Clinical trial results:
A Phase 2 Trial to Investigate the Efficacy, Safety, and Tolerability of Efgartigimod PH20 SC in Adult Patients with Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

Summary

EudraCT number	2019-003076-39
Trial protocol	DE PL HU ES LV CZ GB BE NL BG DK AT IT RO
Global end of trial date	11 May 2023

Results information

Result version number	v1 (current)
This version publication date	25 May 2024
First version publication date	25 May 2024

Trial information

Trial identification

Sponsor protocol code	ARGX-113-1802

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04281472
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	21 November 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 May 2023
Global end of trial reached?	Yes
Global end of trial date	11 May 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Stage A: To assess the activity of efgartigimod PH20 SC (efgartigimod co-formulated with recombinant human hyaluronidase PH20 [rHuPH20]) based on the percentage of patients classified as treatment responders.

Stage B: To determine the efficacy of efgartigimod PH20 SC compared to placebo based on the time needed for the first evidence of clinical deterioration.

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 assent, if applicable) and the dated signature of the investigator or investigator’s delegate.

Background therapy: -

Evidence for comparator:

This study is placebo-controlled and Placebo PH20 SC (placebo) is used for comparator.

Actual start date of recruitment	14 April 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 5
Country: Number of subjects enrolled	Poland: 18
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	United Kingdom: 13
Country: Number of subjects enrolled	Austria: 8
Country: Number of subjects enrolled	Belgium: 7
Country: Number of subjects enrolled	Bulgaria: 9
Country: Number of subjects enrolled	Denmark: 17
Country: Number of subjects enrolled	France: 17
Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	Italy: 14
Country: Number of subjects enrolled	China: 58
Country: Number of subjects enrolled	Georgia: 16

Country: Number of subjects enrolled	Israel: 1
Country: Number of subjects enrolled	Japan: 24
Country: Number of subjects enrolled	Romania: 11
Country: Number of subjects enrolled	Russian Federation: 16
Country: Number of subjects enrolled	Serbia: 9
Country: Number of subjects enrolled	Taiwan: 5
Country: Number of subjects enrolled	Türkiye: 3
Country: Number of subjects enrolled	Ukraine: 12
Country: Number of subjects enrolled	United States: 48
Worldwide total number of subjects	322
EEA total number of subjects	117

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)	247
From 65 to 84 years	75
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Up to 360 participants were planned to be enrolled in Stage A. A total of 322 participants received efgartigimod PH20 SC in Stage A, and 221 of those participants continued to Stage B where they were randomized in a 1:1 ratio to efgartigimod PH20 SC (N=111) or placebo (N=110) in Stage B.

Pre-assignment

Screening details:

In total, 629 participants were screened, and 342 entered the study: 36 entered Stage A directly, and 306 started the run-in period, of whom 286 entered Stage A. Overall, 322 participants entered Stage A. 221 participants from Stage A were randomized in Stage B.

Period 1

Period 1 title	Stage A period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Stage A was open-label.

Arms

Arm title	efgartigimod PH20 SC - Stage A

Arm description:

Up to 360 participants were planned to be enrolled in Stage A. Open-label efgartigimod PH20 SC was administered once weekly in Stage A for up to 12 weeks (with an optional additional week for ECI confirmation), with a minimum of 4 administrations. ECI (evidence of clinical improvement) was achieved through improvement of the INCAT score, or improvement on I-RODS or mean grip strength. Participants remained in Stage A until ECI was confirmed at 2 consecutive visits. Participants who had ECI at 2 consecutive visits during Stage A entered Stage B. Participants without confirmed ECI during Stage A were withdrawn from the study.

Arm type	Experimental
Investigational medicinal product name	efgartigimod PH20 SC
Investigational medicinal product code	
Other name	Efgartigimod (ARGX-113)
Pharmaceutical forms	Solution for injection in vial
Routes of administration	Subcutaneous use

Dosage and administration details:

Stage A: up to 12 weeks (with an optional additional week). Efgartigimod PH20 SC 1000 mg was administered once weekly for at least 4 and up to 13 administrations.

Number of subjects in period 1	efgartigimod PH20 SC - Stage A
Started	322
Completed	221
Not completed	101
death	1
physician decision	1
AEs	20

prohibited medications	2
Rollover to OLE	22
other	5
Lost to follow-up	2
withdrawal by participant	11
IMP noncompliance	1
Lack of efficacy	36

Period 2

Period 2 title	Stage B period
Is this the baseline period?	Yes[1]
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

Stage B was double-blinded.

Arms

Are arms mutually exclusive?	Yes
Arm title	efgartigimod PH20 SC - Stage B

Arm description:

In Stage B, participants were randomized in a 1:1 ratio to receive once-weekly injections of efgartigimod PH20 SC or placebo. 111 subjects were randomized to receive the efgartigimod PH20 SC.

Arm type	Experimental
Investigational medicinal product name	efgartigimod PH20 SC
Investigational medicinal product code	
Other name	Efgartigimod (ARGX-113)
Pharmaceutical forms	Solution for injection in vial
Routes of administration	Subcutaneous use

Dosage and administration details:

Stage B: Efgartigimod PH20 SC 1000 mg once weekly for up to 48 weeks.

Arm title	placebo PH20 SC - Stage B

Arm description:

In Stage B, participants were randomized in a 1:1 ratio to receive once-weekly injections of efgartigimod PH20 SC or placebo. 110 subjects were randomized to receive the placebo.

Arm type	Placebo
Investigational medicinal product name	Placebo PH20 SC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in vial
Routes of administration	Subcutaneous use

Dosage and administration details:

Stage B: 1000 mg placebo PH20 SC (placebo) once weekly for up to 48 weeks.

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: Stage B is the baseline period.

Number of subjects in period 2[2]	efgartigimod PH20 SC - Stage B	placebo PH20 SC - Stage B
Started	111	110
Completed	64	74
Not completed	47	36
death	-	1
AEs	3	-
prohibited medications	2	1
Rollover after 88th event	35	26
other	3	-
Sponsor decision	-	1
Lost to follow-up	-	2
withdrawal by participant	3	3
Protocol deviation	1	1
Lack of efficacy	-	1

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Reported results are for Stage B period which is baseline period of the study.

Baseline characteristics

Reporting groups	
Reporting group title	efgartigimod PH20 SC - Stage B
Reporting group description:	
In Stage B, participants were randomized in a 1:1 ratio to receive once-weekly injections of efgartigimod PH20 SC or placebo. 111 subjects were randomized to receive the efgartigimod PH20 SC.	
Reporting group title	placebo PH20 SC - Stage B
Reporting group description:	
In Stage B, participants were randomized in a 1:1 ratio to receive once-weekly injections of efgartigimod PH20 SC or placebo. 110 subjects were randomized to receive the placebo.	

Reporting group values	efgartigimod PH20 SC - Stage B	placebo PH20 SC - Stage B	Total
Number of subjects	111	110	221
Age categorical			
Units: Subjects			
Adults (18-64 years)	86	88	174
From 65-84 years	25	22	47
Age continuous			
Units: years			
arithmetic mean	54.5	51.3	
standard deviation	± 13.18	± 14.47	-
Gender categorical			
Units: Subjects			
Female	38	41	79
Male	73	69	142

End points

End points reporting groups

Reporting group title	efgartigimod PH20 SC - Stage A

Reporting group description:

Up to 360 participants were planned to be enrolled in Stage A. Open-label efgartigimod PH20 SC was administered once weekly in Stage A for up to 12 weeks (with an optional additional week for ECI confirmation), with a minimum of 4 administrations. ECI (evidence of clinical improvement) was achieved through improvement of the INCAT score, or improvement on I-RODS or mean grip strength. Participants remained in Stage A until ECI was confirmed at 2 consecutive visits. Participants who had ECI at 2 consecutive visits during Stage A entered Stage B. Participants without confirmed ECI during Stage A were withdrawn from the study.

Reporting group title	efgartigimod PH20 SC - Stage B

Reporting group description:

In Stage B, participants were randomized in a 1:1 ratio to receive once-weekly injections of efgartigimod PH20 SC or placebo. 111 subjects were randomized to receive the efgartigimod PH20 SC.

Reporting group title	placebo PH20 SC - Stage B

Reporting group description:

In Stage B, participants were randomized in a 1:1 ratio to receive once-weekly injections of efgartigimod PH20 SC or placebo. 110 subjects were randomized to receive the placebo.

Primary: Stage B -Time to First Occurrence of Clinical Deterioration: Hazard ratio

End point title	Stage B -Time to First Occurrence of Clinical Deterioration: Hazard ratio

End point description:

Hazard ratio for time to first adjusted INCAT deterioration, comparing efgartigimod PH20 SC over placebo PH20 SC

End point type	Primary

End point timeframe:

Up to 48 weeks during the randomized placebo-controlled stage B

End point values	efgartigimod PH20 SC - Stage B	placebo PH20 SC - Stage B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111[1]	110[2]		
Units: Hazard ratio rate				
number (confidence interval 95%)				
Hazard ratio	0.394 (0.253 to 0.614)	999 (999 to 999)		

Notes:

[1] - The hazard ratio compares efgartigimod(111) with placebo(110) in one value. 999 is a dummy value.

[2] - The hazard ratio compares efgartigimod(111) with placebo(110) in one value. 999 is a dummy value.

Statistical analyses

Statistical analysis title	Cox Proportional Hazard Model
Comparison groups	efgartigimod PH20 SC - Stage B v placebo PH20 SC - Stage B

Number of subjects included in analysis	221
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.000039
Method	Cox Proportional Hazard Model
Parameter estimate	Cox proportional hazard
Point estimate	0.394
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.253
upper limit	0.614
Variability estimate	Standard deviation

Primary: Stage A - Percentage of participants with confirmed ECI

End point title	Stage A - Percentage of participants with confirmed ECI[3]

End point description:

Percentage of participants in Stage A with confirmed ECI (Evidence of clinical Improvement)

End point type	Primary

End point timeframe:

Up to 12 weeks during the open-label stage A

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis for this Primary End Point.

End point values	efgartigimod PH20 SC - Stage A			
Subject group type	Reporting group			
Number of subjects analysed	322			
Units: percent				
number (not applicable)				
Number of participants with confirmed ECI	66.5			

Statistical analyses

No statistical analyses for this end point

Primary: Stage B mITT: Time to First Adjusted INCAT Deterioration Compared to Stage B Baseline: Hazard Ratio

End point title	Stage B mITT: Time to First Adjusted INCAT Deterioration Compared to Stage B Baseline: Hazard Ratio[4]

End point description:

Hazard ratio for time to first adjusted INCAT deterioration, comparing efgartigimod PH20 SC over placebo PH20 SC

End point type	Primary

End point timeframe:

Up to 48 weeks during randomized placebo-controlled Stage B

Notes:

[4] - 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: Cox Proportional Hazard Model has been added as Statistical analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Stage A - Time to initial confirmed ECI

End point title	Stage A - Time to initial confirmed ECI

End point description:

End point type	Secondary

End point timeframe:

Up to 12 weeks during the open-label stage A

End point values	efgartigimod PH20 SC - Stage A			
Subject group type	Reporting group			
Number of subjects analysed	322			
Units: days				
median (confidence interval 95%)				
25th percentile (95% CI) (days)	22.0 (22.0 to 23.0)			
50th percentile (95% CI) (days)	43.0 (31.00 to 51.0)			
75th percentile (95% CI) (days)	71.0 (70.0 to 78.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Stage A - Change from Stage A baseline over time during Stage A in aINCAT score, MRC sum score, 24-item I-RODS score, TUG score and Mean grip strength

End point title	Stage A - Change from Stage A baseline over time during Stage A in aINCAT score, MRC sum score, 24-item I-RODS

	score, TUG score and Mean grip strength

End point description:

INCAT: Adjusted Inflammatory Neuropathy Cause and Treatment (INCAT) scores range from 0-10 with a score of 10 indicating the greatest degree of disability.
MRC: The Medical Research Council (MRC) Sum scores range from 0 to 60 with a lower score indicating greater muscle weakness.
I-RODS: The Inflammatory Rasch-built Overall Disability Scale (I-RODS) score ranges from 0-100, with lower scores indicating the greatest degree of disability.
TUG: The Timed Up and Go (TUG) score is calculated as the number of seconds needed to complete a series of actions. The longer time needed to complete this test (expressed in seconds) indicates lower mobility.

End point type	Secondary

End point timeframe:

Up to 12 weeks during the open-label stage A

End point values	efgartigimod PH20 SC - Stage A			
Subject group type	Reporting group			
Number of subjects analysed	322			
Units: number				
arithmetic mean (standard deviation)				
aINCAT score	-0.9 (± 1.71)			
I-RODS score	7.7 (± 15.48)			
Mean grip strength – dominant hand (kPa)	12.3 (± 18.68)			
Mean grip strength – nondominant hand (kPa)	11.2 (± 21.12)			
MRC Sum Score	3.8 (± 0.41)			
TUG score	-4.3 (± 0.83)			

Statistical analyses

No statistical analyses for this end point

Secondary: Stage A - Changes From Stage A Baseline to Last Assessment in Stage A, in EQ-5D-5L Visual Analog Scale (VAS) Over Time

End point title	Stage A - Changes From Stage A Baseline to Last Assessment in Stage A, in EQ-5D-5L Visual Analog Scale (VAS) Over Time

End point description:

Scores range from 0-100 with 100 indicating the best health state. Therefore, positive changes indicate higher health-related quality of life reported by the patient.

End point type	Secondary

End point timeframe:

Up to 12 weeks during the open-label stage A

End point values	efgartigimod PH20 SC - Stage A			
Subject group type	Reporting group			
Number of subjects analysed	322			
Units: number				
arithmetic mean (standard error)				
Baseline Stage A	50.8 (± 1.17)			
Last assessment Stage A	61.7 (± 1.23)			

Statistical analyses

No statistical analyses for this end point

Secondary: Stage A: Exposure Adjusted Occurrence of Treatment-emergent Adverse Events and Serious Adverse Events

End point title	Stage A: Exposure Adjusted Occurrence of Treatment-emergent Adverse Events and Serious Adverse Events

End point description:

Treatment-emergent (serious) AEs expressed in number of events/100 PYFU (participant years of follow-up)

End point type	Secondary

End point timeframe:

Up to 12 weeks during the open-label stage A

End point values	efgartigimod PH20 SC - Stage A			
Subject group type	Reporting group			
Number of subjects analysed	322			
Units: events/100 PYFU				
number (not applicable)				
treatment-emergent adverse events	1343.1			
treatment-emergent serious adverse events	51.2			

Statistical analyses

No statistical analyses for this end point

Secondary: Stage A - Predose efgartigimod PH20 SC serum concentrations over time

End point title	Stage A - Predose efgartigimod PH20 SC serum concentrations over time

End point description:

End point type	Secondary

End point timeframe:

Up to 12 weeks during the open-label stage A

End point values	efgartigimod PH20 SC - Stage A			
Subject group type	Reporting group			
Number of subjects analysed	298			
Units: number				
arithmetic mean (standard deviation)				
Week 1	14.9 (± 6.92)			
Week 2	19.6 (± 8.55)			
Week 3	19.7 (± 9.62)			
Week 4	18.9 (± 9.96)			
Week 5	18.4 (± 8.38)			
Week 6	19.2 (± 9.62)			
Week 7	17.3 (± 8.89)			
Week 8	18.8 (± 8.93)			
Week 9	17.8 (± 8.84)			
Week 10	17.3 (± 7.62)			
Week 11	20.1 (± 9.64)			
Week 12	20.0 (± 6.89)			
Week 13	14.9 (± 7.24)			

Statistical analyses

No statistical analyses for this end point

Secondary: Stage A - Percent Changes From Stage A Baseline of Serum IgG Levels Over Time

End point title	Stage A - Percent Changes From Stage A Baseline of Serum IgG Levels Over Time

End point description:

End point type	Secondary

End point timeframe:

Up to 12 weeks during the open-label stage A

End point values	efgartigimod PH20 SC - Stage A			
Subject group type	Reporting group			
Number of subjects analysed	321			
Units: percent				
arithmetic mean (standard error)				

Week 1	-36.1 (± 0.58)			
Week 2	-54.6 (± 0.80)			
Week 3	-63.5 (± 0.71)			
Week 4	-66.2 (± 0.89)			
Week 5	-67.9 (± 0.74)			
Week 6	-67.7 (± 1.42)			
Week 7	-66.4 (± 1.96)			
Week 8	-64.5 (± 4.28)			
Week 9	-68.8 (± 1.17)			
Week 10	-67.1 (± 1.90)			
Week 11	-70.0 (± 1.41)			
Week 12	-67.3 (± 4.44)			
Week 13	-51.0 (± 10.00)			

Statistical analyses

No statistical analyses for this end point

Secondary: Stage A - Incidence of Binding Antidrug Antibodies (ADA) Towards Efgartigimod or Antibodies (Ab) Against rHuPH20 and Neutralizing Antibodies (NAb) Against Efgartigimod and/or rHuPH20

End point title	Stage A - Incidence of Binding Antidrug Antibodies (ADA) Towards Efgartigimod or Antibodies (Ab) Against rHuPH20 and Neutralizing Antibodies (NAb) Against Efgartigimod and/or rHuPH20

End point description:

End point type	Secondary

End point timeframe:

Up to 12 weeks during the open-label stage A

End point values	efgartigimod PH20 SC - Stage A			
Subject group type	Reporting group			
Number of subjects analysed	317			
Units: Incidence				
number (not applicable)				
ADA towards Efgartigimod incidence	20			
Ab towards rHuPH20 incidence	45			
NAb against Efgartigimod incidence	1			
NAb against rHuPH20 incidence	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Stage B - Time to CIDP Disease Progression

End point title	Stage B - Time to CIDP Disease Progression

End point description:

Time to chronic inflammatory demyelinating polyneuropathy (CIDP) disease progression is defined by the time from first dose of double-blind IMP to the first I-RODS score decrease ≥4 points compared to Stage B baseline using the centile metric. '00' is reported as the median (95% CI) time to CIDP Disease Progression could not be calculated because less than 50% of the participants showed CIDP Disease Progression in the efgartigimod PH20 SC group

End point type	Secondary

End point timeframe:

Up to 48 weeks during the randomized placebo-controlled stage B

End point values	efgartigimod PH20 SC - Stage B	placebo PH20 SC - Stage B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111[5]	110		
Units: days				
median (confidence interval 95%)				
Time to CIDP Disease Progression	999 (247.0 to 999)	85 (50.0 to 253.0)		

Notes:

[5] - '999' is a dummy value as it should be 'NA'

Statistical analyses

No statistical analyses for this end point

Secondary: Stage B - Percentage of participants with improved functional level compared to Stage B baseline, as measured by an increase in the 24-item I-RODS score up to week 48

End point title	Stage B - Percentage of participants with improved functional level compared to Stage B baseline, as measured by an increase in the 24-item I-RODS score up to week 48

End point description:

End point type	Secondary

End point timeframe:

Up to 48 weeks during the randomized placebo-controlled stage B

End point values	efgartigimod PH20 SC - Stage B	placebo PH20 SC - Stage B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	110		
Units: percent				
number (not applicable)				
Improved Functional Level	45.0	36.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Stage B - Change from Stage B baseline over time in aINCAT score, MRC sum score, 24-item I-RODS score, TUG score and Mean grip strength

End point title	Stage B - Change from Stage B baseline over time in aINCAT score, MRC sum score, 24-item I-RODS score, TUG score and Mean grip strength

End point description:

aINCAT: Adjusted Inflammatory Neuropathy Cause and Treatment (INCAT) scores range from 0-10 with a score of 10 indicating the greatest degree of disability.
MRC: The Medical Research Council (MRC) Sum scores range from 0 to 60 with a lower score indicating greater muscle weakness.
I-RODS: The Inflammatory Rasch-built Overall Disability Scale (I-RODS) score ranges from 0-100, with lower scores indicating the greatest degree of disability.
TUG: The Timed Up and Go (TUG) score is calculated as the number of seconds needed to complete a series of actions. The longer time needed to complete this test (expressed in seconds) indicates lower mobility.

End point type	Secondary

End point timeframe:

Up to 48 weeks during the randomized placebo-controlled stage B

End point values	efgartigimod PH20 SC - Stage B	placebo PH20 SC - Stage B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	110		
Units: number				
arithmetic mean (standard deviation)				
aINCAT score	0.1 (± 1.08)	0.9 (± 1.98)		
I-RODS score	0.8 (± 12.33)	-7.0 (± 19.10)		
Mean grip strength – dominant hand (kPa)	2.1 (± 13.29)	-8.2 (± 20.69)		
Mean grip strength – nondominant hand (kPa)	2.0 (± 17.33)	-6.9 (± 21.30)		
MRC Sum score	-0.3 (± 0.43)	-3 (± 0.86)		
TUG score	0.8 (± 0.36)	1.9 (± 0.60)		

Statistical analyses

No statistical analyses for this end point

Secondary: Stage B - Exposure Adjusted Occurrence of Treatment-emergent Adverse Events and Serious Adverse Events

End point title	Stage B - Exposure Adjusted Occurrence of Treatment-emergent Adverse Events and Serious Adverse Events

End point description:

Treatment-emergent (serious) AEs expressed in number of events/100 PYFU (participant years of follow-up)

End point type	Secondary

End point timeframe:

Up to 48 weeks during the randomized placebo-controlled stage B

End point values	efgartigimod PH20 SC - Stage B	placebo PH20 SC - Stage B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	110		
Units: Events/100 PYFU				
number (not applicable)				
treatment-emergent adverse events	347.6	510.9		
treatment-emergent serious adverse events	14.1	19.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Stage B - Predose efgartigimod PH20 SC serum concentrations over time

End point title	Stage B - Predose efgartigimod PH20 SC serum concentrations over time

End point description:

End point type	Secondary

End point timeframe:

Up to 48 weeks during the randomized placebo-controlled stage B

End point values	efgartigimod PH20 SC - Stage B	placebo PH20 SC - Stage B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	110		
Units: number				
arithmetic mean (standard deviation)				

Week 4	18.4 (± 10.3)	0.267 (± 0.365)		
Week 8	17.2 (± 9.11)	0 (± 0)		
Week 12	18.1 (± 9.48)	0 (± 0)		
Week 16	16.9 (± 9.03)	0 (± 0)		
Week 20	16.8 (± 8.36)	0 (± 0)		
Week 24	16.0 (± 7.89)	0 (± 0)		
Week 28	18.5 (± 10.2)	0 (± 0)		
Week 32	18.0 (± 9.50)	0 (± 0)		
Week 36	17.9 (± 10.7)	0 (± 0)		
Week 40	16.2 (± 8.20)	0 (± 0)		
Week 44	18.1 (± 10.2)	0 (± 0)		
Week 48	16.3 (± 8.18)	0 (± 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Stage B - Percent Changes of Serum IgG Levels Over Time

End point title	Stage B - Percent Changes of Serum IgG Levels Over Time

End point description:

End point type	Secondary

End point timeframe:

Up to 48 weeks during the randomized placebo-controlled stage B

End point values	efgartigimod PH20 SC - Stage B	placebo PH20 SC - Stage B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	110		
Units: percent				
arithmetic mean (standard error)				
Week 4	-68.2 (± 1.14)	-36.7 (± 1.91)		
Week 8	-68.2 (± 1.24)	-10.9 (± 2.41)		
Week 12	-69.8 (± 1.09)	-7.1 (± 2.54)		
Week 16	-67.4 (± 1.49)	-2.1 (± 3.09)		
Week 20	-67.8 (± 1.30)	2.0 (± 3.61)		
Week 24	-67.2 (± 1.52)	1.7 (± 4.22)		
Week 28	-67.9 (± 1.42)	-2.3 (± 4.31)		
Week 32	-68.5 (± 1.63)	0.6 (± 5.18)		
Week 36	-64.7 (± 2.82)	-3.6 (± 4.12)		
Week 40	-68.0 (± 1.91)	-4.2 (± 4.98)		
Week 44	-67.8 (± 1.92)	-3.6 (± 6.50)		
Week 48	-66.6 (± 1.85)	-0.9 (± 7.36)		

Statistical analyses

No statistical analyses for this end point

Secondary: Stage B - Incidence of ADA against efgartigimod and antibodies against rHuPH20

End point title	Stage B - Incidence of ADA against efgartigimod and antibodies against rHuPH20

End point description:

End point type	Secondary

End point timeframe:

Up to 48 weeks during the randomized placebo-controlled stage B

End point values	efgartigimod PH20 SC - Stage B	placebo PH20 SC - Stage B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	109		
Units: Incidence				
number (not applicable)				
ADA towards Efgartigimod incidence	2	64		
Ab towards rHuPH20 incidence	52	32		
NAb against efgartigimod incidence	0	13		
NAb against rHuPH20 incidence	5	2		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
AEs reported from the first dose of IMP until 28 days after the last dose of IMP were considered treatment-emergent and were summarized descriptively.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups	
Reporting group title	efgartigimod PH20 SC - Stage B
Reporting group description:	
Participants who completed stage A and received efgartigimod PH20 SC in stage B	
Reporting group title	placebo PH20 SC - Stage B
Reporting group description:	
Participants who completed stage A and received placebo PH20 SC in stage B	
Reporting group title	efgartigimod PH20 SC - Stage A
Reporting group description:	
Participants receiving efgartigimod PH20 SC in stage A	

Serious adverse events	efgartigimod PH20 SC - Stage B	placebo PH20 SC - Stage B	efgartigimod PH20 SC - Stage A
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 111 (5.41%)	6 / 110 (5.45%)	21 / 322 (6.52%)
number of deaths (all causes)	0	1	2
number of deaths resulting from adverse events	0	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lipoma			
subjects affected / exposed	0 / 111 (0.00%)	1 / 110 (0.91%)	0 / 322 (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
Prostate cancer			
subjects affected / exposed	1 / 111 (0.90%)	0 / 110 (0.00%)	0 / 322 (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
Transitional cell carcinoma			
subjects affected / exposed	1 / 111 (0.90%)	0 / 110 (0.00%)	0 / 322 (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

Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 111 (0.00%)	0 / 110 (0.00%)	1 / 322 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	1 / 111 (0.90%)	0 / 110 (0.00%)	0 / 322 (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
Foot fracture			
subjects affected / exposed	1 / 111 (0.90%)	0 / 110 (0.00%)	0 / 322 (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
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 111 (0.00%)	0 / 110 (0.00%)	1 / 322 (0.31%)
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			
Chronic inflammatory demyelinating polyradiculoneuropathy			
subjects affected / exposed	0 / 111 (0.00%)	1 / 110 (0.91%)	14 / 322 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Quadriparesis			
subjects affected / exposed	0 / 111 (0.00%)	0 / 110 (0.00%)	1 / 322 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Deafness unilateral			
subjects affected / exposed	0 / 111 (0.00%)	1 / 110 (0.91%)	0 / 322 (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
Hepatobiliary disorders			
Cholelithiasis			

subjects affected / exposed	1 / 111 (0.90%)	0 / 110 (0.00%)	0 / 322 (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
Renal and urinary disorders			
Urethral stenosis			
subjects affected / exposed	1 / 111 (0.90%)	0 / 110 (0.00%)	0 / 322 (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
Urinary bladder polyp			
subjects affected / exposed	1 / 111 (0.90%)	0 / 110 (0.00%)	0 / 322 (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
Calculus urinary			
subjects affected / exposed	0 / 111 (0.00%)	0 / 110 (0.00%)	1 / 322 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 111 (0.00%)	1 / 110 (0.91%)	0 / 322 (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
COVID-19 pneumonia			
subjects affected / exposed	1 / 111 (0.90%)	0 / 110 (0.00%)	1 / 322 (0.31%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 111 (0.00%)	2 / 110 (1.82%)	0 / 322 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 111 (0.00%)	0 / 110 (0.00%)	1 / 322 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			

subjects affected / exposed	0 / 111 (0.00%)	0 / 110 (0.00%)	1 / 322 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suspected COVID-19			
subjects affected / exposed	0 / 111 (0.00%)	0 / 110 (0.00%)	1 / 322 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 111 (0.00%)	1 / 110 (0.91%)	0 / 322 (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

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

Non-serious adverse events	efgartigimod PH20 SC - Stage B	placebo PH20 SC - Stage B	efgartigimod PH20 SC - Stage A
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 111 (27.93%)	15 / 110 (13.64%)	60 / 322 (18.63%)
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 111 (3.60%)	2 / 110 (1.82%)	16 / 322 (4.97%)
occurrences (all)	6	2	28
General disorders and administration site conditions			
Injection site bruising			
subjects affected / exposed	6 / 111 (5.41%)	1 / 110 (0.91%)	4 / 322 (1.24%)
occurrences (all)	6	1	5
Injection site erythema			
subjects affected / exposed	6 / 111 (5.41%)	0 / 110 (0.00%)	33 / 322 (10.25%)
occurrences (all)	6	0	53
Infections and infestations			
COVID-19			
subjects affected / exposed	19 / 111 (17.12%)	14 / 110 (12.73%)	6 / 322 (1.86%)
occurrences (all)	20	14	7
Upper respiratory tract infection			

subjects affected / exposed occurrences (all)	2 / 111 (1.80%) 3	11 / 110 (10.00%) 11	11 / 322 (3.42%) 12

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 January 2020	The primary endpoint of Stage B was updated: 1. The time window for confirmation of the first occurrence of clinical deterioration (defined by an increase of ≥1 point in aINCAT score compared with Stage B baseline) was shortened to reduce the time of clinical deterioration and offer follow-up treatment as soon as possible. 2. A clarification was added that to prevent further deterioration, no confirmation was needed for a clinical deterioration (increase in aINCAT score of ≥2 points compared with baseline). Clarification of the eligibility criterion was added: The lowest possible INCAT score of 2 had to be exclusively from leg disability.
04 May 2020	COVID-19 mitigation measures were added. Additional IMP blinding measures were added (using blinded IMP vials and masked syringes). A withdrawal criterion was added for Stage A. The requirement of a 4-week minimum in the run-in period before entering Stage A was removed.
30 November 2020	The definition of ECI was updated to include I-RODS and/or grip strength (for participants with no change in aINCAT during run-in). Inclusion criterion #6 was updated to specify that "current" CIDP treatment at screening means "within the last 6 months." Based on nonclinical teratogenicity and reproductive toxicity data, female participants could use acceptable contraception methods (in addition to highly effective methods) and male contraception was no longer required; however, male participants had to agree not to donate sperm during the study and for 90 days after. Clarification was added for INCAT scores at baseline (with different baselines during the study) and aINCAT scores at postbaseline visits. The safety section was updated based on the current Investigator's Brochure at the time of the amendment. Further clarification was provided on how to perform a home visit during the COVID-19 pandemic.
12 October 2022	EQ-5D-5L was escalated from an exploratory endpoint to a secondary endpoint. As an additional blinding precaution, local IgG measurements were no longer allowed, and total protein and albumin results were not sent to the sites (or not measured if a local laboratory was used) after the Stage B baseline. IgG subtype measurements were removed from the protocol. A change was made to allow participants in the run-in period at the time the study stopped (ie, at the 88th event) to roll over to the OLE study. The maximum number of 180 randomized participants in Stage B was removed. Clarification was added that additional tests could be performed to confirm the CIDP diagnosis. The list of prohibited medications was updated.Based on nonclinical teratogenicity and reproductive toxicity data, the inclusion and exclusion criteria were updated: 1) Female participants could stop their contraception method at the date of the last IMP dose; 2) Female participants could become pregnant immediately after the study; 3) Male participants could donate sperm. Integration of country-specific requirements (except for China) in the global protocol.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported