N=48) Different numbers of patients analyzed in each group due to patient discontinuation.

End point type	Secondary

End point timeframe:

From start of the trial till Week 16

End point values	Placebo	Octagam 10%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	45		
Units: U/L				
arithmetic mean (standard deviation)	-19.79 (± 142.012)	-11.04 (± 165.252)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline (Week 0) to Extension Period (Week 40) in Enzymes (Lactate Dehydrogenase)

End point title	Mean Change From Baseline (Week 0) to Extension Period (Week 40) in Enzymes (Lactate Dehydrogenase)

End point description:

Full Analysis Set : Octagam (N=47) Placebo (N=48) Different numbers of patients analyzed in each group due to patient discontinuation.

End point type	Secondary

End point timeframe:

From start of the trial till Week 40.

End point values	Placebo	Octagam 10%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	34		
Units: U/L				
arithmetic mean (standard deviation)	-33.43 (± 63.651)	-59.21 (± 92.801)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline (Week 0) to End of First Period (Week 16) in Enzymes (Aldolase)

End point title	Mean Change From Baseline (Week 0) to End of First Period (Week 16) in Enzymes (Aldolase)

End point description:

Full Analysis Set : Octagam (N=47) Placebo (N=48) Different numbers of patients analyzed in each group due to patient discontinuation.

End point type	Secondary

End point timeframe:

From start of the trial till Week 16

End point values	Placebo	Octagam 10%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	42		
Units: U/L				
arithmetic mean (standard deviation)	-2.51 (± 12.077)	-0.48 (± 7.743)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline (Week 0) to Extension Period (Week 40) in Enzymes (Aldolase)

End point title	Mean Change From Baseline (Week 0) to Extension Period (Week 40) in Enzymes (Aldolase)

End point description:

Full Analysis Set : Octagam (N=47) Placebo (N=48) Different numbers of patients analyzed in each group due to patient discontinuation.

End point type	Secondary

End point timeframe:

From start of the trial till Week 40

End point values	Placebo	Octagam 10%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	32		
Units: U/L				
arithmetic mean (standard deviation)	-0.59 (± 7.839)	-1.48 (± 3.644)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline (Week 0) to End of First Period (Week 16) in Enzymes (Creatine Kinase)

End point title	Mean Change From Baseline (Week 0) to End of First Period (Week 16) in Enzymes (Creatine Kinase)

End point description:

Full Analysis Set : Octagam (N=47) Placebo (N=48) Different numbers of patients analyzed in each group due to patient discontinuation.

End point type	Secondary

End point timeframe:

From start of the trial till Week 16

End point values	Placebo	Octagam 10%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	44		
Units: U/L				
arithmetic mean (standard deviation)	-352.79 (± 2141.534)	-169.20 (± 434.224)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline (Week 0) to Extension Period (Week 40) in Enzymes (Creatine Kinase)

End point title	Mean Change From Baseline (Week 0) to Extension Period (Week 40) in Enzymes (Creatine Kinase)

End point description:

Full Analysis Set : Octagam (N=47) Placebo (N=48) Different numbers of patients analyzed in each group due to patient discontinuation.

End point type	Secondary

End point timeframe:

From start of the trial till Week 40

End point values	Placebo	Octagam 10%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	34		
Units: U/L				
arithmetic mean (standard deviation)	-56.54 (± 556.928)	-169.38 (± 449.210)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline (Week 0) to End of First Period (Week 16) in: Extra-muscular Activity

End point title	Mean Change From Baseline (Week 0) to End of First Period (Week 16) in: Extra-muscular Activity

End point description:

Full Analysis Set : Octagam (N=47) Placebo (N=48) Different numbers of patients analyzed in each group due to patient discontinuation.

End point type	Secondary

End point timeframe:

From start of the trial until Week 16

End point values	Placebo	Octagam 10%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	45		
Units: Score				
arithmetic mean (standard deviation)	-0.94 (± 2.287)	-2.18 (± 2.134)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline (Week 0) to Extension Period (Week 40) in: Extra-muscular Activity

End point title	Mean Change From Baseline (Week 0) to Extension Period (Week 40) in: Extra-muscular Activity

End point description:

Full Analysis Set : Octagam (N=47) Placebo (N=48) Different numbers of patients analyzed in each group due to patient discontinuation.

End point type	Secondary

End point timeframe:

From start of the trial until Week 40

End point values	Placebo	Octagam 10%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	34		
Units: Score				
arithmetic mean (standard deviation)	-2.64 (± 2.092)	-2.67 (± 2.061)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean TIS From Baseline (Week 0) to End of First Period (Week 16)

End point title	Mean TIS From Baseline (Week 0) to End of First Period (Week 16)

End point description:

The TIS (Total Improvement Score) is a scale from 0 to 100 that allows for the discrimination between minimal, moderate and major responders depending on their improvement in the combined 6 CSM: ≥20 to 39 points being minimal improvement, ≥40 to 59 points being moderate improvement, and ≥60 points being major improvement.
Full Analysis Set : Octagam (N=47) Placebo (N=48) Different numbers of patients analyzed in each group due to patient discontinuation.

End point type	Secondary

End point timeframe:

Up to 16 weeks

End point values	Placebo	Octagam 10%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	45		
Units: Score				
arithmetic mean (standard deviation)	21.57 (± 20.185)	48.44 (± 24.444)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean TIS From Baseline (Week 0) to End of Extension Period (Week 40)

End point title	Mean TIS From Baseline (Week 0) to End of Extension Period (Week 40)

End point description:

The TIS (Total Improvement Score) is a scale from 0 to 100 that allows for the discrimination between minimal, moderate and major responders depending on their improvement in the combined 6 CSM: ≥20 to 39 points being minimal improvement, ≥40 to 59 points being moderate improvement, and ≥60 points being major improvement.
Full Analysis Set : Octagam (N=47) Placebo (N=48) Different numbers of patients analyzed in each group due to patient discontinuation.

End point type	Secondary

End point timeframe:

Up to 40 weeks

End point values	Placebo	Octagam 10%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	34		
Units: Score				
arithmetic mean (standard deviation)	51.07 (± 18.314)	55.44 (± 21.712)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Minimal Improvement in TIS

End point title	Time to Minimal Improvement in TIS

End point description:

When interpreting these time to event evaluations, one has to keep in mind that eventually all patients were treated with octagam 10%, so that differences in time to response for the Overall Period reflect this delayed start of treatment rather than the true difference between treatment with octagam 10%

and placebo.
Full Analysis Set: Octagam (N=47) Placebo (N=48)

End point type	Secondary

End point timeframe:

Up to 40 weeks

End point values	Time to Minimal Improvement Placebo	Time to Minimal Improvement Octagam 10%		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	41	47		
Units: days				
number (not applicable)	114	35		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Moderate Improvement in TIS

End point title	Time to Moderate Improvement in TIS

End point description:

When interpreting these time to event evaluations, one has to keep in mind that eventually all patients were treated with octagam 10%, so that differences in time to response for the Overall Period reflect this delayed start of treatment rather than the true difference between treatment with octagam 10% and placebo.
Full Analysis Set: Octagam (N=47) Placebo (N=48)

End point type	Secondary

End point timeframe:

up to 40 weeks

End point values	Time to Moderate Improvement Placebo	Time to Moderate Improvement Octagam 10%		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	36	39		
Units: days				
number (not applicable)	197	85		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Confirmed Deterioration in the First Period

End point title	Time to Confirmed Deterioration in the First Period

End point description:

Full Analysis Set : Octagam (N=47) Placebo (N=48)

End point type	Secondary

End point timeframe:

Up to week 16

End point values	Placebo	Octagam 10%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	47		
Units: days				
number (not applicable)				
Number of patients analyzed	3	0		
Time	117	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Confirmed Deterioration Overall

End point title	Time to Confirmed Deterioration Overall

End point description:

Full Analysis Set : Octagam (N=47) Placebo (N=48)

End point type	Secondary

End point timeframe:

Up to 40 weeks

End point values	Placebo	Octagam 10%		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48[1]	47[2]		
Units: days				
number (not applicable)				
Number of patients analyzed	3	1		
Time	0	0		

Notes:

[1] - No result due to limited sample size

[2] - No result due to limited sample size

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Major Improvement in TIS

End point title	Time to Major Improvement in TIS

End point description:

When interpreting these time to event evaluations, one has to keep in mind that eventually all patients were treated with octagam 10%, so that differences in time to response for the Overall Period reflect this delayed start of treatment rather than the true difference between treatment with octagam 10% and placebo.
Full Analysis Set: Octagam (N=47) Placebo (N=48)

End point type	Secondary

End point timeframe:

Up to 40 weeks

End point values	Time to Major Improvement Placebo	Time to Major Improvement Octagam 10%		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20	25		
Units: days				
number (not applicable)	283	283		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 40 weeks	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.0
Reporting groups	
Reporting group title	First Period Placebo
Reporting group description: -	
Reporting group title	Overall Period Octagam
Reporting group description: -	

Serious adverse events	First Period Placebo	Overall Period Octagam	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 48 (4.17%)	14 / 95 (14.74%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma			
subjects affected / exposed	0 / 48 (0.00%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 48 (0.00%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	1 / 48 (2.08%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure congestive			

subjects affected / exposed	0 / 48 (0.00%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus tachycardia			
subjects affected / exposed	1 / 48 (2.08%)	0 / 95 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular extrasystoles			
subjects affected / exposed	0 / 48 (0.00%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	0 / 48 (0.00%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	0 / 48 (0.00%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoaesthesia			
subjects affected / exposed	0 / 48 (0.00%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss of consciousness			
subjects affected / exposed	0 / 48 (0.00%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Condition aggravated			
subjects affected / exposed	0 / 48 (0.00%)	2 / 95 (2.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 48 (0.00%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 48 (0.00%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 48 (0.00%)	3 / 95 (3.16%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 48 (0.00%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	0 / 48 (0.00%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Atypical pneumonia			
subjects affected / exposed	0 / 48 (0.00%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia bacteraemia			
subjects affected / exposed	0 / 48 (0.00%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	0 / 48 (0.00%)	1 / 95 (1.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 48 (0.00%)	2 / 95 (2.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tropical spastic paresis			
subjects affected / exposed	1 / 48 (2.08%)	0 / 95 (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	First Period Placebo	Overall Period Octagam	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 48 (58.33%)	83 / 95 (87.37%)	
Investigations			
Blood pressure increased			
subjects affected / exposed	3 / 48 (6.25%)	4 / 95 (4.21%)	
occurrences (all)	4	8	
Body temperature increased			
subjects affected / exposed	0 / 48 (0.00%)	5 / 95 (5.26%)	
occurrences (all)	0	8	
Coombs test positive			
subjects affected / exposed	0 / 48 (0.00%)	5 / 95 (5.26%)	
occurrences (all)	0	5	
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 48 (6.25%)	5 / 95 (5.26%)	
occurrences (all)	3	6	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	2 / 48 (4.17%)	5 / 95 (5.26%)	
occurrences (all)	2	6	

Nervous system disorders			
Headache			
subjects affected / exposed	4 / 48 (8.33%)	46 / 95 (48.42%)	
occurrences (all)	10	102	
Dizziness			
subjects affected / exposed	3 / 48 (6.25%)	5 / 95 (5.26%)	
occurrences (all)	3	6	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	3 / 48 (6.25%)	17 / 95 (17.89%)	
occurrences (all)	3	26	
Condition aggravated			
subjects affected / exposed	9 / 48 (18.75%)	9 / 95 (9.47%)	
occurrences (all)	22	13	
Fatigue			
subjects affected / exposed	4 / 48 (8.33%)	5 / 95 (5.26%)	
occurrences (all)	4	6	
Chills			
subjects affected / exposed	1 / 48 (2.08%)	7 / 95 (7.37%)	
occurrences (all)	2	12	
Chest pain			
subjects affected / exposed	3 / 48 (6.25%)	3 / 95 (3.16%)	
occurrences (all)	3	3	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	2 / 48 (4.17%)	18 / 95 (18.95%)	
occurrences (all)	2	30	
Vomiting			
subjects affected / exposed	0 / 48 (0.00%)	9 / 95 (9.47%)	
occurrences (all)	0	12	
Constipation			
subjects affected / exposed	0 / 48 (0.00%)	5 / 95 (5.26%)	
occurrences (all)	0	5	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			

subjects affected / exposed	1 / 48 (2.08%)	5 / 95 (5.26%)	
occurrences (all)	1	5	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 48 (2.08%)	6 / 95 (6.32%)	
occurrences (all)	1	6	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 48 (8.33%)	7 / 95 (7.37%)	
occurrences (all)	5	8	
Myalgia			
subjects affected / exposed	0 / 48 (0.00%)	9 / 95 (9.47%)	
occurrences (all)	0	12	
Pain in extremity			
subjects affected / exposed	0 / 48 (0.00%)	6 / 95 (6.32%)	
occurrences (all)	0	9	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 48 (2.08%)	6 / 95 (6.32%)	
occurrences (all)	1	8	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 July 2017	Amendment 3: -Following a recommendation of the Steering Committee inclusion of patients with Dermatomyositis who are under no current treatment due to intolerance and/or non-responsiveness to DM-related medication has been added -upon recommendation by the Steering Committee exclusion criterion was amended to shorten the waiting period for patients after excision of basal or squamous cell skin cancer -Following a recommendation by the Steering Committee Subjects diagnosed with Juvenile Dermatomyositis were excluded from the study. - further specification of some exclusion criteria -Maximally allowed stable dose as concomitant therapy for Hydroxychloroquine was re-defined -in accoedance with the Steering Committee the definition of "Confirmed deterioration" was updated -As requested by the study's Independent Adjudication Committee Thyroid-stimulating hormone (TSH) was added to the clinical chemistry test panel - Details on breaking the blind have been udated upon request of the Czech Regulatory Authority
18 July 2018	Amendment 4: -The maximum infusion rate has been reduced to 0.04 mL/kg/min upon request of FDA -Duration of infusion cycles for extension period changed from 2 days to 2-5 days -Upon FDA request a new stopping rule was implemented for TEEs observed on or after the cut-off date of 04-Jul-2018 (since introduction of reduced maximum infusion rate of 0.04 mL/kg/min) -Thromboembolic events will be reported as SAE (medical occurrence that at any dose is another important medical event) - Exclusion criterion with reference to forbidden medication has been added for clarification -Time window defined for Direct Coombs' test taken prior infusion cycle has been extended for administrative reason
05 November 2018	Amendment 6: -Exclusion criterion was extended so that patients with any prior TEE event, regardless of the onset of the event, are not be eligible for participation in the study -References were added to explicitly state the higher risk for thromboembolic events in "newly" diagnosed patients with DM. -For the safety of patients with risk factors for thromboembolic events or patients who are in the initial disease stage after diagnosis the Permitted Concomitant Therapy Section has been amended wit the information that TEE prophylaxis, if deemed necessary by the investigator, is allowed as a precautionary measure and should follow standard of care. Its use must be documented.
12 March 2019	Amendment 7: Early Termination section has been updated based on the opinion of the IDMC. TEEs with a likely temporal and cause-effect relationship which occur in a single subject within a short clinical time period should be counted as a single adverse events of special interest (AESI) including for the calculations performed for stopping rules.
03 July 2019	Amendment 8: -As requested by FDA the definition of responders in study protocol was reworded and the primary endpoint was reworded subsequently in order to be unambiguous

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported