Clinical trial results:
A Phase 2/3, Double-Blind, Randomized, Placebo-Controlled, Parallel Group, Multicenter Study to Evaluate the Efficacy and Safety of Ravulizumab in Adult Participants with Dermatomyositis

Summary

EudraCT number	2021-001200-15
Trial protocol	DE FR ES IT
Global end of trial date	08 May 2024

Results information

Result version number	v2 (current)
This version publication date	28 February 2025
First version publication date	06 November 2024
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	ALXN1210-DM-310

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04999020
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Alexion Pharmaceuticals Inc.
Sponsor organisation address	121 Seaport Boulevard, Boston, MA, United States, 02210
Public contact	European Clinical Trial Information, Alexion Pharmaceuticals Inc., +35 3874162507, clinicaltrials.eu@alexion.com
Scientific contact	European Clinical Trial Information, Alexion Pharmaceuticals, Inc., +35 3874162507, 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	08 May 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 May 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to determine the effect of ravulizumab compared with placebo in the treatment of dermatomyositis (DM) based on improvement in Total Improvement Score (TIS) International Myositis Assessment and Clinical Studies Total Improvement Score (IMAC-TIS).

Protection of trial subjects:

This study was conducted in accordance with the protocol and consensus ethical principles derived from international guidelines including the Declaration of Helsinki, Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines, applicable International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP) Guidelines, and other applicable laws and regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 November 2021
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	France: 2
Country: Number of subjects enrolled	Germany: 5
Country: Number of subjects enrolled	Italy: 14
Country: Number of subjects enrolled	Japan: 1
Country: Number of subjects enrolled	Korea, Republic of: 4
Country: Number of subjects enrolled	Spain: 2
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	United States: 8
Worldwide total number of subjects	38
EEA total number of subjects	23

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)	33
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study was planned to be conducted in 2 parts – Part A and Part B. The study was terminated early and participants were not enrolled into Part B. Therefore, results are presented for Part A of the study only. Part A consisted of a Randomized Controlled Period (RCP) and an Open-Label Extension (OLE) period.

Period 1

Period 1 title	Randomized Controlled Period (RCP)
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	RCP: Ravulizumab

Arm description:

Participants received a loading dose of ravulizumab on Day 1 followed by a maintenance dose at Week 2 and then ravulizumab once every 8 weeks (Q8W) during the 26-week RCP.

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

Dosage and administration details:

Ravulizumab per dosage and administration specified in the arm description.

Arm title	RCP: Placebo

Arm description:

Participants received placebo on Day 1, and Weeks 2, 10, and 18 during the 26-week RCP.

Arm type	Placebo
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:

Placebo per administration specified in the arm description.

Number of subjects in period 1	RCP: Ravulizumab	RCP: Placebo
Started	26	12
Received at Least 1 Dose of Treatment	26	12
Completed	22	9
Not completed	4	3
Consent withdrawn by subject	1	2
Physician decision	1	1
Adverse event, non-fatal	2	-

Period 2

Period 2 title	Open-Label Extension (OLE) Period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	OLE: Ravulizumab to Ravulizumab

Arm description:

Participants who received ravulizumab during the RCP continued to receive ravulizumab during the 130-week OLE. Participants received a blinded ravulizumab dose at Week 26, a maintenance dose at Week 28, then ravulizumab Q8W for the remainder of the OLE period.

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

Dosage and administration details:

Ravulizumab per dosage and administration specified in the arm description.

Arm title	OLE: Placebo to Ravulizumab

Arm description:

Participants who received placebo during the RCP received ravulizumab during the 130-week OLE. Participants received a blinded ravulizumab dose at Week 26, a maintenance dose at Week 28, then ravulizumab Q8W for the remainder of the OLE period.

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

Dosage and administration details:

Ravulizumab per dosage and administration specified in the arm description.

Number of subjects in period 2	OLE: Ravulizumab to Ravulizumab	OLE: Placebo to Ravulizumab
Started	22	9
Received at Least 1 Dose of Treatment	22	9
Completed	0	0
Not completed	22	9
Consent withdrawn by subject	3	3
Physician decision	1	-
Adverse event, non-fatal	-	2
Study Terminated by Sponsor	17	4
Lost to follow-up	1	-

Baseline characteristics

Reporting groups	
Reporting group title	RCP: Ravulizumab
Reporting group description:	
Participants received a loading dose of ravulizumab on Day 1 followed by a maintenance dose at Week 2 and then ravulizumab once every 8 weeks (Q8W) during the 26-week RCP.	
Reporting group title	RCP: Placebo
Reporting group description:	
Participants received placebo on Day 1, and Weeks 2, 10, and 18 during the 26-week RCP.	

Reporting group values	RCP: Ravulizumab	RCP: Placebo	Total
Number of subjects	26	12	38
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	24	9	33
From 65-84 years	2	3	5
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	50.7	59.3	
standard deviation	± 10.38	± 9.31	-
Sex: Female, Male Units: participants			
Female	18	9	27
Male	8	3	11
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	3	2	5
Not Hispanic or Latino	23	10	33
Unknown or Not Reported	0	0	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	4	2	6
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	3	0	3
White	18	10	28
More than one race	0	0	0
Unknown or Not Reported	1	0	1

End points

End points reporting groups

Reporting group title	RCP: Ravulizumab
Reporting group description:	
Participants received a loading dose of ravulizumab on Day 1 followed by a maintenance dose at Week 2 and then ravulizumab once every 8 weeks (Q8W) during the 26-week RCP.	
Reporting group title	RCP: Placebo
Reporting group description:	
Participants received placebo on Day 1, and Weeks 2, 10, and 18 during the 26-week RCP.	
Reporting group title	OLE: Ravulizumab to Ravulizumab
Reporting group description:	
Participants who received ravulizumab during the RCP continued to receive ravulizumab during the 130-week OLE. Participants received a blinded ravulizumab dose at Week 26, a maintenance dose at Week 28, then ravulizumab Q8W for the remainder of the OLE period.	
Reporting group title	OLE: Placebo to Ravulizumab
Reporting group description:	
Participants who received placebo during the RCP received ravulizumab during the 130-week OLE. Participants received a blinded ravulizumab dose at Week 26, a maintenance dose at Week 28, then ravulizumab Q8W for the remainder of the OLE period.	

Primary: Number of Participants with International Myositis Assessment and Clinical Studies Total Improvement Score (IMACS-TIS) (TIS40) Response at Week 26 of the Randomized Controlled Period

End point title	Number of Participants with International Myositis Assessment and Clinical Studies Total Improvement Score (IMACS-TIS) (TIS40) Response at Week 26 of the Randomized Controlled Period
End point description:	
Data are presented for the number of participants with a TIS40 response, defined as an IMACS-TIS score ≥ 40 at Week 26. IMACS-TIS is a clinical instrument that encompasses 6 core set measure (CSMs) (physician, patient, extra-muscular global activity, muscle strength, Health Assessment Questionnaire [HAQ], and muscle enzyme levels). A Total Improvement Score (TIS: 0–100), was determined by summing scores in each CSM, and was based on the improvement and relative weight of each CSM. A higher score indicated greater improvement. TIS40 was considered a moderate improvement score. Randomized Set, which included all randomized participants grouped by randomized treatment group.	
End point type	Primary
End point timeframe:	
Week 26	

End point values	RCP: Ravulizumab	RCP: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	12		
Units: participants	9	6		

Statistical analyses

Statistical analysis title	Ravulizumab vs placebo
Comparison groups	RCP: Ravulizumab v RCP: Placebo
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4192
Method	Barnard’s unconditional exact test
Parameter estimate	Difference in response rates
Point estimate	-15.38
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-38.55
upper limit	8.48

Secondary: TIS at Week 26

End point title	TIS at Week 26

End point description:

TIS scores ranged from 0–100 with higher scores indicating a greater improvement. Scores were determined by summing scores in each of the 6 CSMs of the IMAC (physician, patient, extra-muscular global activity, muscle strength, HAQ, and muscle enzyme levels). Clinically meaningful thresholds for improvement were defined as ≥ 20 point improvement response on IMACS-TIS (TIS20; mild), ≥ 40 point improvement response on IMACS TIS (TIS40; moderate) and ≥ 60 point improvement response on IMACS-TIS (TIS60; severe). Scores were based on the improvement and relative weight of each CSM. Data are presented for TIS (least squares mean) at Week 26. Randomized Set, which included all randomized participants grouped by randomized treatment group. Number of participants analyzed = participants with evaluable data for the outcome measure.

End point type	Secondary

End point timeframe:

Week 26

End point values	RCP: Ravulizumab	RCP: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	12		
Units: scores on a scale				
least squares mean (standard error)	31.16 (± 4.185)	43.28 (± 6.650)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline In Cutaneous Dermatomyositis Disease Area And Severity Index (CDASI) Activity Score at Week 26

End point title	Change from Baseline In Cutaneous Dermatomyositis Disease Area And Severity Index (CDASI) Activity Score at Week 26

End point description:

The CDASI is an instrument that separately measures activity and damage in the skin of dermatomyositis (DM) participants. It is a 1-page instrument that contains 3 activity measures (erythema, scale, and erosion/ulceration) and 2 damage measures (poikiloderma and calcinosis). CDASI score is calculated by rating the severity of skin disease in 15 anatomical locations on the body based on activity and damage components. CDASI was completed by the Clinician/Clinician-Investigator. Total CDASI scores ranged from 0-100, higher scores =greater disease severity. Change from baseline in CDASI Total Activity Score at Week 26 was analyzed using a mixed model repeated measures (MMRM). The MMRM model included the observed Total Activity Score values at post baseline visits (Week 26) as the dependent variable. Randomized Set, which included all randomized participants grouped by randomized treatment group. Number of participants analyzed = participants with evaluable data for the outcome measure.

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	RCP: Ravulizumab	RCP: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	12		
Units: scores on a scale				
least squares mean (standard error)	-3.80 (± 1.249)	-7.47 (± 2.021)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Response Related to Muscle Enzymes: Normalization of Most Abnormal Baseline Enzyme at Week 26

End point title	Number of Participants with Response Related to Muscle Enzymes: Normalization of Most Abnormal Baseline Enzyme at Week 26

End point description:

Laboratory tests were conducted to measure serum activities of muscle associated enzymes including creatine kinase (CK), alanine aminotransferase (ALT), aspartate aminotransferase (AST), lactate dehydrogenase (LDH), and aldolase. Data are presented for the number of participants who had an abnormal muscle enzyme at baseline that had been normalized at Week 26. Randomized Set, which included all randomized participants grouped by randomized treatment group.

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	RCP: Ravulizumab	RCP: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	12		
Units: participants	4	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline In IMACS CSMs: Extra-Muscular Disease Activity Based on Myositis Disease Activity Assessment Tool (MDAAT) at Week 26

End point title	Change from Baseline In IMACS CSMs: Extra-Muscular Disease Activity Based on Myositis Disease Activity Assessment Tool (MDAAT) at Week 26

End point description:

The MDAAT assesses disease activity of extra-muscular organ systems and muscles in participants with DM. The validated MDAAT tool measures the degree of disease activity of extra-muscular organ systems and muscle on a 0-10 centimeter (cm) visual analog scale (VAS). Extra-muscular activity ranged between 0 and 10, where, 0 cm = absent and 10 cm = maximum disease activity. Randomized Set, which included all randomized participants grouped by randomized treatment group. Number of participants analyzed = participants with evaluable data for the outcome measure.

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	RCP: Ravulizumab	RCP: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	12		
Units: scores on a scale				
least squares mean (standard error)	-0.92 (± 0.383)	-2.13 (± 0.614)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline In IMACS CSMs: Physician Global Activity Assessment at Week 26

End point title	Change from Baseline In IMACS CSMs: Physician Global Activity Assessment at Week 26

End point description:

The physician global activity assessment provides an overall rating of disease activity related to myositis. Disease activity is judged by the physician based on all information available at the time of evaluation, including the participant’s appearance, medical history, physical examination, laboratory testing, and prescribed medical therapy. The global disease activity score is recorded on a 10-cm VAS, where 0 cm= no evidence of disease activity and 10 cm= extremely severe disease activity. Randomized Set, which included all randomized participants grouped by randomized treatment group. Number of

participants analyzed = participants with evaluable data for the outcome measure.

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	RCP: Ravulizumab	RCP: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	12		
Units: scores on a scale				
least squares mean (standard error)	-1.18 (± 0.413)	-1.97 (± 0.649)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline In IMACS CSMs: Patient Global Activity Assessment at Week 26

End point title	Change from Baseline In IMACS CSMs: Patient Global Activity Assessment at Week 26

End point description:

The patient global activity assessment provides an overall rating of disease activity related to myositis from the participant's perspective. Participants were asked to consider all of the active inflammation in their own muscles, skin, joints, intestines, heart, lungs, or other parts of the body that can improve with treatment. The patient global disease activity score was recorded on a 10-cm VAS that contained a smiley face at the 0-cm anchor and a sad face at the 10 cm anchor to help participants understand the scale. Scores ranged from 0 (no evidence of disease activity) to 10 (extremely active or severe disease activity). Randomized Set, which included all randomized participants grouped by randomized treatment group. Number of participants analyzed = participants with evaluable data for the outcome measure.

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	RCP: Ravulizumab	RCP: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	12		
Units: scores on a scale				
least squares mean (standard error)	-1.43 (± 0.432)	-1.12 (± 0.699)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline In IMACS CSMs: Manual Muscle Testing Subset 8 Muscles (MMT-8) at Week 26

End point title	Change from Baseline In IMACS CSMs: Manual Muscle Testing Subset 8 Muscles (MMT-8) at Week 26

End point description:

The purpose of the MMT-8 was to measure muscle strength as part of the physical examination. It included a subset of 8 muscle groups: neck flexors, deltoids, biceps, wrist, extensors, gluteus maximus and medius, quadriceps, and ankle dorsiflexors. Total MMT8 scores ranged from 0 (lowest strength) to 150 (highest strength). Randomized Set, which included all randomized participants grouped by randomized treatment group. Number of participants analyzed = participants with evaluable data for the outcome measure.

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	RCP: Ravulizumab	RCP: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	12		
Units: scores on a scale				
least squares mean (standard error)	9.5 (± 1.85)	12.6 (± 2.98)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with CDASI Response (>=7-point Improvement) at Week 26

End point title	Number of Participants with CDASI Response (>=7-point Improvement) at Week 26

End point description:

The CDASI is an instrument that separately measures activity and damage in the skin of dermatomyositis (DM) participants. It is a 1-page instrument that contains 3 activity measures (erythema, scale, and erosion/ulceration) and 2 damage measures (poikiloderma and calcinosis). CDASI score is calculated by rating the severity of skin disease in 15 anatomical locations on the body based on the activity and damage components. CDASI was completed by the Clinician or Clinician-Investigator while examining the participant. Total CDASI scores ranged from 0-100, with higher scores indicating a greater disease severity.

Data are presented for the number of participants with a CDASI response. Response was defined as a >=7 point improvement in participants who did not have an intercurrent event at or prior to the relevant timepoint. Randomized Set, which included all randomized participants grouped by randomized treatment group.

End point type	Secondary

End point timeframe:

Week 26

End point values	RCP: Ravulizumab	RCP: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	12		
Units: participants	6	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline In IMACS CSMs: Health Assessment Questionnaire (HAQ) at Week 26

End point title	Change from Baseline In IMACS CSMs: Health Assessment Questionnaire (HAQ) at Week 26

End point description:

The HAQ is a brief self-report questionnaire that assesses physical function pertaining to activities of daily living in a variety of domains. The HAQ includes 20 questions relating to 8 domains of function: dressing and grooming, arising, eating, walking, hygiene, reach, grip and usual activities. For each of the categories, participants reported the amount of difficulty they had in performing 2 or 3 specific subcategory items. The standard disability score is calculated from the 8 categories by dividing the sum of the individual categories by the number of categories answered, yielding a score from 0 (without any difficulty) to 3 (unable to do), with higher values indicating higher disability. Randomized Set, which included all randomized participants grouped by randomized treatment group. Number of participants analyzed = participants with evaluable data for the outcome measure.

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	RCP: Ravulizumab	RCP: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	12		
Units: scores on a scale				
least squares mean (standard error)	-0.1289 (± 0.08607)	-0.4188 (± 0.13676)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Cutaneous Dermatomyositis Activity Physician's Global Assessment (CDA-IGA) Response at Week 26

End point title	Number of Participants with Cutaneous Dermatomyositis Activity Physician's Global Assessment (CDA-IGA) Response at Week 26

End point description:

CDA-IGA is a scale that was created to measure disease severity in participants with skin disease. It is a 5-point scale (0 = clear; 1 = almost clear; 2 = mild; 3 = moderate; 4 = severe) with morphologic descriptors for each score. The CDA-IGA was completed by the Investigator and was used to describe

the overall appearance of lesions at a given time point. Data are presented for the number of participants with a CDA-IGA response at Week 26. A response was defined as participants with clear or almost clear skin (score of 0 or 1) who did not have an intercurrent event at or before the relevant timepoint. Randomized Set, which included all randomized participants grouped by randomized treatment group.

End point type	Secondary

End point timeframe:

Week 26

End point values	RCP: Ravulizumab	RCP: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	12		
Units: participants	5	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with ≥ 20-Point Improvement Response on IMACS-TIS (TIS20) Response at Week 26

End point title	Number of Participants with ≥ 20-Point Improvement Response on IMACS-TIS (TIS20) Response at Week 26

End point description:

TIS20 was defined as a ≥20-point improvement response on IMACS-TIS. IMACS-TIS is a clinical instrument that encompasses 6 CSMs (physician, patient, extra-muscular global activity, muscle strength, HAQ, and muscle enzyme levels). A Total Improvement Score (TIS: 0–100), was determined by summing scores in each CSM, and was based on the improvement and relative weight of each CSM. Higher scores indicated greater improvement/response. TIS20 is considered a mild improvement score. Randomized Set, which included all randomized participants grouped by randomized treatment group.

End point type	Secondary

End point timeframe:

Week 26

End point values	RCP: Ravulizumab	RCP: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	12		
Units: participants	14	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with ≥ 60-Point Improvement Response on

IMACS-TIS (TIS60) Response at Week 26

End point title	Number of Participants with ≥ 60-Point Improvement Response on IMACS-TIS (TIS60) Response at Week 26

End point description:

TIS60 was defined as a ≥60-point improvement response on IMACS-TIS. IMACS-TIS is a clinical instrument that encompasses 6 CSMs (physician, patient, extra-muscular global activity, muscle strength, HAQ, and muscle enzyme levels). A Total Improvement Score (TIS: 0–100), was determined by summing scores in each CSM, and was based on the improvement and relative weight of each CSM. Higher scores indicated greater improvement/response. TIS60 is considered a severe improvement score. Randomized Set, which included all randomized participants grouped by randomized treatment group.

End point type	Secondary

End point timeframe:

Week 26

End point values	RCP: Ravulizumab	RCP: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	12		
Units: participants	3	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Response of TIS20, TIS40, or TIS60

End point title	Time to First Response of TIS20, TIS40, or TIS60

End point description:

TIS20, 40 and 60 were defined as a ≥20,≥40 and≥60-point improvement response on IMACS-TIS respectively. TIS20, 40 and 60 were considered mild, moderate and severe improvement scores respectively. The median time to TIS20, TIS40, and TIS60 was defined at the time in which 50% of the participants experienced TIS20, TIS40, or TIS60, respectively, based on a Kaplan-Meier analysis. 99999=As fewer than 50% of the participants experienced the event of TIS40 and the median time to TIS40 event was close to the maximum follow-up period, there was not enough information on longer follow-up times to estimate the upper bound of the confidence interval. 9999= <50% of the participants experienced TIS60 response during the RCP (the Week 26 period), the median time could not be estimated along with the associated 80% confidence interval(s) using Kaplan-Meier analysis.

End point type	Secondary

End point timeframe:

Baseline through Week 26

End point values	RCP: Ravulizumab	RCP: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	12		
Units: weeks				
median (confidence interval 80%)				

Time to TIS20 (n=17, n=10)	10.43 (10.14 to 17.86)	10.14 (2.14 to 10.14)		
Time to TIS40 (n=10, n=6)	25.86 (18.14 to 99999)	26.0 (10.14 to 26.29)		
Time to TIS60 (n=3, n=2)	9999 (9999 to 9999)	9999 (26.14 to 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Clinical Worsening (CW) During the RCP At 2 Consecutive Visits

End point title	Number of Participants with Clinical Worsening (CW) During the RCP At 2 Consecutive Visits

End point description:

CW was defined as one of the following:

a. Physician’s global activity VAS worsening ≥ 2 cm and MMT-8 worsening ≥ 20% compared to baseline
b. Global extra muscular activity worsening ≥ 2 cm on the MDAAT VAS compared to baseline
c. Any 3 of 5 CSMs (excluding muscle enzymes) worsening by ≥ 30% compared to baseline

Data are presented for the number of participants with clinical worsening during the RCP at 2 consecutive visits. Randomized Set, which included all randomized participants grouped by randomized treatment group.

End point type	Secondary

End point timeframe:

Baseline through Week 26

End point values	RCP: Ravulizumab	RCP: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	12		
Units: participants	2	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Received Acute Rescue Therapy with Standard DM Treatment

End point title	Number of Participants who Received Acute Rescue Therapy with Standard DM Treatment

End point description:

Acute rescue therapy with standard DM treatment included an increased dose of a medication that was being taken for DM or the initiation of a new DM treatment (glucocorticoid and/or immunosuppressive/immunomodulatory therapy [ISTs]). Data are presented for the number of participants who received acute rescue therapy with standard DM treatment. Randomized Set, which included all randomized participants grouped by randomized treatment group.

End point type	Secondary

End point timeframe:

Baseline through Week 26

End point values	RCP: Ravulizumab	RCP: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	12		
Units: participants	2	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to approximately 130 weeks

Adverse event reporting additional description:

Safety Set for RCP = participants who received ≥1 dose of treatment. Participants were analyzed according to treatment received. One participant who was randomized to ravulizumab during RCP received placebo and was analyzed in placebo group. OLE Set for the OLE period= participants who received at least 1 dose of ravulizumab from Week 26

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	RCP: Ravulizumab

Reporting group description:

Participants received a loading dose of ravulizumab on Day 1 followed by a maintenance dose at Week 2 and then ravulizumab once every 8 weeks (Q8W) during the 26-week RCP.

Reporting group title	OLE: Ravulizumab to Ravulizumab

Reporting group description:

Participants who received ravulizumab during the RCP continued to receive ravulizumab during the 130-week OLE. Participants received a blinded ravulizumab dose at Week 26, a maintenance dose at Week 28, then ravulizumab Q8W for the remainder of the OLE period.

Reporting group title	OLE: Placebo to Ravulizumab

Reporting group description:

Participants who received placebo during the RCP received ravulizumab during the 130-week OLE. Participants received a blinded ravulizumab dose at Week 26, a maintenance dose at Week 28, then ravulizumab Q8W for the remainder of the OLE period.

Reporting group title	RCP: Placebo

Reporting group description:

Participants received placebo on Day 1, and Weeks 2, 10, and 18 during the 26-week RCP.

Serious adverse events	RCP: Ravulizumab	OLE: Ravulizumab to Ravulizumab	OLE: Placebo to Ravulizumab
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 25 (8.00%)	4 / 22 (18.18%)	4 / 9 (44.44%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			

Hypovolaemic shock			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Coronary artery stenosis			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 25 (4.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Agranulocytosis			
subjects affected / exposed	0 / 25 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Impaired healing			

subjects affected / exposed	0 / 25 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 25 (4.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal haemorrhage			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Endometrial hyperplasia	Additional description: Number at risk has been adjusted as this is a sex-specific event.		
subjects affected / exposed[1]	0 / 18 (0.00%)	1 / 16 (6.25%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Cutaneous calcification			
subjects affected / exposed	0 / 25 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 25 (0.00%)	1 / 22 (4.55%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia urinary tract infection			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	RCP: Placebo		
Total subjects affected by serious adverse events			

subjects affected / exposed	0 / 13 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypovolaemic shock			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Coronary artery stenosis			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac failure			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Agranulocytosis			

subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anaemia			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Impaired healing			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intestinal haemorrhage			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Endometrial hyperplasia	Additional description: Number at risk has been adjusted as this is a sex-specific event.		
subjects affected / exposed[1]	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Cutaneous calcification			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
COVID-19			

subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Escherichia urinary tract infection			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Number at risk has been adjusted as this is a sex-specific event.

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

Non-serious adverse events	RCP: Ravulizumab	OLE: Ravulizumab to Ravulizumab	OLE: Placebo to Ravulizumab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 25 (36.00%)	11 / 22 (50.00%)	7 / 9 (77.78%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Vaccination site swelling			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 25 (0.00%)	2 / 22 (9.09%)	0 / 9 (0.00%)
occurrences (all)	0	3	0
Respiratory, thoracic and mediastinal disorders			
Pulmonary mass			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1

Cough			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Vocal cord leukoplakia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	0 / 25 (0.00%)	2 / 22 (9.09%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Contusion			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Compression fracture			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Neuralgia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Taste disorder			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Eye disorders			

Diabetic retinopathy			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	4 / 25 (16.00%)	0 / 22 (0.00%)	2 / 9 (22.22%)
occurrences (all)	5	0	2
Constipation			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Anal erosion			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Abdominal pain			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Tongue movement disturbance			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	0
Large intestine polyp			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Hypoaesthesia oral			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Diverticulum intestinal			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Enterocolitis			

subjects affected / exposed	0 / 25 (0.00%)	2 / 22 (9.09%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Skin and subcutaneous tissue disorders			
Skin lesion			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	3 / 25 (12.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	3	0	0
Eczema			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Diffuse alopecia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Dermatomyositis			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Cushingoid			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Rotator cuff syndrome			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Osteoporosis			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Back pain			

subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Arthralgia			
subjects affected / exposed	2 / 25 (8.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
occurrences (all)	2	0	1
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 25 (0.00%)	2 / 22 (9.09%)	1 / 9 (11.11%)
occurrences (all)	0	2	1
COVID-19			
subjects affected / exposed	2 / 25 (8.00%)	2 / 22 (9.09%)	0 / 9 (0.00%)
occurrences (all)	2	2	0
Pyoderma			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 25 (0.00%)	2 / 22 (9.09%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Influenza			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Genital infection fungal			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Sepsis			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Urinary tract infection			
subjects affected / exposed	0 / 25 (0.00%)	0 / 22 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	2
Upper respiratory tract infection			
subjects affected / exposed	0 / 25 (0.00%)	2 / 22 (9.09%)	0 / 9 (0.00%)
occurrences (all)	0	2	0

Non-serious adverse events	RCP: Placebo		
Total subjects affected by non-serious adverse events			

subjects affected / exposed	10 / 13 (76.92%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Vaccination site swelling			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Influenza like illness			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary mass			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Cough			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Vocal cord leukoplakia			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		

Contusion subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Compression fracture subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Nervous system disorders Neuralgia subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 2		
Taste disorder subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 2		
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Eye disorders Diabetic retinopathy subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Constipation subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Anal erosion subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Abdominal pain			

subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Tongue movement disturbance			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Large intestine polyp			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Hypoaesthesia oral			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Diverticulum intestinal			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Enterocolitis			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Skin lesion			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Eczema			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Diffuse alopecia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		

Dermatomyositis subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Endocrine disorders Cushingoid subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Musculoskeletal and connective tissue disorders Rotator cuff syndrome subjects affected / exposed occurrences (all) Osteoporosis subjects affected / exposed occurrences (all) Myalgia subjects affected / exposed occurrences (all) Muscle spasms subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0 1 / 13 (7.69%) 1 1 / 13 (7.69%) 1 1 / 13 (7.69%) 1 0 / 13 (0.00%) 0 1 / 13 (7.69%) 1		
Infections and infestations Bronchitis subjects affected / exposed occurrences (all) COVID-19 subjects affected / exposed occurrences (all) Pyoderma subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0 3 / 13 (23.08%) 3 1 / 13 (7.69%) 1		

Nasopharyngitis			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Influenza			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Genital infection fungal			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Sepsis			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 August 2021	• Provided information on the Independent Data Monitoring Committee (IDMC) role • Clarified Part A interim analysis • Clarified individual and study closure criteria
30 August 2022	• Broadened the target population • Reduced the risk of screen failures • Improved participant experience • Facilitated recruitment of participants
23 June 2023	• Extended RCP in Part B from 26 weeks to 50 weeks • Extended OLE Period in Part A from 74 weeks to 130 weeks • Implemented requirements for conducting a clinical study under European Union Clinical Trials Regulation (EU CTR)

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.

Part A did not meet its primary endpoint and the study was terminated.

Notes: