Clinical trial results:
A Phase 3, Randomized, Open-Label, Parallel-Group Study to Compare the Pharmacodynamics, Pharmacokinetics, Efficacy, Safety, Tolerability, and Immunogenicity of Multiple Subcutaneous Injections of Efgartigimod PH20 SC with Multiple Intravenous Infusions of Efgartigimod in Patients with Generalized Myasthenia Gravis

Summary

EudraCT number	2020-004085-19
Trial protocol	HU NL BE DE ES IT
Global end of trial date	13 December 2021

Results information

Result version number	v1 (current)
This version publication date	15 December 2022
First version publication date	15 December 2022

Trial information

Trial identification

Sponsor protocol code	ARGX-113-2001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04735432
WHO universal trial number (UTN)	-
Other trial identifiers	IND: 152843

Notes:

Sponsors

Sponsor organisation name	argenx BV
Sponsor organisation address	Industriepark Zwijnaarde 7, Zwijnaarde (Ghent), Belgium, 9052
Public contact	argenx BV, argenx BV, 32 9310 3400, regulatory@argenx.com
Scientific contact	argenx BV, argenx BV, 32 9310 3400, 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	16 August 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 December 2021
Global end of trial reached?	Yes
Global end of trial date	13 December 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that the pharmacodynamic (PD) effect of injections of 1000 mg efgartigimod PH20 SC (efgartigimod coformulated with recombinant human
hyaluronidase PH20 for subcutaneous administration), administered once weekly for 4 administrations, is NI (noninferior) to IV infusions of efgartigimod (efgartigimod formulation for intravenous infusion) at a dose of 10 mg/kg administered once weekly for 4 administrations.

Secondary objectives:
To compare the PD effect of efgartigimod PH20 SC and efgartigimod IV over time
To evaluate the pharmacokinetics (PK) of efgartigimod PH20 SC and efgartigimod IV
To evaluate the safety, tolerability, and immunogenicity of efgartigimod PH20 SC and efgartigimod IV
To evaluate the clinical efficacy of efgartigimod PH20 SC and efgartigimod IV

Protection of trial subjects:

This study was conducted according to ICH GCP, the principles of the Declaration of Helsinki, and other applicable local ethical and legal requirements. The participant's informed consent was documented by the dated signature of the participant (and/or assent, if applicable) and the dated signature of the investigator or investigator's delegate. Evaluation of eligibility was performed at screening and confirmed at visit 1.

Background therapy:

Efgartigimod was administered concomitantly with a stable dose of the participant's current gMG therapy, which could have included AChE (acetylcholinesterase) inhibitors, steroids, and NSIDs (nonsteroidal immunosuppressive drugs). At the end of the study, eligible participants could roll over to ARGX-113-2002 to receive efgartigimod PH20 SC. This is the open label long term safety extension study.

Evidence for comparator:

Open label parallel-group, non-inferiority study

Actual start date of recruitment	05 February 2021
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	1 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 4
Country: Number of subjects enrolled	Poland: 36
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Germany: 3

Country: Number of subjects enrolled	Hungary: 5
Country: Number of subjects enrolled	Italy: 6
Country: Number of subjects enrolled	Georgia: 20
Country: Number of subjects enrolled	Japan: 8
Country: Number of subjects enrolled	Russian Federation: 4
Country: Number of subjects enrolled	United States: 19
Worldwide total number of subjects	111
EEA total number of subjects	60

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)	81
From 65 to 84 years	30
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subject’s evaluation of eligibility was performed at screening and confirmed at randomization visit 1. The overall study duration per subject was approximately 12 weeks spanning the study periods - 2 weeks for screening, 3 weeks for treatment, and 7 weeks for follow-up.

Pre-assignment

Screening details:

153 patients were screened, 111 patients were randomized, 110 patients were treated 1:1 at the day 1 visit to receive efgartigimod PH20 SC 1000 mg or efgartigimod IV 10 mg/kg once weekly for 4 administrations (4 doses on days 1, 8, 15, and 22). One participant was randomized to the efgartigimod IV arm but did not receive efgartigimod due to an AE.

Period 1

Period 1 title	Treatment period (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Efgartigimod PH20 SC

Arm description:

Efgartigimod drug product of 180 mg/mL for a fixed dose of 1000 mg for SC injection coformulated with 2000 U/mL rHuPH20 once weekly for 4 administrations (4 doses on days 1, 8, 15, and 22) - Efgartigimod PH20 SC was administered at the site by the study staff or by the participant (or their caregiver, as appropriate), under supervision of the site staff.

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

Dosage and administration details:

1000 mg once weekly for a total of 4 SC injections

Arm title	Efgartigimod IV

Arm description:

Efgartigimod drug product of 20 mg/mL for dosing of 10 mg/kg for IV infusion once weekly for 4 administrations (4 doses on days 1, 8, 15, and 22) - Efgartigimod IV was administered by a 1-hour infusion performed by the site staff.

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

Dosage and administration details:

10 mg/kg once weekly for a total of 4 IV infusions

Number of subjects in period 1[1]	Efgartigimod PH20 SC	Efgartigimod IV
Started	55	55
Completed	52	55
Not completed	3	0
Adverse event, non-fatal	2	-
Other	1	-

Notes:

[1] - 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: 111 participants were enrolled and randomized to receive the investigational medicinal product (IMP): 55 participants in the efgartigimod PH20 SC arm and 56 participants in the efgartigimod IV arm. There were 110 participants (55 in each arm) in the safety analysis set and the intent to treat (ITT) and modified intent-to-treat (mITT) analysis sets.

Baseline characteristics

Reporting groups	
Reporting group title	Efgartigimod PH20 SC
Reporting group description:	
Efgartigimod drug product of 180 mg/mL for a fixed dose of 1000 mg for SC injection coformulated with 2000 U/mL rHuPH20 once weekly for 4 administrations (4 doses on days 1, 8, 15, and 22) - Efgartigimod PH20 SC was administered at the site by the study staff or by the participant (or their caregiver, as appropriate), under supervision of the site staff.	
Reporting group title	Efgartigimod IV
Reporting group description:	
Efgartigimod drug product of 20 mg/mL for dosing of 10 mg/kg for IV infusion once weekly for 4 administrations (4 doses on days 1, 8, 15, and 22) - Efgartigimod IV was administered by a 1-hour infusion performed by the site staff.	

Reporting group values	Efgartigimod PH20 SC	Efgartigimod IV	Total
Number of subjects	55	55	110
Age categorical			
Units: Subjects			
Adults (18-64 years)	43	37	80
From 65-84 years	12	18	30
Age continuous			
Units: years			
median	53.0	59.0	
full range (min-max)	19 to 84	24 to 83	-
Gender categorical			
Units: Subjects			
Female	31	34	65
Male	24	21	45

Subject analysis sets	
Subject analysis set title	ITT analysis set
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All randomized participants who were exposed to the IMP.	
Subject analysis set title	mITT analysis set
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
All randomized participants with a value for total IgG levels at baseline and at least 1 postbaseline time point.	
Subject analysis set title	Safety analysis set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All randomized participants who were exposed to IMP.	
Subject analysis set title	PK analysis set
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
A subset of the safety analysis set with at least 1 post dose PK measurement.	

Reporting group values	ITT analysis set	mITT analysis set	Safety analysis set
Number of subjects	110	110	110
Age categorical Units: Subjects			
Adults (18-64 years)	80	80	80
From 65-84 years	30	30	30
Age continuous Units: years			
median	53.5	53.5	53.5
full range (min-max)	19 to 84	19 to 84	19 to 84
Gender categorical Units: Subjects			
Female	65	65	65
Male	45	45	45

Reporting group values	PK analysis set		
Number of subjects	98		
Age categorical Units: Subjects			
Adults (18-64 years)			
From 65-84 years			
Age continuous Units: years			
median			
full range (min-max)			
Gender categorical Units: Subjects			
Female			
Male			

End points

End points reporting groups

Reporting group title	Efgartigimod PH20 SC
Reporting group description:	
Efgartigimod drug product of 180 mg/mL for a fixed dose of 1000 mg for SC injection coformulated with 2000 U/mL rHuPH20 once weekly for 4 administrations (4 doses on days 1, 8, 15, and 22) - Efgartigimod PH20 SC was administered at the site by the study staff or by the participant (or their caregiver, as appropriate), under supervision of the site staff.	
Reporting group title	Efgartigimod IV
Reporting group description:	
Efgartigimod drug product of 20 mg/mL for dosing of 10 mg/kg for IV infusion once weekly for 4 administrations (4 doses on days 1, 8, 15, and 22) - Efgartigimod IV was administered by a 1-hour infusion performed by the site staff.	
Subject analysis set title	ITT analysis set
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All randomized participants who were exposed to the IMP.	
Subject analysis set title	mITT analysis set
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
All randomized participants with a value for total IgG levels at baseline and at least 1 postbaseline time point.	
Subject analysis set title	Safety analysis set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All randomized participants who were exposed to IMP.	
Subject analysis set title	PK analysis set
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
A subset of the safety analysis set with at least 1 post dose PK measurement.	

Primary: Percent reduction from baseline in total IgG levels at day 29 (mITT Analysis set)

End point title	Percent reduction from baseline in total IgG levels at day 29 (mITT Analysis set)
End point description:	
ANCOVA Analysis of Percent Change From Baseline in Total IgG Level at Day 29 (ie, 7 days after the fourth IV or SC administration). The results were consistent when the ANCOVA analysis was repeated for the per-protocol analysis set and for the AChR-Ab seropositive population in the mITT analysis set.	
End point type	Primary
End point timeframe:	
From week 0 to week 4	

End point values	Efgartigimod PH20 SC	Efgartigimod IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	52		
Units: percent				
least squares mean (confidence interval 95%)				
mITT	-66.4 (-68.91 to -63.86)	-62.2 (-64.67 to -59.72)		

Statistical analyses

Statistical analysis title	Statistical Analysis Plan - EFG PH20 SC vs EFG IV

Statistical analysis description:

The primary endpoint was analyzed using an ANCOVA model with treatment as a factor and total IgG levels at baseline as a covariate. The NI evaluation was based on a percent reduction from baseline in total IgG levels at day 29 (week 4) using an NI margin of 10%. Only the results for mITT analysis set are entered. The results were consistent when the ANCOVA analysis was repeated for the per-protocol analysis set and for the AChR-Ab seropositive population in the mITT analysis set.

Comparison groups	Efgartigimod PH20 SC v Efgartigimod IV
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-4.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.73
upper limit	-0.66
Variability estimate	Standard error of the mean
Dispersion value	1.782

Secondary: Percent reduction from baseline in total IgG levels over time (mITT Analysis Set)

End point title	Percent reduction from baseline in total IgG levels over time (mITT Analysis Set)

End point description:

Total IgG level percent change from baseline over time for the overall population.

End point type	Secondary

End point timeframe:

From baseline to week 10

End point values	Efgartigimod PH20 SC	Efgartigimod IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	55	55		
Units: percent				
arithmetic mean (standard error)				
Week 1	-40.1 (± 1.45)	-39.6 (± 1.51)		
Week 2	-56.9 (± 1.57)	-55.1 (± 1.85)		
Week 3	-62.2 (± 1.41)	-59 (± 2)		
Week 4	-64.7 (± 1.95)	-62.3 (± 1.24)		
Week 5	-57.4 (± 1.7)	-49.9 (± 2.17)		
Week 6	-44 (± 2.52)	-38.9 (± 2.24)		
Week 7	-31.2 (± 4.67)	-25.3 (± 2.78)		
Week 8	-8.9 (± 8.65)	-14.6 (± 3.13)		
Week 10	7.8 (± 7.78)	-3.1 (± 3.82)		

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute values, change from baseline and percent reduction from baseline in AChR-Ab levels over time in AChR- Ab positive patients (mITT Analysis Set)

End point title	Absolute values, change from baseline and percent reduction from baseline in AChR-Ab levels over time in AChR- Ab positive patients (mITT Analysis Set)

End point description:

Absolute values, change from baseline and percent reduction from baseline in AChR-Ab levels over time in AChR-Ab positive patients measured in mITT Analysis Set.
Descriptive statistics have been used for this secondary end point.

End point type	Secondary

End point timeframe:

From baseline to week 10

End point values	Efgartigimod PH20 SC	Efgartigimod IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	46		
Units: percent				
arithmetic mean (standard error)				
Week 1	-42.5 (± 1.5)	-43.7 (± 1.55)		
Week 2	-57.4 (± 1.39)	-55.1 (± 1.52)		
Week 3	-61.8 (± 1.6)	-59.2 (± 1.66)		
Week 4	-62.2 (± 1.76)	-59.6 (± 1.74)		
Week 5	-55.3 (± 1.52)	-47.2 (± 2.98)		
Week 6	-40.4 (± 3.13)	-29.9 (± 4.61)		
Week 7	-26.7 (± 4.76)	-15.8 (± 5.63)		
Week 8	-14.5 (± 7.82)	-7.1 (± 6.02)		
Week 10	13.5 (± 23.16)	10.3 (± 7.85)		

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute values, change from baseline, and percent reduction from baseline in IgG subtype levels over time (mITT Analysis Set)

End point title	Absolute values, change from baseline, and percent reduction from baseline in IgG subtype levels over time (mITT Analysis Set)

End point description:

Median (IQR) Percent Change From Baseline and AUEC for the Percent Change From Baseline for the IgG Subtypes (IgG1, IgG2, IgG3, and IgG4) in the Overall Population.
The highest number of patients among all weeks for the analysis is chosen for each arm.
Descriptive statistics have been used for this secondary end point.

End point type	Secondary

End point timeframe:

Baseline to week 10

End point values	Efgartigimod PH20 SC	Efgartigimod IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	55	55		
Units: percent x days				
median (inter-quartile range (Q1-Q3))				
Percent change from baseline at week 4 IgG1	-71 (-79.3 to -56.6)	-68.4 (-73 to -61.5)		
Percent change from baseline at week 4 IgG2	-65.6 (-72.2 to -58.1)	-64.5 (-73 to -57.4)		
Percent change from baseline at week 4 IgG3	-69.6 (-78.3 to -58.4)	-64.7 (-76.9 to -59.5)		
Percent change from baseline at week 4 IgG4	-56.4 (-64.4 to -37.2)	-55.5 (-64.2 to -42.1)		
AUEC percent change from baseline to week 10 IgG1	-3054.1 (-3679.2 to -1933.1)	-2935.2 (-3195.0 to -2422.0)		
AUEC percent change from baseline to week 10 IgG2	-2709.9 (-3551.5 to -1932.2)	-2796.3 (-3187.9 to -2076.3)		
AUEC percent change from baseline to week 10 IgG3	-2732.9 (-3437.9 to -1602.7)	-2566.5 (-3567.4 to -1973.9)		
AUEC percent change from baseline to week 10 IgG4	-2060.5 (-2815.7 to -874.3)	-1979.4 (-2730.6 to -1160.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: AUEC of the Percent Change From Baseline in Total IgG Level (mITT Analysis Set)

End point title	AUEC of the Percent Change From Baseline in Total IgG Level (mITT Analysis Set)

End point description:

AUEC of the percent reduction from baseline total IgG per dosing interval (days 1-8, days 8-15, days 15-22, and days 22-29), days 1-29, days 1-57 and over the entire study (days 1-71).
The highest number of patients among all weeks for the analysis is chosen for each arm.
Descriptive statistics have been used for this secondary end point.

End point type	Secondary

End point timeframe:

From baseline to week 10

End point values	Efgartigimod PH20 SC	Efgartigimod IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	55	55		
Units: percent days				
arithmetic mean (standard error)				
Days 1-8 (baseline-week 1)	-138.9 (± 5.48)	-139.1 (± 5.67)		
Days 8-15 (week 1-week 2)	-341.9 (± 9.9)	-328.3 (± 10.98)		
Days 15-22 (week 2-week 3)	-416.0 (± 12.06)	-399.8 (± 14.46)		
Days 22-29 (week 3-week 4)	-447.3 (± 9.24)	-427.0 (± 9.76)		
Days 1-29 (baseline-week 4)	-1332.5 (± 30.78)	-1311.6 (± 26.35)		
Days 1-57 (baseline-week 8)	-2515.9 (± 96.98)	-2387.6 (± 77.61)		
Days 1-71 (baseline-week 10)	-2562.9 (± 171.86)	-2500.3 (± 116.10)		

Statistical analyses

No statistical analyses for this end point

Secondary: Efgartigimod IV and PH20 SC serum pharmacokinetic parameter Ctrough

End point title	Efgartigimod IV and PH20 SC serum pharmacokinetic parameter Ctrough

End point description:

Evaluation of observed predose concentration (Ctrough) (after all doses for the IV and SC treatment arms). The analysis will present data from Week 1 to Week 4.
Descriptive statistics have been used for this secondary end point.

End point type	Secondary

End point timeframe:

From Week 1 to Week 4.

End point values	Efgartigimod PH20 SC	Efgartigimod IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	51		
Units: µg/mL				
arithmetic mean (standard deviation)				
Ctrough week 1	18.3 (± 8.05)	16.4 (± 33.0)		
Ctrough week 2	21.4 (± 8.36)	14.0 (± 6.92)		
Ctrough week 3	22.5 (± 9.61)	15.2 (± 8.05)		
Ctrough week 4	22.0 (± 8.12)	14.9 (± 6.43)		

Statistical analyses

No statistical analyses for this end point

Secondary: Efgartigimod IV serum pharmacokinetic parameter Cmax

End point title	Efgartigimod IV serum pharmacokinetic parameter Cmax[1]

End point description:

Evaluation of maximum observed concentration (Cmax) (after all doses for the IV treatment arm). The analysis will present data from Baseline to Week 3.
Descriptive statistics have been used for this secondary end point.

End point type	Secondary

End point timeframe:

From Baseline to week 3

Notes:

[1] - 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: Descriptive statistics have been performed for this secondary endpoint.

End point values	Efgartigimod IV			
Subject group type	Reporting group			
Number of subjects analysed	54			
Units: µg/mL				
arithmetic mean (standard deviation)				
Cmax Baseline	199 (± 62.8)			
Cmax week 1	215 (± 63.0)			
Cmax week 2	211 (± 75.0)			
Cmax week 3	206 (± 59.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence and prevalence of ADA against Efgartigimod (Safety Analysis Set)

End point title	Incidence and prevalence of ADA against Efgartigimod (Safety Analysis Set)

End point description:

Classification, incidence, and prevalence of antidrug antibodies (ADA) against Efgartigimod in the overall population.
Descriptive statistics have been used for this secondary end point.

End point type	Secondary

End point timeframe:

From baseline to week 10

End point values	Efgartigimod PH20 SC	Efgartigimod IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	55	55		
Units: percent				
number (not applicable)				
Baseline ADA positive sample	12.7	9.1		
Baseline ADA negative sample	87.3	90.9		
ADA+ treatment boosted (prs classif)	1.8	1.8		
ADA+ treatment induced (prs classif)	32.7	18.2		
ADA- treatment unaffected (prs classif)	10.9	7.3		
ADA- (prs classif)	54.5	72.7		
ADA incidence	34.5	20.0		
ADA prevalence	45.5	27.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence and prevalence of antibodies against rHuPH20 in the SC treatment arm (Safety Analysis Set)

End point title	Incidence and prevalence of antibodies against rHuPH20 in the SC treatment arm (Safety Analysis Set)[2]

End point description:

Participant classification, incidence, and prevalence of antibodies against rHuPH20 in the Efgartigimod PH20 SC Arm.
Descriptive statistics have been used for this secondary end point.

End point type	Secondary

End point timeframe:

From baseline to week 10

Notes:

[2] - 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 endpoint is not applicable to the EFG IV arm.

End point values	Efgartigimod PH20 SC			
Subject group type	Reporting group			
Number of subjects analysed	55			
Units: percent				
number (not applicable)				
Baseline rHuPH20 Ab - sample	89.1			
Baseline rHuPH20 Ab + sample	10.9			
rHuPH20 Ab - (prs classif)	85.5			
Treatment-unaffected rHuPH20 Ab - (prs classif)	9.1			
Treatment-induced rHuPH20 Ab + (prs classif)	3.6			
Treatment-boosted rHuPH20 Ab + (prs classif)	1.8			
rHuPH20 antibody incidence	5.5			
rHuPH20 antibody prevalence	14.5			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence and severity of AEs and SAEs (Safety Analysis Set)

End point title	Incidence and severity of AEs and SAEs (Safety Analysis Set)

End point description:

Evaluation of incidence and severity of treatment-emergent adverse events (TEAEs) and incidence of serious AEs (SAEs).
Descriptive statistics have been used for this secondary end point.

End point type	Secondary

End point timeframe:

From baseline to week 10

End point values	Efgartigimod PH20 SC	Efgartigimod IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	55	55		
Units: percent				
number (not applicable)				
≥1 AE	67.3	50.9		
≥1 SAE	14.5	7.3		
≥1 Grade 3 or higher AE	16.4	7.3		
≥1 AESI	18.2	16.4		
≥1 Injection site reaction (localized)	38.2	1.8		
≥1 Infusion- or injection-related reaction	25.5	3.6		
≥1 Fatal AE	0	0		
≥1 Treatment-related AE according to PI	43.6	21.8		
≥1 Procedure-related AE according to PI	25.5	3.6		

≥1 Treatment-related SAE	0	0		
≥1 AE for which the IMP was interrupted	1.8	0		
≥1 AE for which the IMP was discontinued	3.6	0		

Statistical analyses

No statistical analyses for this end point

Secondary: MG-ADL Responders (ITT Analysis Set)

End point title	MG-ADL Responders (ITT Analysis Set)

End point description:

Evaluation of number and percentage of Myasthenia Gravis Activities of Daily Living (MG-ADL) responders in the overall population (ITT Analysis Set).
Descriptive statistics have been used for this secondary end point.

End point type	Secondary

End point timeframe:

From baseline to week 10

End point values	Efgartigimod PH20 SC	Efgartigimod IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	55	55		
Units: percent				
number (not applicable)				
Overall	69.1	69.1		

Statistical analyses

No statistical analyses for this end point

Secondary: QMG Responders (ITT Analysis Set)

End point title	QMG Responders (ITT Analysis Set)

End point description:

Evaluation of number and percentage of Quantitative Myasthenia Gravis (QMG) responders in the overall population (ITT Analysis Set).
Descriptive statistics have been used for this secondary end point.
One subject in the EFG IV arm had no post-baseline QMG assessment and thus was excluded from the denominator.

End point type	Secondary

End point timeframe:

From baseline to week 10

End point values	Efgartigimod PH20 SC	Efgartigimod IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	55	54		
Units: percent				
number (not applicable)				
Overall	65.5	51.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in MG-ADL total score over time (ITT Analysis Set)

End point title	Change from baseline in MG-ADL total score over time (ITT Analysis Set)

End point description:

Evaluation of MG-ADL Total Score Change from baseline over time for the overall population (ITT Analysis Set).
Descriptive statistics have been used for this secondary end point.

End point type	Secondary

End point timeframe:

From baseline to week 10

End point values	Efgartigimod PH20 SC	Efgartigimod IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	55	55		
Units: Total score				
arithmetic mean (standard error)				
Week 1	-2.2 (± 0.33)	-2.0 (± 0.30)		
Week 2	-3.6 (± 0.40)	-3.2 (± 0.35)		
Week 3	-4.7 (± 0.36)	-4.3 (± 0.33)		
Week 4	-5.1 (± 0.38)	-4.7 (± 0.37)		
Week 5	-4.9 (± 0.36)	-4.3 (± 0.41)		
Week 6	-4.2 (± 0.35)	-3.7 (± 0.44)		
Week 7	-3.9 (± 0.35)	-3.6 (± 0.44)		
Week 8	-3.3 (± 0.34)	-2.9 (± 0.4)		
Week 10	-2.2 (± 0.44)	-2.1 (± 0.43)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in QMG score over time (ITT Analysis Set)

End point title	Change from baseline in QMG score over time (ITT Analysis Set)

End point description:

Evaluation of QMG Total Score change from baseline over time for the overall population (ITT Analysis Set).
Descriptive statistics have been used for this secondary end point.

End point type	Secondary

End point timeframe:

From baseline to week 10

End point values	Efgartigimod PH20 SC	Efgartigimod IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	55	55		
Units: Total score				
arithmetic mean (standard error)				
Week 1	-3 (± 0.48)	-2 (± 0.44)		
Week 2	-4.3 (± 0.58)	-3.4 (± 0.44)		
Week 3	-5.7 (± 0.61)	-4.5 (± 0.5)		
Week 4	-6.1 (± 0.62)	-5.2 (± 0.52)		
Week 5	-5.9 (± 0.61)	-5 (± 0.57)		
Week 6	-5.2 (± 0.6)	-5 (± 0.61)		
Week 7	-3.9 (± 0.61)	-4.1 (± 0.55)		
Week 8	-3.7 (± 0.66)	-3.3 (± 0.53)		
Week 10	-2.3 (± 0.6)	-2.8 (± 0.53)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Throughout the treatment period.

Adverse event reporting additional description:

Both efgartigimod PH20 SC and IV were well tolerated and had a favorable safety profile in participants with gMG, with most AE being mild to moderate in severity. No deaths or grade 4 AE occurred during the study period. 11.8% of patients had Grade 3 AE reported. The frequency of AE leading to treatment interruption and discontinuation was low.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Efgartigimod PH20 SC

Reporting group description:

Efgartigimod drug product of 180 mg/mL for a fixed dose of 1000 mg for SC injection coformulated with 2000 U/mL rHuPH20 once weekly for 4 administrations (4 doses on days 1, 8, 15, and 22) - Efgartigimod PH20 SC was administered at the site by the study staff or by the participant (or their caregiver, as appropriate), under supervision of the site staff.

Reporting group title	Efgartigimod IV

Reporting group description:

Efgartigimod drug product of 20 mg/mL for dosing of 10 mg/kg for IV infusion once weekly for 4 administrations (4 doses on days 1, 8, 15, and 22) - Efgartigimod IV was administered by a 1-hour infusion performed by the site staff.

Serious adverse events	Efgartigimod PH20 SC	Efgartigimod IV	
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 55 (14.55%)	4 / 55 (7.27%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Humerus fracture			
subjects affected / exposed	1 / 55 (1.82%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure congestive			
subjects affected / exposed	0 / 55 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			

Myasthenia gravis			
subjects affected / exposed	5 / 55 (9.09%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Optic neuritis			
subjects affected / exposed	1 / 55 (1.82%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 55 (1.82%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 55 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Testicular cyst			
subjects affected / exposed	0 / 55 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 55 (1.82%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 55 (1.82%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Efgartigimod PH20 SC	Efgartigimod IV	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	37 / 55 (67.27%)	23 / 55 (41.82%)	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 55 (0.00%)	3 / 55 (5.45%)	
occurrences (all)	0	3	
Fall			
subjects affected / exposed	1 / 55 (1.82%)	3 / 55 (5.45%)	
occurrences (all)	1	3	
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 55 (12.73%)	7 / 55 (12.73%)	
occurrences (all)	10	11	
Myasthenia gravis			
subjects affected / exposed	6 / 55 (10.91%)	1 / 55 (1.82%)	
occurrences (all)	8	2	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 55 (3.64%)	3 / 55 (5.45%)	
occurrences (all)	2	3	
Injection site bruising			
subjects affected / exposed	4 / 55 (7.27%)	0 / 55 (0.00%)	
occurrences (all)	4	0	
Injection site erythema			
subjects affected / exposed	7 / 55 (12.73%)	0 / 55 (0.00%)	
occurrences (all)	7	0	
Injection site pain			
subjects affected / exposed	3 / 55 (5.45%)	0 / 55 (0.00%)	
occurrences (all)	3	0	
Injection site pruritus			
subjects affected / exposed	5 / 55 (9.09%)	0 / 55 (0.00%)	
occurrences (all)	5	0	

Injection site rash subjects affected / exposed occurrences (all)	8 / 55 (14.55%) 14	0 / 55 (0.00%) 0	
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	1 / 55 (1.82%) 5	3 / 55 (5.45%) 3	
Infections and infestations Urinary tract infection subjects affected / exposed occurrences (all)	1 / 55 (1.82%) 1	3 / 55 (5.45%) 3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 July 2021	• Increased sample size from 76 to 110 to quantify the clinical safety and efficacy profile of the efgartigimod PH20 SC formulation • Defined IVIg and immunoglobulin administered SC as rescue medication • Removed "suspected transmission of any infectious agent" as an SAE • Updated the potential risk to the teratogenicity/fetotoxicity mitigation strategy

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported