Clinical trial results:
A Phase 2, Randomized, Double-Blinded, Placebo-Controlled, Parallel-Group, Multicenter Trial to Evaluate the Safety and Tolerability, Efficacy, Pharmacokinetics, Pharmacodynamics, and Immunogenicity of 2 Dose Regimens of ARGX-117 in Adults With Multifocal Motor Neuropathy

Summary

EudraCT number	2021-003302-50
Trial protocol	FR ES DE BE IT PL AT NL
Global end of trial date	04 June 2024

Results information

Result version number	v1 (current)
This version publication date	20 June 2025
First version publication date	20 June 2025

Trial information

Trial identification

Sponsor protocol code	ARGX-117-2002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05225675
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	argenx BV
Sponsor organisation address	Industriepark Zwijnaarde 7, Zwijnaarde (Ghent), Belgium, 9052
Public contact	Regulatory, argenx, regulatory@argenx.com
Scientific contact	Regulatory, argenx, regulatory@argenx.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	10 April 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 June 2024
Global end of trial reached?	Yes
Global end of trial date	04 June 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of empasiprubart (ARGX-117) compared to placebo in adult participants previously stabilized with IVIg

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, applicable ICH GCP guidelines, and applicable laws and regulations.
The participant’s informed consent was documented by the dated signature of the participant and the dated signature of the investigator or investigator’s delegate before enrollment.

Background therapy: -

Evidence for comparator:

This study is placebo-controlled and Placebo IV is used for comparator.

Actual start date of recruitment	31 March 2022
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	15 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 6
Country: Number of subjects enrolled	Poland: 3
Country: Number of subjects enrolled	Spain: 8
Country: Number of subjects enrolled	Austria: 1
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	France: 6
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Italy: 6
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	United States: 13
Worldwide total number of subjects	54
EEA total number of subjects	36

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)	46
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

78 participants were screened: 27 directly entered IVIg monitoring period (IVMP), and 30 entered IVMP after completing IVIg dependency period (IVDP). Of the 57 participants who entered IVMP, 54 completed IVMP and were enrolled in 2 cohorts. In each cohort, 27 participants were randomized (2:1) to receive: EMP IV (N=18) or PBO (N=9).

Pre-assignment

Screening details:

Screening period: Up to 28 days

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	ARGX-117 Cohort 1

Arm description:

Participants received dosing regimen 1 of ARGX-117 via intravenous (IV) infusion

Arm type	Experimental
Investigational medicinal product name	Empasiprubart
Investigational medicinal product code	
Other name	ARGX-117
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received dosing regimen 1 of ARGX-117 via intravenous (IV) infusion.

Arm title	Placebo Cohort 1

Arm description:

Participants received placebo via intravenous (IV) infusion

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

Dosage and administration details:

Participants received Placebo via intravenous (IV) infusion.

Arm title	ARGX-117 Cohort 2

Arm description:

Participants received dosing regimen 2 of ARGX-117 via intravenous (IV) infusion

Arm type	Experimental

Investigational medicinal product name	Empasiprubart
Investigational medicinal product code	
Other name	ARGX-117
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received dosing regimen 2 of ARGX-117 via intravenous (IV) infusion.

Arm title	Placebo Cohort 2

Arm description:

Participants received placebo via intravenous (IV) infusion

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

Dosage and administration details:

Participants received Placebo via intravenous (IV) infusion.

Number of subjects in period 1	ARGX-117 Cohort 1	Placebo Cohort 1	ARGX-117 Cohort 2
Started	18	9	18
Completed	17	8	18
Not completed	1	1	0
Adverse event, non-fatal	1	-	-
Withdrawal by participant	-	1	-

Number of subjects in period 1	Placebo Cohort 2
Started	9
Completed	9
Not completed	0
Adverse event, non-fatal	-
Withdrawal by participant	-

Baseline characteristics

Reporting groups	
Reporting group title	ARGX-117 Cohort 1
Reporting group description:	
Participants received dosing regimen 1 of ARGX-117 via intravenous (IV) infusion	
Reporting group title	Placebo Cohort 1
Reporting group description:	
Participants received placebo via intravenous (IV) infusion	
Reporting group title	ARGX-117 Cohort 2
Reporting group description:	
Participants received dosing regimen 2 of ARGX-117 via intravenous (IV) infusion	
Reporting group title	Placebo Cohort 2
Reporting group description:	
Participants received placebo via intravenous (IV) infusion	

Reporting group values	ARGX-117 Cohort 1	Placebo Cohort 1	ARGX-117 Cohort 2
Number of subjects	18	9	18
Age categorical Units: Subjects			
Adults (18-64 years)	16	7	16
From 65-84 years	2	2	2
Age continuous Units: years			
median	54.5	44.0	55.5
inter-quartile range (Q1-Q3)	47.0 to 61.0	42.0 to 54.0	50.0 to 59.0
Gender categorical Units: Subjects			
Female	7	4	6
Male	11	5	12

Reporting group values	Placebo Cohort 2	Total	
Number of subjects	9	54	
Age categorical Units: Subjects			
Adults (18-64 years)	7	46	
From 65-84 years	2	8	
Age continuous Units: years			
median	58.0		
inter-quartile range (Q1-Q3)	55.0 to 61.0	-	
Gender categorical Units: Subjects			
Female	4	21	
Male	5	33	

End points

End points reporting groups

Reporting group title	ARGX-117 Cohort 1
Reporting group description:	
Participants received dosing regimen 1 of ARGX-117 via intravenous (IV) infusion	
Reporting group title	Placebo Cohort 1
Reporting group description:	
Participants received placebo via intravenous (IV) infusion	
Reporting group title	ARGX-117 Cohort 2
Reporting group description:	
Participants received dosing regimen 2 of ARGX-117 via intravenous (IV) infusion	
Reporting group title	Placebo Cohort 2
Reporting group description:	
Participants received placebo via intravenous (IV) infusion	
Subject analysis set title	ENR - enrolled analysis set
Subject analysis set type	Full analysis
Subject analysis set description:	
All participants who signed an informed consent to participate in the study	
Subject analysis set title	SAF - safety analysis set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All enrolled participants who were randomized and who received at least 1 dose or part of a dose of IMP (empasiprubart or placebo). Participants were analyzed according to the treatment they received.	
Subject analysis set title	PK set - pharmacokinetic(s)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All participants in the SAF for whom at least 1 postdose serum PK concentration was available, excluding participants who received placebo.	
Subject analysis set title	PD set - pharmacodynamic(s) set
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All participants in the SAF for whom at least 1 postbaseline value for PD parameters (including free C2, total C2, and CH50) was available	
Subject analysis set title	Total Placebo (Cohort 1 and 2 Combined)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Total Placebo (Cohort 1 and 2 Combined)	

Primary: Number of participants with AEs and SAEs

End point title	Number of participants with AEs and SAEs[1]
End point description:	
AE: adverse events, SAE: serious adverse events	
End point type	Primary
End point timeframe:	
Up to 80 weeks	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analyses were performed for the primary safety endpoint

End point values	ARGX-117 Cohort 1	Placebo Cohort 1	ARGX-117 Cohort 2	Placebo Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	9	18	9
Units: Number of participants with AEs and SAEs				
Number of participants with a AE	14	5	14	6
Number of participants with a Treatment-related AE	7	0	2	2
Number of participants with a SAE	2	0	0	0
Number of participants with a Treatment-related SA	1	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Retreatment with IVIg

End point title	Time to First Retreatment with IVIg

End point description:

The time to first retreatment with intravenous immunoglobulin (IVIg) is defined as the time from the last IVIg administration before randomization until the first IVIg retreatment during the 16-week treatment period.

End point type	Secondary

End point timeframe:

Up to 16 weeks

End point values	ARGX-117 Cohort 1	Placebo Cohort 1	ARGX-117 Cohort 2	Placebo Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18[2]	9[3]	18[4]	9[5]
Units: days				
median (confidence interval 95%)				
Time to first retreatment with IVIg	0.00 (0.00 to 0.00)	37.0 (16.0 to 9999)	0.00 (0.00 to 0.00)	0.00 (0.00 to 0.00)

Notes:

[2] - Not evaluable because fewer than 50% of participants were re-treated with IVIg during the DBTP

[3] - Too few participants were retreated with IVIg to estimate the 95% CI. “9999” = data not estimable

[4] - Not evaluable because fewer than 50% of participants were re-treated with IVIg during the DBTP

[5] - Not evaluable because fewer than 50% of participants were re-treated with IVIg during the DBTP

Statistical analyses

Statistical analysis title	Cox regression model
Comparison groups	ARGX-117 Cohort 1 v Placebo Cohort 1

Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	other[6]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.02
upper limit	0.44

Notes:

[6] - Descriptive analysis

Statistical analysis title	Cox regression model
Comparison groups	ARGX-117 Cohort 2 v Placebo Cohort 2
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	other[7]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.02
upper limit	1.6

Notes:

[7] - Descriptive analysis

Secondary: Time-to-Relapse

End point title	Time-to-Relapse

End point description:

Time-to-Relapse is defined as the time from randomization until a participant met the threshold for clinically meaningful deterioration.

End point type	Secondary

End point timeframe:

Up to 16 weeks

End point values	ARGX-117 Cohort 1	Placebo Cohort 1	ARGX-117 Cohort 2	Placebo Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18[8]	9[9]	18[10]	9
Units: days				
median (confidence interval 95%)				
Time-to-Relapse	9999 (17.0 to 9999)	26.0 (7.0 to 9999)	9999 (70.0 to 9999)	28.0 (7.0 to 99.0)

Notes:

[8] - "9999" is a dummy value as the data is not estimable

[9] - "9999" is a dummy value as the data is not estimable

[10] - "9999" is a dummy value as the data is not estimable

Statistical analyses

No statistical analyses for this end point

Secondary: iAUC of the Change From Baseline in mMRC-10 Sum Score

End point title	iAUC of the Change From Baseline in mMRC-10 Sum Score

End point description:

The Incremental Area Under Curve (iAUC) is the area under the curve of the change from baseline in the Modified Medical Research Council (mMRC)-10 score. A positive AUC indicates a favourable outcome while a negative AUC indicates a nonfavourable outcome.

End point type	Secondary

End point timeframe:

Up to 16 weeks

End point values	ARGX-117 Cohort 1	Placebo Cohort 1	ARGX-117 Cohort 2	Placebo Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	9	18	9
Units: score on a scale				
median (inter-quartile range (Q1-Q3))	110.25 (-32.25 to 228.75)	-182.50 (-362.50 to 130.50)	283.75 (-17.50 to 432.00)	-93.50 (-158.50 to 13.00)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Average Score of the 2 Most Important Muscle Groups as Assessed by the mMRC-14 Sum Score

End point title	Change From Baseline in the Average Score of the 2 Most Important Muscle Groups as Assessed by the mMRC-14 Sum Score

End point description:

The Modified Medical Research Council (mMRC)-14 assesses muscle strength of 14 muscles groups, both sides (left and right). A score between 0 and 5 (normal strength) is assigned. This endpoint is the change from baseline in the average score of the 2 most important muscle groups affected by the disease. It ranges between 0 and 5. A change of more than 0 represents an improvement in strength, and a change less than 0 represents worsening.

End point type	Secondary

End point timeframe:

At week 16

End point values	ARGX-117 Cohort 1	Placebo Cohort 1	ARGX-117 Cohort 2	Placebo Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	9	18	9
Units: score on a scale				
median (inter-quartile range (Q1-Q3))	0.50 (0.50 to 0.50)	0.00 (0.00 to 0.50)	0.50 (0.00 to 1.00)	0.00 (0.00 to 0.50)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the mMRC-14 Sum Score

End point title	Change From Baseline in the mMRC-14 Sum Score

End point description:

The Modified Medical Research Council (mMRC)-14 scores range from 0 to 140 with a higher score representing better muscle strength. A change of more than 0 represents an improvement in strength, and a change less than 0 represents worsening.

End point type	Secondary

End point timeframe:

At week 16

End point values	ARGX-117 Cohort 1	Placebo Cohort 1	ARGX-117 Cohort 2	Placebo Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	9	18	9
Units: score on a scale				
median (inter-quartile range (Q1-Q3))				
Change From Baseline in the mMRC-14 Sum Score	4.0 (2.0 to 8.0)	0.0 (-8.0 to 0.0)	7.0 (1.0 to 11.0)	1.0 (-2.0 to 8.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Participants Showing a Deterioration of at Least 2 Points as Assessed by the mMRC-10 Sum Score

End point title	Proportion of Participants Showing a Deterioration of at Least 2 Points as Assessed by the mMRC-10 Sum Score

End point description:

The Modified Medical Research Council (mMRC)-10 scores evaluates motor strength/weakness from 10 predetermined muscle groups. A higher proportion of participants showing a deterioration represents a worsening of the outcome.

End point type	Secondary

End point timeframe:

Up to 16 weeks

End point values	ARGX-117 Cohort 1	Placebo Cohort 1	ARGX-117 Cohort 2	Placebo Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	9	18	9
Units: Percentage of participants				
number (not applicable)	5.6	44.4	11.1	22.2

Statistical analyses

No statistical analyses for this end point

Secondary: iAUC of the Change From Baseline in GS daily average

End point title	iAUC of the Change From Baseline in GS daily average

End point description:

Measurement of grip strength (GS) has been done using the Martin vigorimeter in kPa.
The incremental Area Under Curve (iAUC) is the area under the curve of the change from baseline of GS daily average. The 3 daily measurements of GS from the left hand and the 3 daily measurements of GS from the right hand have been recorded and the daily average for the left hand and right hand has been calculated, respectively.
Safety analysis set – Only participants with data for these timepoints are included

End point type	Secondary

End point timeframe:

Up to 16 weeks

End point values	ARGX-117 Cohort 1	Placebo Cohort 1	ARGX-117 Cohort 2	Placebo Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	9	18	9
Units: kPa				
median (inter-quartile range (Q1-Q3))				
Most affected Hand	508.25 (237.17 to 1788.08)	-63.75 (-591.42 to 671.08)	1269.67 (289.00 to 3139.17)	1.67 (-267.67 to 124.00)
Least affected Hand	356.08 (-57.17 to 1372.42)	-363.17 (-975.67 to 655.50)	554.00 (111.00 to 2847.00)	-100.33 (-291.00 to 478.50)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in GS 3-day moving average

End point title	Percent Change From Baseline in GS 3-day moving average

End point description:

Measurement of grip strength (GS) has been done using the Martin vigorimeter in kPa.
The 3 daily measurements of GS from the left hand and the 3 daily measurements of GS from the right hand have been recorded and the daily average for the left hand and right hand has been calculated, respectively. A 3-day moving average has been generated based on the average over the last 3 days of the obtained daily averages for each hand.

End point type	Secondary

End point timeframe:

At week 16

End point values	ARGX-117 Cohort 1	Placebo Cohort 1	ARGX-117 Cohort 2	Placebo Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	9	18	9
Units: percent change				
median (inter-quartile range (Q1-Q3))				
Most Affected Hand	31.88 (0.00 to 53.91)	1.63 (-1.96 to 10.42)	61.48 (8.12 to 101.10)	3.68 (-3.64 to 16.67)
Least Affected Hand	13.13 (0.25 to 37.68)	5.69 (-0.52 to 7.07)	17.97 (6.43 to 69.38)	4.90 (1.61 to 7.69)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the MMN-RODS centile score

End point title	Change From Baseline in the MMN-RODS centile score

End point description:

The Rasch-built Overall Disability Scale for MMN (MMN-RODS) is a disease-specific PRO instrument constructed to capture activity limitations in patients with MMN. Raw sum scores of the 25-item MMN-RODS (range, 0-50) were converted to a centile metric score ranging from 0 to 100. Lower scores indicated a greater degree of disability.

End point type	Secondary

End point timeframe:

At week 16

End point values	ARGX-117 Cohort 1	Placebo Cohort 1	ARGX-117 Cohort 2	Placebo Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	9	18	9
Units: score on a scale				
median (inter-quartile range (Q1-Q3))	6.0 (0.0 to 14.0)	0.0 (-2.0 to 0.0)	7.5 (0.0 to 17.0)	0.0 (-5.0 to 1.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change From Baseline in the Average Time for Upper Extremity (Arm and Hand) Function

End point title	Percent change From Baseline in the Average Time for Upper Extremity (Arm and Hand) Function

End point description:

The 9-Hole Peg Test (9-HPT) results are based on the time to complete the assessment with a shorter time representing better muscle strength. A change of less than 0 represents an improvement in strength, and a change more than 0 represents worsening.

End point type	Secondary

End point timeframe:

At week 16

End point values	ARGX-117 Cohort 1	Placebo Cohort 1	ARGX-117 Cohort 2	Placebo Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	9	17	9
Units: seconds				
median (inter-quartile range (Q1-Q3))				
Dominant hand	-10.760 (-41.463 to -1.250)	-5.691 (-16.049 to 9.254)	-8.571 (-20.907 to 0.000)	-12.150 (-16.212 to 2.500)
Non-Dominant hand	-5.236 (-23.529 to 6.343)	-3.394 (-20.690 to 5.000)	-14.286 (-25.714 to -8.725)	-1.402 (-7.368 to 4.762)

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Participants by Level of Severity on Each Dimension of the EQ-5D-5L Scale

End point title	Proportion of Participants by Level of Severity on Each Dimension of the EQ-5D-5L Scale

End point description:

The EuroQol 5-Dimension 5-Level (EQ-5D-5L) scale includes five dimensions: mobility, self-care, usual activities, pain or discomfort, and anxiety or depression. Each dimension is ranked with a level 1-5 with level 1 being no problems and level 5 representing extreme problems.

End point type	Secondary

End point timeframe:

At weeks 16

End point values	ARGX-117 Cohort 1	Placebo Cohort 1	ARGX-117 Cohort 2	Placebo Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	9	18	9
Units: participants				
Mobility - 1 No Problem	9	3	11	2
Mobility - 2 Slight Problem	2	3	2	6
Mobility - 3 Moderate Problem	6	2	3	1
Mobility - 4 Severe Problem	1	1	1	0
Mobility - 5 Unable to	0	0	1	0
Self-Care - 1 No Problem	5	3	8	3
Self-Care - 2 Slight Problem	8	4	8	5
Self-Care - 3 Moderate Problem	4	2	1	1
Self-Care - 4 Severe Problem	1	0	0	0
Self-Care - 5 Unable to	0	0	1	0
Usual Activities - 1 No Problem	5	2	8	2
Usual Activities - 2 Slight Problem	6	4	5	4
Usual Activities - 3 Moderate Problem	6	2	4	3
Usual Activities - 4 Severe Problem	1	1	0	0
Usual Activities - 5 Unable to	0	0	1	0
Pain/Discomfort - 1 No Problem	9	6	10	2
Pain/Discomfort - 2 Slight Problem	5	1	5	5
Pain/Discomfort - 3 Moderate Problem	3	2	2	2
Pain/Discomfort - 4 Severe Problem	1	0	1	0
Pain/Discomfort - 5 Unable to	0	0	0	0
Anxiety/Depression - 1 No Problem	13	2	15	5
Anxiety/Depression - 2 Slight Problem	4	6	1	2
Anxiety/Depression - 3 Moderate Problem	1	1	2	2
Anxiety/Depression - 4 Severe Problem	0	0	0	0
Anxiety/Depression - 5 Unable to	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Quality of Life Using EQ-5D-5L Visual Analog Scale

End point title	Change From Baseline in Quality of Life Using EQ-5D-5L Visual Analog Scale

End point description:

The EQ-5D-5L visual analog scale is from 0-100 with 0 representing the worst health. A change of more than 0 represents an improvement in health, and a change of less than 0 represents worsening.

End point type	Secondary

End point timeframe:

At week 16

End point values	ARGX-117 Cohort 1	Placebo Cohort 1	ARGX-117 Cohort 2	Placebo Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	9	18	9
Units: score on a scale				
median (inter-quartile range (Q1-Q3))	5.0 (0.0 to 13.0)	7.0 (-8.0 to 10.0)	6.0 (2.0 to 8.0)	-6.0 (-10.0 to 9.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the CAP-PRI

End point title	Change From Baseline in the CAP-PRI

End point description:

The Chronic Acquired Polyneuropathy Patient-reported Index (CAP-PRI) assesses disease-specific quality of life. This instrument includes the assessment of 15 items yielding a total score ranging from 0 to 30. A change of less than 0 represents an improvement in health, and a change more than 0 represents worsening.

End point type	Secondary

End point timeframe:

At week 16

End point values	ARGX-117 Cohort 1	Placebo Cohort 1	ARGX-117 Cohort 2	Placebo Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	9	18	9
Units: score on a scale				
median (inter-quartile range (Q1-Q3))				
Change From Baseline in the CAP-PRI	-2.5 (-6.0 to -1.0)	0.0 (-1.0 to 2.0)	-2.0 (-5.0 to -1.0)	1.0 (-1.0 to 2.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Participants by Level of Improvement Using the PGI-C Scale

End point title	Proportion of Participants by Level of Improvement Using the PGI-C Scale

End point description:

Patient Global Impression of Change (PGI-C) scale ranks a patients condition from 1-7 with 1 representing the most improvement and 7 representing the most decline in their condition.

End point type	Secondary

End point timeframe:

Up to 16 weeks

End point values	ARGX-117 Cohort 1	Placebo Cohort 1	ARGX-117 Cohort 2	Placebo Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	9	18	9
Units: participants				
1 - Very much improved	7	0	4	0
2 - Much improved	3	1	8	2
3 - Minimally improved	7	0	3	2
4 - No change	0	3	2	2
5 - Minimally worse	1	2	0	2
6 - Much worse	0	1	1	1
7 - Very much worse	0	2	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the 9-item FSS average Total Score

End point title	Change From Baseline in the 9-item FSS average Total Score

End point description:

9-item Fatigue Severity Scale (FSS) average score is the sum of the 9 items divided by the number of items. It ranges from 0 to 7 with a higher score representing more severe fatigue. A change of less than 0 indicates an improvement.

End point type	Secondary

End point timeframe:

Up to 16 weeks

End point values	ARGX-117 Cohort 1	Placebo Cohort 1	ARGX-117 Cohort 2	Placebo Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	9	18	9
Units: score on a scale				
median (inter-quartile range (Q1-Q3))	-0.444 (-1.556 to 0.000)	0.222 (0.111 to 1.222)	-0.111 (-0.556 to 0.111)	0.222 (-0.222 to 1.000)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Total Hours for Work-related and Household Chore Activities Lost, as Part of the HRPQ

End point title	Percent of Total Hours for Work-related and Household Chore Activities Lost, as Part of the HRPQ

End point description:

The Health-Related Productivity Questionnaire (HRPQ) provides data related to missed hours at work or educational activities and reduced effectiveness during any attempted work.
Safety analysis set - only participants with HRPQ data are shown. This is limited to employed/partially employed participants.

End point type	Secondary

End point timeframe:

Up to 16 weeks

End point values	ARGX-117 Cohort 1	Placebo Cohort 1	ARGX-117 Cohort 2	Placebo Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	9	18	9
Units: percent				
median (inter-quartile range (Q1-Q3))				
Work Activities lost	10.00 (0.00 to 15.00)	36.00 (0.00 to 46.00)	0.00 (0.00 to 12.13)	24.17 (17.50 to 37.78)
Household Chore Activities lost	33.33 (10.00 to 60.00)	20.00 (12.50 to 64.50)	15.00 (0.00 to 35.00)	43.75 (27.62 to 60.00)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Effectiveness, Side Effects, Convenience, and Overall Satisfaction Scores as Assessed by the TSQM-14

End point title	Change From Baseline in Effectiveness, Side Effects, Convenience, and Overall Satisfaction Scores as Assessed by the TSQM-14

End point description:

Each Treatment Satisfaction Questionnaire for Medication–14 items (TSQM-14) domain score ranges from 0-100 with higher scores representing greater satisfaction with the treatment. A change greater than 0 indicates an improvement in satisfaction.

End point type	Secondary

End point timeframe:

Up to 16 weeks

End point values	ARGX-117 Cohort 1	Placebo Cohort 1	ARGX-117 Cohort 2	Placebo Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	9	18	9
Units: score on a scale				
median (inter-quartile range (Q1-Q3))				
Effectiveness	0.000 (-16.667 to 27.778)	-22.222 (-33.333 to -16.667)	25.000 (0.000 to 38.889)	-11.111 (-16.667 to 5.556)
Side effects	0.000 (0.000 to 18.750)	0.000 (0.000 to 18.750)	0.000 (0.000 to 0.000)	0.000 (0.000 to 12.500)
Convenience	5.556 (0.000 to 22.222)	5.556 (0.000 to 5.556)	5.556 (0.000 to 11.111)	-5.556 (-11.111 to 5.556)
Overall Satisfaction	3.6 (-7.1 to 28.6)	-14.3 (-28.6 to -14.3)	3.6 (0.0 to 28.6)	-14.3 (-21.4 to -7.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Empasiprubart Serum Concentrations (Cmax)

End point title	Maximum Empasiprubart Serum Concentrations (Cmax)[11]

End point description:

PK set - All participants for whom at least 1 postdose serum PK concentration was available, excluding participants who received placebo.

End point type	Secondary

End point timeframe:

Up to 16 weeks

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The participants who received placebo (placebo cohorts 1 and 2) have been excluded from the PK analysis

End point values	ARGX-117 Cohort 1	ARGX-117 Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	18		
Units: µg/mL				
arithmetic mean (standard deviation)				
Day 1	777.1 (± 202.6)	400.1 (± 73.4)		
Day 8	590.8 (± 164.0)	273.8 (± 88.1)		
Day 15	672.3 (± 118.4)	340.5 (± 59.0)		
Day 22	802.3 (± 202.4)	356.2 (± 42.3)		
Day 29	725.2 (± 176.5)	394.1 (± 60.6)		
Day 43	797.3 (± 153.2)	0.0 (± 0.0)		

Day 57	819.9 (± 187.6)	391.6 (± 128.1)		
Day 71	871.9 (± 183.4)	0.0 (± 0.0)		
Day 85	876.3 (± 222.5)	349.4 (± 71.1)		
Day 99	891.8 (± 125.2)	0.0 (± 0.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Free C2, Total C2, and Functional Complement Activity (CH50)

End point title	Percent Change From Baseline in Free C2, Total C2, and Functional Complement Activity (CH50)[12]

End point description:

PD set - All participants for whom at least 1 postbaseline value for pharmacodynamic parameters was available. Only participants with available data at week 16.

End point type	Secondary

End point timeframe:

At week 16

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data from the placebo cohorts 1 and 2 has been pooled in a single "Total placebo" group for this endpoint

End point values	ARGX-117 Cohort 1	ARGX-117 Cohort 2	Total Placebo (Cohort 1 and 2 Combined)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	18	18	18	
Units: Percent change				
median (inter-quartile range (Q1-Q3))				
Free C2	-98.915 (-99.031 to -98.635)	-98.079 (-98.532 to -97.324)	-0.669 (-13.876 to 7.625)	
Total C2	331.82 (314.29 to 475.34)	296.34 (219.80 to 332.00)	331.82 (314.29 to 475.34)	
CH50	-89.01 (-95.68 to -83.92)	-64.33 (-69.00 to -45.27)	296.34 (219.80 to 332.00)	

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Antidrug Antibodies (ADA) Against Empasiprubart

End point title	Incidence of Antidrug Antibodies (ADA) Against

End point description:

Only ADA-evaluable participants were analyzed for this outcome measure. ADA-evaluable participants were classified as treatment-boosted ADA, treatment-induced ADA, treatment-unaffected ADA, or ADA negative.

End point type	Secondary

End point timeframe:

Up to 16 weeks

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data from the placebo cohorts 1 and 2 has been pooled in a single "Total placebo" group for this endpoint

End point values	ARGX-117 Cohort 1	ARGX-117 Cohort 2	Total Placebo (Cohort 1 and 2 Combined)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	18	18	
Units: participants	0	1	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: AEs have been reported from the start of the DBTP (Double-Blinded Treatment Period - 16 weeks) until the end of the safety follow-up period (15 months).	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups	
Reporting group title	ARGX-117 Cohort 1
Reporting group description: Participants received dosing regimen 1 of ARGX-117 via intravenous (IV) infusion	
Reporting group title	Placebo Cohort 1
Reporting group description: Participants received placebo via intravenous (IV) infusion	
Reporting group title	ARGX-117 Cohort 2
Reporting group description: Participants received dosing regimen 2 of ARGX-117 via intravenous (IV) infusion	
Reporting group title	Placebo Cohort 2
Reporting group description: Participants received placebo via intravenous (IV) infusion	

Serious adverse events	ARGX-117 Cohort 1	Placebo Cohort 1	ARGX-117 Cohort 2
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 18 (11.11%)	0 / 9 (0.00%)	0 / 18 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	0 / 18 (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
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	0 / 18 (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

Serious adverse events	Placebo Cohort 2		
Total subjects affected by serious			

adverse events			
subjects affected / exposed	0 / 9 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	ARGX-117 Cohort 1	Placebo Cohort 1	ARGX-117 Cohort 2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 18 (72.22%)	1 / 9 (11.11%)	14 / 18 (77.78%)
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 18 (0.00%)	0 / 9 (0.00%)	2 / 18 (11.11%)
occurrences (all)	0	0	2
Infusion site rash			
subjects affected / exposed	0 / 18 (0.00%)	0 / 9 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Oedema peripheral			
subjects affected / exposed	0 / 18 (0.00%)	1 / 9 (11.11%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Vaccination site pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 9 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Asthenia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 9 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Catheter site haematoma			

subjects affected / exposed	0 / 18 (0.00%)	0 / 9 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 18 (0.00%)	1 / 9 (11.11%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Chest pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 9 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Chills			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Feeling cold			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Injection site pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 9 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 18 (0.00%)	1 / 9 (11.11%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 18 (0.00%)	0 / 9 (0.00%)	3 / 18 (16.67%)
occurrences (all)	0	0	3
Oropharyngeal pain			
subjects affected / exposed	0 / 18 (0.00%)	1 / 9 (11.11%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Asthma			
subjects affected / exposed	0 / 18 (0.00%)	0 / 9 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Choking			

subjects affected / exposed	0 / 18 (0.00%)	0 / 9 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Nasal congestion			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Sneezing			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 9 (11.11%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Investigations			
Blood urine present			
subjects affected / exposed	0 / 18 (0.00%)	0 / 9 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Protein urine			
subjects affected / exposed	0 / 18 (0.00%)	0 / 9 (0.00%)	2 / 18 (11.11%)
occurrences (all)	0	0	2
Alanine aminotransferase increased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Haemoglobin decreased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 9 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Serum ferritin decreased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 9 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Procedural headache			
subjects affected / exposed	0 / 18 (0.00%)	0 / 9 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Arthropod bite			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Contusion			

subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Foot fracture			
subjects affected / exposed	0 / 18 (0.00%)	0 / 9 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Head injury			
subjects affected / exposed	0 / 18 (0.00%)	0 / 9 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Limb crushing injury			
subjects affected / exposed	0 / 18 (0.00%)	0 / 9 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	0 / 18 (0.00%)	1 / 9 (11.11%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Traumatic haematoma			
subjects affected / exposed	0 / 18 (0.00%)	0 / 9 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Antinuclear antibody increased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 9 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Bilirubin urine			
subjects affected / exposed	0 / 18 (0.00%)	0 / 9 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 18 (27.78%)	1 / 9 (11.11%)	5 / 18 (27.78%)
occurrences (all)	5	1	5
Amnesia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 9 (11.11%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Fine motor skill dysfunction			
subjects affected / exposed	0 / 18 (0.00%)	0 / 9 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Somnolence			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0

Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 9 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Eye disorders			
Eye irritation			
subjects affected / exposed	0 / 18 (0.00%)	0 / 9 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal rigidity			
subjects affected / exposed	0 / 18 (0.00%)	0 / 9 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	0 / 18 (0.00%)	0 / 9 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Dysphagia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Gastritis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Pigmentation disorder			
subjects affected / exposed	0 / 18 (0.00%)	0 / 9 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Rash papular			
subjects affected / exposed	0 / 18 (0.00%)	0 / 9 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Rash pruritic			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Urticaria			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0

Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 18 (5.56%)	1 / 9 (11.11%)	0 / 18 (0.00%)
occurrences (all)	1	1	0
Arthritis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Muscle spasms			
subjects affected / exposed	0 / 18 (0.00%)	0 / 9 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	0 / 18 (0.00%)	1 / 9 (11.11%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Back pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 9 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Myalgia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 9 (11.11%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Neck pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 9 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Spinal pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 9 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Fall			
subjects affected / exposed	0 / 18 (0.00%)	0 / 9 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 9 (0.00%)	4 / 18 (22.22%)
occurrences (all)	0	0	4

Influenza			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Urinary tract infection			
subjects affected / exposed	2 / 18 (11.11%)	0 / 9 (0.00%)	1 / 18 (5.56%)
occurrences (all)	2	0	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 18 (0.00%)	1 / 9 (11.11%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Anal fungal infection			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
COVID-19			
subjects affected / exposed	1 / 18 (5.56%)	0 / 9 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal infection			
subjects affected / exposed	0 / 18 (0.00%)	1 / 9 (11.11%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 18 (0.00%)	0 / 9 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Paronychia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 9 (11.11%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Sinusitis bacterial			
subjects affected / exposed	0 / 18 (0.00%)	0 / 9 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Tooth abscess			
subjects affected / exposed	0 / 18 (0.00%)	0 / 9 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1

Non-serious adverse events	Placebo Cohort 2		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 9 (66.67%)		
General disorders and administration site conditions			

Fatigue				
subjects affected / exposed	2 / 9 (22.22%)			
occurrences (all)	2			
Infusion site rash				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Oedema peripheral				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Vaccination site pain				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Asthenia				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Catheter site haematoma				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Chest discomfort				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Chest pain				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Chills				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Feeling cold				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Injection site pain				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Pyrexia				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			

Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Asthma			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Choking			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Nasal congestion			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Sneezing			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Investigations			
Blood urine present			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Protein urine			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Alanine aminotransferase increased			

subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Haemoglobin decreased			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Serum ferritin decreased			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Procedural headache			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Arthropod bite			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Contusion			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Foot fracture			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Head injury			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Limb crushing injury			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Skin abrasion			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Traumatic haematoma			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Antinuclear antibody increased			

subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Bilirubin urine			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Amnesia			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Fine motor skill dysfunction			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Somnolence			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Eye disorders			
Eye irritation			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal rigidity			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Dysphagia			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Gastritis			

subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Pigmentation disorder			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Rash papular			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Rash pruritic			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Urticaria			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Arthritis			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Back pain			

subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Neck pain			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Spinal pain			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Fall			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	3 / 9 (33.33%)		
occurrences (all)	3		
Influenza			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Anal fungal infection			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
COVID-19			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Gastrointestinal infection			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		

Lower respiratory tract infection subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0		
Paronychia subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0		
Sinusitis bacterial subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Tooth abscess subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 February 2022	Amendment 1 (v2.0) - Revised contraception guidelines and defined sexual abstinence and unacceptable forms of contraception per Clinical Trials Facilitation and Coordination Group guidelines. The timing of pregnancy tests for women of childbearing potential was also clarified. - Clarified that a delay in the first visit (IDV1 or IMV1) to align with a participant's IVIg dosing schedule would not result in screen failure. - Clarified that all assessments were performed before IMP administration unless otherwise specified. Added sampling for immunogenicity at screening. - Extended the safety follow-up period from 9 to 12 months and adapted the timing of the visits. - Corrected mMRC endpoint from percentage of time to proportion of participants. - Specified liver and renal exclusion cutoff values in the exclusion criteria. Also clarified that individuals who had a splenectomy were excluded from the study. - Expanded criteria for early treatment discontinuation to include the detection of a new malignancy during the DBTP and participants whose blinding code was broken. - Updated safety and monitoring criteria. - Added C-reactive protein to the collected laboratory parameters.
12 December 2022	Amendment 2 (v3.0): - Revised the definition of clinically meaningful deterioration to align with the clinical presentation of MMN. - Clarified that the investigator determined whether deterioration in objective MMN measurements necessitated retreatment with IVIg. - Updated the safety follow-up period and requirements for contraception from 12 to 15 months to reflect the half-life of empasiprubart. - Clarified that bilateral vasectomy was considered an effective form of contraception. - Clarified that the final causality assessment was made by the sponsor after careful review of all relevant information, including recommendations/suggestions from the principal investigator and IDMC. - Clarified that "stable" IVIg regimen was at least 3 months before screening or recently initiated. - Clarified that IDMC review of cohort 1 data also considered early discontinuations within the DBTP. - Clarified the timing of assessments. - Clarified the secondary endpoints of the study: mMRC, 9-HPT, EQ-5D-5L, PGI-C, HRPQ, TSQM-14, and ADA. The endpoint planned to assess the difference between the time to the first retreatment with IVIg (cycle) and the second time to retreatment with IVIg was removed because it was unlikely to be meaningful. - Replaced the full analysis set with the safety analysis set, because participants were analyzed according to the treatment received and not planned. The per protocol analysis set was deleted. - Added that interim analyses could have been performed for regulatory interactions.

02 March 2023	Amendment 3 (v4.0): - Added AEs of clinical interest. - Added 3 dosing regimen options for cohort 2. - Added details about maintaining blinding throughout cohort 2. - Updated potential risks and mitigation strategies. - Updated ANA titer reporting to ≥1:100. - Updated pregnancy follow-up and SAE reporting language and clarified that any female who became pregnant while participating in the study would discontinue IMP. - Added details for the interim analyses after the completion of cohort 1 and cohort 2. - Clarified the timeline for the final database lock. - Updated language to reflect that the EDRT would select the final dosing regimen in cohort 2, if applicable.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported