Clinical trial results:
A Phase 3, Multicenter, Randomized, Double-Blinded, Placebo-Controlled Trial to Evaluate the Efficacy and the Safety of Efgartigimod (ARGX-113) PH20 Subcutaneous in Adult Patients With Primary Immune Thrombocytopenia

Summary

EudraCT number	2020-004032-21
Trial protocol	IE PT DE BG NO DK GR IT FR RO ES
Global end of trial date	09 October 2023

Results information

Result version number	v1 (current)
This version publication date	24 October 2024
First version publication date	24 October 2024

Trial information

Trial identification

Sponsor protocol code	ARGX-113-2004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04687072
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 manager, argenx BV, regulatory@argenx.com
Scientific contact	Regulatory manager, argenx BV, 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	31 July 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 October 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of efgartigimod PH20 SC compared to placebo PH20 SC in achieving a sustained platelet count response in participants with chronic primary ITP, with a sustained platelet count response defined as platelet counts of ≥50×10^9/L for at least 4 of the 6 visits between week 19 and week 24 of the trial.

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 International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Good Clinical Practice guidelines, and applicable laws and regulations. The sponsor appointed an independent Data and Safety Monitoring Board (DSMB) consisting of clinical experts and a statistician not involved in the study management. The DSMB reviewed all unblinded safety and immunoglobulin (Ig)G data as specified in the DSMB charter.

Background therapy:

Participants were permitted to continue ≥1 protocol-specified concurrent ITP therapy if at a stable dosage and frequency for ≥4 weeks before randomization.

Evidence for comparator: -

Actual start date of recruitment	16 December 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	Australia: 7
Country: Number of subjects enrolled	Argentina: 4
Country: Number of subjects enrolled	Bulgaria: 4
Country: Number of subjects enrolled	Chile: 3
Country: Number of subjects enrolled	China: 30
Country: Number of subjects enrolled	Georgia: 11
Country: Number of subjects enrolled	Greece: 6
Country: Number of subjects enrolled	Ireland: 1
Country: Number of subjects enrolled	Italy: 6
Country: Number of subjects enrolled	Japan: 9
Country: Number of subjects enrolled	Jordan: 20
Country: Number of subjects enrolled	Korea, Republic of: 6
Country: Number of subjects enrolled	Mexico: 1

Country: Number of subjects enrolled	New Zealand: 1
Country: Number of subjects enrolled	Norway: 2
Country: Number of subjects enrolled	Poland: 6
Country: Number of subjects enrolled	Portugal: 3
Country: Number of subjects enrolled	Romania: 9
Country: Number of subjects enrolled	Russian Federation: 7
Country: Number of subjects enrolled	South Africa: 6
Country: Number of subjects enrolled	Thailand: 14
Country: Number of subjects enrolled	Tunisia: 13
Country: Number of subjects enrolled	Türkiye: 23
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	United States: 9
Worldwide total number of subjects	207
EEA total number of subjects	37

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)	169
From 65 to 84 years	38
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A regionally diverse participant population was enrolled (including but not limited to North America, East Asia, Europe, and the rest of world [ROW]).

Pre-assignment

Screening details:

A total of 207 participants were randomized to IMP: 137 participants in the efgartigimod PH20 subcutaneous (SC) arm and 70 participants in the placebo PH20 SC arm.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Efgartigimod PH20 SC

Arm description:

Participants receiving efgartigimod PH20 SC treatment.

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

Dosage and administration details:

Subcutaneous injection with efgartigimod PH20 SC.

Arm title	Placebo PH20 SC

Arm description:

Participants receiving placebo PH20 SC treatment.

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

Dosage and administration details:

Subcutaneous injection with placebo PH20 SC.

Number of subjects in period 1	Efgartigimod PH20 SC	Placebo PH20 SC
Started	137	70
Completed	113	62
Not completed	24	8
Adverse event, serious fatal	1	-
Physician decision	1	-
Adverse event, non-fatal	2	-
Requires prohibited medication	2	-
Pregnancy	1	-
Miscellaneous	4	1
Withdrawal of consent	11	6
Lack of efficacy	2	1

Baseline characteristics

Reporting groups	
Reporting group title	Efgartigimod PH20 SC
Reporting group description:	
Participants receiving efgartigimod PH20 SC treatment.	
Reporting group title	Placebo PH20 SC
Reporting group description:	
Participants receiving placebo PH20 SC treatment.	

Reporting group values	Efgartigimod PH20 SC	Placebo PH20 SC	Total
Number of subjects	137	70	207
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	47.3	50.0	
standard deviation	± 17.22	± 15.29	-
Gender categorical Units: Subjects			
Female	88	43	131
Male	49	27	76
Ethnicity Units: Subjects			
Hispanic or Latino	8	2	10
Not Hispanic or Latino	129	68	197
Unknown or Not Reported	0	0	0
Race Units: Subjects			
Asian	44	18	62
Black or African American	4	2	6
White	88	49	137
Other	1	1	2

End points

End points reporting groups

Reporting group title	Efgartigimod PH20 SC
Reporting group description:	
Participants receiving efgartigimod PH20 SC treatment.	
Reporting group title	Placebo PH20 SC
Reporting group description:	
Participants receiving placebo PH20 SC treatment.	

Primary: Percentage of Participants With Chronic Immune Thrombocytopenia (ITP) With a Sustained Platelet Count Response Between Weeks 19 and 24

End point title	Percentage of Participants With Chronic Immune Thrombocytopenia (ITP) With a Sustained Platelet Count Response Between Weeks 19 and 24

End point description:

A participant was considered a responder for this endpoint (i.e., had a sustained platelet count response) if the participant had platelet counts of ≥50 × 10^9/L for ≥4 of the 6 analysis visits between Weeks 19 and 24.

Full Analysis Set (FAS)-Chronic: Participants from the FAS (all randomized participants) including only participants with chronic ITP.

End point type	Primary

End point timeframe:

Up to 6 weeks (between Weeks 19 and 24)

End point values	Efgartigimod PH20 SC	Placebo PH20 SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	124	68		
Units: percentage of participants				
number (not applicable)	13.7	16.2		

Statistical analyses

Statistical analysis title	Efgartigimod PH20 SC versus (vs.) Placebo PH20 SC

Statistical analysis description:

The adjusted difference in percentages and 95% confidence interval (CI) (Klingenberg approach) were presented.

Comparison groups	Efgartigimod PH20 SC v Placebo PH20 SC

Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5081 [1]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentage
Point estimate	-3.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.7
upper limit	7

Notes:

[1] - The p-value was calculated using the Cochran-Mantel-Haenszel test used in the hierarchical testing procedure.

Secondary: Extent of Disease Control Over the 24-Week Treatment Period in the Chronic ITP Population

End point title	Extent of Disease Control Over the 24-Week Treatment Period in the Chronic ITP Population

End point description:

Extent of disease control was defined as the number of cumulative weeks over the planned 24-week treatment period with platelet counts of ≥50×10^9/L in the chronic ITP population.

FAS-Chronic: Participants from the FAS (all randomized participants) including only participants with chronic ITP.

End point type	Secondary

End point timeframe:

Up to 24 weeks

End point values	Efgartigimod PH20 SC	Placebo PH20 SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	124	68		
Units: weeks				
median (full range (min-max))	0.5 (0 to 24)	0.0 (0 to 23)		

Statistical analyses

Statistical analysis title	Efgartigimod PH20 SC vs. Placebo PH20 SC

Statistical analysis description:

The Hodges-Lehmann estimator of the treatment difference and 95% CI are presented.

Comparison groups	Efgartigimod PH20 SC v Placebo PH20 SC

Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4925 [2]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Location shift
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0

Notes:

[2] - The p-value was calculated using the stratified Mann-Whitney test used in the hierarchical testing procedure.

Secondary: Percentage of Participants in the Overall Population (Chronic and Persistent ITP) With a Sustained Platelet Count Response Between Weeks 19 and 24

End point title	Percentage of Participants in the Overall Population (Chronic and Persistent ITP) With a Sustained Platelet Count Response Between Weeks 19 and 24

End point description:

A participant was considered a responder for this endpoint (i.e., had a sustained platelet count response) if the participant had platelet counts of ≥50 × 10^9/L for ≥4 of the 6 analysis visits between Weeks 19 and 24.

FAS: All randomized participants.

End point type	Secondary

End point timeframe:

Up to 6 weeks (between Weeks 19 and 24)

End point values	Efgartigimod PH20 SC	Placebo PH20 SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	137	70		
Units: percentage of participants				
number (not applicable)	16.1	15.7		

Statistical analyses

Statistical analysis title	Efgartigimod PH20 SC vs. Placebo PH20 SC

Statistical analysis description:

The adjusted difference in percentages and 95% CI (Klingenberg approach) were presented.

Comparison groups	Efgartigimod PH20 SC v Placebo PH20 SC

Number of subjects included in analysis	207
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9314 [3]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentage
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.7
upper limit	10

Notes:

[3] - The p-value was calculated using the Cochran-Mantel-Haenszel test used in the hierarchical testing procedure.

Secondary: Percentage of Participants in the Overall Population With Sustained Platelet Count Response Between Weeks 17 and 24

End point title	Percentage of Participants in the Overall Population With Sustained Platelet Count Response Between Weeks 17 and 24

End point description:

A participant was considered a responder for this endpoint (i.e., had a sustained platelet count response) if the participant had platelet counts of ≥50 × 10^9/L for ≥6 of the 8 analysis visits between weeks 17 and 24.

FAS: All randomized participants.

End point type	Secondary

End point timeframe:

Up to 8 weeks (between Weeks 17 and 24)

End point values	Efgartigimod PH20 SC	Placebo PH20 SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	137	70		
Units: percentage of participants				
number (not applicable)	12.4	14.3		

Statistical analyses

Statistical analysis title	Efgartigimod PH20 SC vs. Placebo PH20 SC

Statistical analysis description:

The adjusted difference in percentage and 95% CI (Klingenberg approach) are presented.

Comparison groups	Efgartigimod PH20 SC v Placebo PH20 SC

Number of subjects included in analysis	207
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7379 [4]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentage
Point estimate	-1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.4
upper limit	8.2

Notes:

[4] - The Cochran-Mantel-Haenszel test p-value was used in the hierarchical testing procedure.

Secondary: Percentage of Participants in the Overall Population Achieving Overall Platelet Count Response at Any Time During the 24-week Treatment Period

End point title	Percentage of Participants in the Overall Population Achieving Overall Platelet Count Response at Any Time During the 24-week Treatment Period

End point description:

A participant was considered a responder for this endpoint (i.e., had an overall platelet count response) if the participant had platelet counts of ≥50 × 10^9/L for ≥4 analysis visits at any time during the 24-week treatment period.

FAS: All randomized participants.

End point type	Secondary

End point timeframe:

Up to 24 weeks

End point values	Efgartigimod PH20 SC	Placebo PH20 SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	137	70		
Units: percentage of participants				
number (not applicable)	29.9	25.7		

Statistical analyses

Statistical analysis title	Efgartigimod PH20 SC vs. Placebo PH20 SC

Statistical analysis description:

The 95% Agresti-Min CIs are presented.

Comparison groups	Efgartigimod PH20 SC v Placebo PH20 SC

Number of subjects included in analysis	207
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in percentage
Point estimate	4.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.3
upper limit	16.8

Secondary: Extent of Disease Control Until Week 12 in the Overall Population

End point title	Extent of Disease Control Until Week 12 in the Overall Population

End point description:

Extent of disease control was defined as the number of cumulative weeks until Week 12 with platelet counts of ≥50×10^9/L in the overall population.

End point type	Secondary

End point timeframe:

Up to 12 weeks

End point values	Efgartigimod PH20 SC	Placebo PH20 SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	137	70		
Units: weeks				
median (full range (min-max))	0.00 (0.00 to 12.00)	0.00 (0.00 to 11.00)		

Statistical analyses

Statistical analysis title	Efgartigimod PH20 SC vs. Placebo PH20 SC

Statistical analysis description:

The Hodges-Lehmann estimator of the treatment difference and 95% CI are presented.

Comparison groups	Efgartigimod PH20 SC v Placebo PH20 SC
Number of subjects included in analysis	207
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.726 [5]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Location shift
Point estimate	0

Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0

Notes:

[5] - The p-value was calculated using the stratified Mann-Whitney test.

Secondary: Percentage of Participants in the Overall Population Achieving Overall Platelet Count Response at Any Time Until Week 12

End point title	Percentage of Participants in the Overall Population Achieving Overall Platelet Count Response at Any Time Until Week 12

End point description:

A participant was considered a responder for this endpoint (i.e., had an overall platelet count response) if the participant had platelet counts of ≥50 × 10^9/L for ≥4 analysis visits at any time until Week 12.

FAS: All randomized participants.

End point type	Secondary

End point timeframe:

Up to 12 weeks

End point values	Efgartigimod PH20 SC	Placebo PH20 SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	137	70		
Units: percentage of participants				
number (not applicable)	18.2	15.7		

Statistical analyses

Statistical analysis title	Efgartigimod PH20 SC vs. Placebo PH20 SC

Statistical analysis description:

The 95% Agresti-Min CIs are presented.

Comparison groups	Efgartigimod PH20 SC v Placebo PH20 SC
Number of subjects included in analysis	207
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in percentage
Point estimate	2.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.6
upper limit	13

Secondary: Mean Change From Baseline in Platelet Count at Each Visit in the Overall Population

End point title	Mean Change From Baseline in Platelet Count at Each Visit in the Overall Population

End point description:

Change from Baseline at time point t = value at time point t - Baseline value. Baseline was defined as the last available value prior to first administration of the investigational medicinal product (IMP). Values of "99999" indicate standard deviation could not be calculated as a single participant was analyzed.

FAS: All randomized participants with available data.

End point type	Secondary

End point timeframe:

Baseline and Weeks 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, Safety and Efficacy Follow-up Visit 1 (SEFU1) (up to Week 29), and SEFU2 (up to Week 33)

End point values	Efgartigimod PH20 SC	Placebo PH20 SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	69		
Units: platelets x10^9/L				
arithmetic mean (standard deviation)				
Week 1 (N = 136, 69)	13.84 (± 41.150)	8.82 (± 34.355)		
Week 2 (N = 135, 68)	16.62 (± 49.408)	23.54 (± 85.005)		
Week 3 (N = 133, 69)	17.07 (± 39.855)	19.22 (± 71.947)		
Week 4 (N = 132, 68)	12.39 (± 37.886)	9.31 (± 26.813)		
Week 5 (N = 129, 67)	18.14 (± 54.335)	12.24 (± 30.059)		
Week 6 (N = 127, 65)	34.61 (± 112.204)	16.35 (± 40.891)		
Week 7 (N = 126, 67)	28.25 (± 107.932)	13.46 (± 41.876)		
Week 8 (N = 126, 66)	21.77 (± 52.308)	16.57 (± 42.508)		
Week 9 (N = 123, 64)	19.90 (± 54.542)	20.42 (± 53.488)		
Week 10 (N = 119, 66)	21.73 (± 47.685)	15.42 (± 33.119)		
Week 11 (N = 122, 63)	20.13 (± 42.193)	14.54 (± 25.588)		
Week 12 (N = 120, 62)	21.02 (± 43.882)	22.28 (± 56.173)		
Week 13 (N = 118, 63)	22.29 (± 44.654)	15.51 (± 37.651)		
Week 14 (N = 119, 65)	23.60 (± 47.521)	24.04 (± 55.678)		
Week 15 (N = 116, 59)	21.30 (± 45.776)	28.05 (± 67.897)		
Week 16 (N = 113, 58)	30.32 (± 71.553)	23.09 (± 46.154)		
Week 17 (N = 112, 58)	25.12 (± 54.747)	30.05 (± 56.581)		
Week 18 (N = 115, 60)	28.54 (± 53.115)	31.64 (± 57.309)		

Week 19 (N = 114, 62)	33.86 (± 59.323)	37.26 (± 68.832)		
Week 20 (N = 107, 61)	30.87 (± 55.342)	25.85 (± 48.409)		
Week 21 (N = 108, 59)	30.04 (± 61.438)	26.23 (± 50.323)		
Week 22 (N = 110, 61)	33.26 (± 61.558)	29.23 (± 55.175)		
Week 23 (N = 111, 60)	29.51 (± 53.437)	24.89 (± 41.103)		
Week 24 (N = 113, 59)	25.51 (± 52.203)	24.91 (± 42.972)		
SEFU1 (N = 9, 1)	40.44 (± 64.860)	48.70 (± 99999)		
SEFU2 (N = 10, 2)	30.00 (± 35.011)	56.25 (± 85.206)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Platelet Count Response in the Overall Population

End point title	Time to Platelet Count Response in the Overall Population

End point description:

Time to platelet count response, defined as the time to have 2 consecutive platelet counts of ≥50 × 10^9/L via Kaplan-Meier estimates. Values of "999999" indicate the median and/or confidence intervals were not calculable due to insufficient event data.

FAS: All randomized participants. Participants with no occurrence of platelet count response, early discontinuation of treatment, or dose and/or frequency of concurrent ITP therapy increased or a new ITP therapy were censored. If multiple censoring conditions apply, the earliest censoring date is considered.

End point type	Secondary

End point timeframe:

Up to 24 weeks

End point values	Efgartigimod PH20 SC	Placebo PH20 SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	137[6]	70[7]		
Units: days				
median (confidence interval 95%)	999999 (155.0 to 999999)	999999 (999999 to 999999)		

Notes:

[6] - Median and upper confidence interval were not calculable due to fewer than 50% events.

[7] - Median and confidence intervals were not calculable due to insufficient event data.

Statistical analyses

No statistical analyses for this end point

Secondary: Extent of Disease Control Over the 24-Week Treatment Period in the

Overall Population

End point title	Extent of Disease Control Over the 24-Week Treatment Period in the Overall Population

End point description:

Extent of disease control was defined as the number of cumulative weeks over the planned 24-week treatment period with platelet counts of ≥30×10^9/L with at least ≥20×10^9/L above Baseline in the overall population.

FAS: All randomized participants.

End point type	Secondary

End point timeframe:

Up to 24 weeks

End point values	Efgartigimod PH20 SC	Placebo PH20 SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	137	70		
Units: weeks				
median (full range (min-max))	1.0 (0 to 24)	1.0 (0 to 24)		

Statistical analyses

Statistical analysis title	Efgartigimod PH20 SC vs. Placebo PH20 SC

Statistical analysis description:

The Hodges-Lehmann estimator of the treatment difference and 95% CI are presented.

Comparison groups	Efgartigimod PH20 SC v Placebo PH20 SC
Number of subjects included in analysis	207
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2929 [8]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Location shift
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	1

Notes:

[8] - The p-value was calculated using the stratified Mann-Whitney test.

Secondary: Extent of Disease Control Over the 24-Week Treatment Period in the Overall Population for Participants With Baseline Platelet Count of <15×10^9/L

End point title	Extent of Disease Control Over the 24-Week Treatment Period in the Overall Population for Participants With Baseline Platelet Count of <15×10^9/L

End point description:

Extent of disease control was defined as the number of cumulative weeks over the planned 24-week

treatment period with platelet counts of ≥30×10^9/L with at least ≥20×10^9/L above Baseline in the overall population.

FAS: All randomized participants with Baseline Platelet Count of <15×10^9/L.

End point type	Secondary

End point timeframe:

Up to 24 weeks

End point values	Efgartigimod PH20 SC	Placebo PH20 SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	35		
Units: weeks				
median (full range (min-max))	1.0 (0.0 to 23)	0.0 (0.0 to 24)		

Statistical analyses

Statistical analysis title	Efgartigimod PH20 SC vs. Placebo PH20 SC

Statistical analysis description:

The Hodges-Lehmann estimator of the treatment difference and 95% CI are presented.

Comparison groups	Efgartigimod PH20 SC v Placebo PH20 SC
Number of subjects included in analysis	94
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1475 [9]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Location shift
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	1

Notes:

[9] - The p-value was calculated using the stratified Mann-Whitney test.

Secondary: Number of the World Health Organization (WHO)-Classified Bleeding Events (Grade ≥1) in the Overall Population

End point title	Number of the World Health Organization (WHO)-Classified Bleeding Events (Grade ≥1) in the Overall Population

End point description:

Assessed using the WHO bleeding scale. The WHO bleeding scale is a five-point scale where Grade 0 = no bleeding; Grade 1 = petechial bleeding; Grade 2 = mild blood loss; Grade 3 = gross blood loss (requires transfusion); and Grade 4 = debilitating blood loss, associated with fatality.

FAS: All randomized participants.

End point type	Secondary

End point timeframe:

Up to 24 weeks

End point values	Efgartigimod PH20 SC	Placebo PH20 SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	137	70		
Units: bleeding events				
median (full range (min-max))	9.0 (0.00 to 24)	10.0 (0.00 to 24)		

Statistical analyses

Statistical analysis title	WHO Classified Bleeding Event Grade ≥1

Statistical analysis description:

The Hodges-Lehmann estimator of the treatment difference and 95% CI are presented.

Comparison groups	Efgartigimod PH20 SC v Placebo PH20 SC
Number of subjects included in analysis	207
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7677 [10]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Location shift
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	2

Notes:

[10] - The p-value was calculated using the stratified Mann-Whitney test used in the hierarchical testing procedure.

Secondary: Percentage of Participants With a Platelet Count International Working Group (IWG) Response

End point title	Percentage of Participants With a Platelet Count International Working Group (IWG) Response

End point description:

IWG complete response was defined as platelet counts of ≥100 × 10^9/L and the absence of bleeding events (WHO Grading = 0 [no bleeding]) for at least 2 separate, consecutive analysis visits at least 7 days apart.

IWG response was defined as platelet counts of ≥30 × 10^9/L and a 2-fold increase of platelet count from Baseline and the absence of bleeding events (WHO grading = 0) for at least 2 separate, consecutive analysis visits that were at least 7 days apart.

Initial response was defined as platelet counts of ≥30 × 10^9/L and a 2-fold increase from the Baseline platelet count at analysis visit 5.

FAS: All randomized participants.

End point type	Secondary

End point timeframe:

Up to 24 weeks

End point values	Efgartigimod PH20 SC	Placebo PH20 SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	137	70		
Units: percentage of participants				
number (not applicable)				
IWG Complete Response	10.2	11.4		
IWG Response	28.5	20.0		
Initial Response	19.7	17.1		

Statistical analyses

Statistical analysis title	IWG Complete Response
Statistical analysis description: The 95% Agresti-Min CIs are presented.	
Comparison groups	Efgartigimod PH20 SC v Placebo PH20 SC
Number of subjects included in analysis	207
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in percentage
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.8
upper limit	7.3

Statistical analysis title	IWG Response
Statistical analysis description: The 95% Agresti-Min CIs are presented.	
Comparison groups	Efgartigimod PH20 SC v Placebo PH20 SC
Number of subjects included in analysis	207
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in percentage
Point estimate	8.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.6
upper limit	20.2

Statistical analysis title	Initial Response
Statistical analysis description: The 95% Agresti-Min CIs are presented.	
Comparison groups	Efgartigimod PH20 SC v Placebo PH20 SC
Number of subjects included in analysis	207
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in percentage
Point estimate	2.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.7
upper limit	13.3

Secondary: Rate of Receipt of Rescue Therapy (Rescue Per Participant Per Month) in the Overall Population

End point title	Rate of Receipt of Rescue Therapy (Rescue Per Participant Per Month) in the Overall Population

End point description:

Rescue therapy was defined as an occurrence where the participant needed treatment with 1 or more rescue treatments. An occurrence was defined as a period of maximum 5 days where 1 or more rescue treatments were administered simultaneously or consecutively to the trial participant. The following rescue treatments were permitted: methylprednisolone, dexamethasone, prednisone, normal immunoglobulins, anti-D (Rho) immunoglobins, or platelet transfusions.

FAS: All randomized participants.

End point type	Secondary

End point timeframe:

Up to 24 weeks

End point values	Efgartigimod PH20 SC	Placebo PH20 SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	137	70		
Units: rescues per participant per month				
arithmetic mean (standard deviation)	0.25 (± 0.553)	0.17 (± 0.363)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants for Whom Dose and/or Frequency of Concurrent ITP Therapies Have Increased at Week 12 or Later in the Overall Population

End point title	Percentage of Participants for Whom Dose and/or Frequency of Concurrent ITP Therapies Have Increased at Week 12 or Later in the Overall Population

End point description:

A change in ITP therapy was defined as either an increase in the dose and/or frequency of a concurrent ITP therapy relative to Baseline or the initiation of a new concurrent ITP therapy.

FAS: All randomized participants.

End point type	Secondary

End point timeframe:

Up to 13 weeks (between Weeks 12 and 24)

End point values	Efgartigimod PH20 SC	Placebo PH20 SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	137	70		
Units: percentage of participants				
number (not applicable)	11.7	15.7		

Statistical analyses

Statistical analysis title	Efgartigimod PH20 SC vs. Placebo PH20 SC

Statistical analysis description:

The 95% Agresti-Min CIs are presented.

Comparison groups	Efgartigimod PH20 SC v Placebo PH20 SC
Number of subjects included in analysis	207
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in percentage
Point estimate	-4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.6
upper limit	5.7

Secondary: Change From Baseline in Functional Assessment of Chronic Illness Therapy Fatigue Scale (FACIT-Fatigue) at Week 24 in the Overall Population

End point title	Change From Baseline in Functional Assessment of Chronic Illness Therapy Fatigue Scale (FACIT-Fatigue) at Week 24 in the Overall Population

End point description:

The FACIT-fatigue scale is a short, 13-item, easy-to-administer tool that measures an individual's level of fatigue during his/her usual daily activities over the past week. The level of fatigue was measured by

recording item responses on a 5-point Likert scale ranging from 0 "not at all" to 4 "very much". All items were summed to create a single fatigue score with a range from 0 to 52, where a higher FACIT-F score indicated more severe symptoms. A negative change score from Baseline indicated improvement in quality of life (QoL).

FAS: All randomized participants.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Efgartigimod PH20 SC	Placebo PH20 SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	137	70		
Units: score on a scale				
least squares mean (standard deviation)	-0.025 (± 0.712)	0.741 (± 0.985)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Functional Assessment of Cancer Therapy Questionnaire-Th6 (Fact-Th6) at Week 24 in the Overall Population

End point title	Change From Baseline in Functional Assessment of Cancer Therapy Questionnaire-Th6 (Fact-Th6) at Week 24 in the Overall Population

End point description:

The FACT-Th6 uses a 5-level Likert scale (0=not at all to 4=very much), with participants rating their degree of concern in the past 7 days. The 6 selected items pertain to ability to do usual activities, worry about problems with bleeding or bruising, worry about the possibility of serious bleeding, avoidance of physical or social activity because of concern with bleeding or bruising and frustration due to the inability to carry out usual activities. All items were summed to create a single score with a range from 0 to 24, where a higher score indicated less severe symptoms. A positive change score from Baseline indicated improvement in QoL.

FAS: All randomized participants.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Efgartigimod PH20 SC	Placebo PH20 SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	137	70		
Units: score on a scale				
least squares mean (standard error)				
Week 24	0.225 (± 0.360)	0.359 (± 0.498)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Short Form-36 (SF-36) at Week 24 in the Overall Population

End point title	Change From Baseline in Short Form-36 (SF-36) at Week 24 in the Overall Population

End point description:

The SF-36 is a 36-item scale constructed to survey health-related QoL on 8 domains: limitations in physical activities due to health problems; limitations in social activities due to physical or emotional problems; limitations in usual role activities due to physical health problems; bodily pain; general mental health (psychological distress and well-being); limitations in usual role activities due to emotional problems; vitality (energy and fatigue); and general health perceptions. The scores from the 8 domains were evaluated independently and aggregated into 2 norm-based summary component measures of physical and mental health. The summary component scores could range from 0 to 100, where a higher score indicated improvement in QoL. A positive change score from Baseline indicated improvement in QoL.

FAS: All randomized participants.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Efgartigimod PH20 SC	Placebo PH20 SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	137	70		
Units: score on a scale				
least squares mean (standard error)				
Week 24: Mental Component	1.215 (± 0.620)	0.957 (± 0.841)		
Week 24: Physical Component	-0.848 (± 0.525)	-0.850 (± 0.712)		

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence and Prevalence of Antibodies to Efgartigimod and/or rHuPH20 in the Overall Population

End point title	Incidence and Prevalence of Antibodies to Efgartigimod and/or rHuPH20 in the Overall Population

End point description:

Anti-drug antibody (ADA) incidence was defined as the percentage of participants with treatment-induced or treatment boosted ADA (denominator: number of evaluable participants). ADA prevalence was defined as the percentage of participants with treatment-unaffected ADA, treatment-induced ADA or treatment-boosted ADA (denominator: number of evaluable participants).

SAF: All participants who received at least 1 dose or part of a dose including only antibody-evaluable participants.

End point type	Secondary

End point timeframe:

Up to 35 weeks

End point values	Efgartigimod PH20 SC	Placebo PH20 SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	70		
Units: percentage of participants				
number (not applicable)				
Incidence of Antibodies to Efgartigimod	5.1	2.9		
Prevalence of Antibodies to Efgartigimod	16.2	7.1		
Incidence of Antibodies to rHuPH20	41.2	20.0		
Prevalence of Antibodies to rHuPH20	50.0	31.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Titers of Antibodies to Efgartigimod and/or rHuPH20 in the Overall Population

End point title	Titers of Antibodies to Efgartigimod and/or rHuPH20 in the Overall Population

End point description:

A titer was determined in the samples with a positive assay response. Values of "99999" indicate standard deviation could not be calculated as a single participant was analyzed.

SAF: All participants who received at least 1 dose or part of a dose with available data.

End point type	Secondary

End point timeframe:

Weeks 3, 7, 11, 15, 19, 23, 24, SEFU1 (up to Week 29), and SEFU2 (up to Week 33)

End point values	Efgartigimod PH20 SC	Placebo PH20 SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	16		
Units: titer				
arithmetic mean (standard deviation)				

Week 3: ADA Against Efgartigimod Titer (N = 0, 2)	0.0 (± 0.0)	16.5 (± 15.50)		
Week 7: ADA Against Efgartigimod Titer (N = 1, 3)	1.0 (± 99999)	11.3 (± 10.33)		
Week 11: ADA Against Efgartigimod Titer (N = 0, 3)	0.0 (± 0.0)	6.3 (± 4.84)		
Week 15: ADA Against Efgartigimod Titer (N = 0, 2)	0.0 (± 0.0)	8.5 (± 7.50)		
Week 19: ADA Against Efgartigimod Titer (N = 0, 0)	0.0 (± 0.0)	0.0 (± 0.0)		
Week 23: ADA Against Efgartigimod Titer (N = 0, 1)	0.0 (± 0.0)	2.0 (± 99999)		
Week 24: ADA Against Efgartigimod Titer (N = 3, 2)	16.3 (± 8.95)	1.0 (± 0.00)		
SEFU1: ADA Against Efgartigimod Titer (N = 2, 0)	2.5 (± 1.50)	0.0 (± 0.0)		
SEFU2: ADA Against Efgartigimod Titer (N = 2, 0)	17.0 (± 15.00)	0.0 (± 0.0)		
Week 3: ADA Against rHuPH20 Titer (N = 15, 11)	12.7 (± 2.53)	14.1 (± 3.15)		
Week 7: ADA Against rHuPH20 Titer (N = 23, 8)	645.9 (± 314.79)	14.4 (± 4.27)		
Week 11: ADA Against rHuPH20 Titer (N = 32, 7)	2204.8 (± 1297.43)	11.4 (± 2.37)		
Week 15: ADA Against rHuPH20 Titer (N = 34, 7)	3209.3 (± 1325.96)	15.7 (± 2.02)		
Week 19: ADA Against rHuPH20 Titer (N = 42, 11)	3742.7 (± 1414.15)	49.1 (± 27.87)		
Week 23: ADA Against rHuPH20 Titer (N = 45, 15)	5936.6 (± 2180.33)	58.3 (± 27.83)		
Week 24: ADA Against rHuPH20 Titer (N = 45, 16)	4731.3 (± 1898.96)	69.1 (± 26.60)		
SEFU1: ADA Against rHuPH20 Titer (N = 2, 0)	5122.5 (± 5117.50)	0.0 (± 0.0)		
SEFU2: ADA Against rHuPH20 Titer (N = 2, 0)	5160.0 (± 5080.00)	0.0 (± 0.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence and Prevalence of Neutralizing Antibodies (NAb) to Efgartigimod and/or rHuPH20 in the Overall Population

End point title	Incidence and Prevalence of Neutralizing Antibodies (NAb) to Efgartigimod and/or rHuPH20 in the Overall Population

End point description:

Samples were tested for the presence of NAb against efgartigimod and/or rHuPH20 and titers for NAb against rHuPH20. Values of "9999" indicate no participants were analyzed at that timepoint.

NAb incidence is defined as the total percentage of participants with participant classification “baseline negative–postbaseline positive” and “baseline positive–postbaseline positive”. NAb prevalence is defined as the total percentage of participants with participant classification “baseline negative–postbaseline positive,” “baseline positive–postbaseline positive,” or “baseline positive–postbaseline negative”.

SAF: All participants who received at least 1 dose or part of a dose with available data.

End point type	Secondary

End point timeframe:

Up to 35 weeks

End point values	Efgartigimod PH20 SC	Placebo PH20 SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	70		
Units: percentage of participants				
number (not applicable)				
Incidence of NAb to Efgartigimod	0.7	0.0		
Prevalence of NAb to Efgartigimod	5.1	0.0		
Incidence of NAb to rHuPH20	0.0	0.0		
Prevalence of NAb to rHuPH20	0.0	0.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Efgartigimod Trough Concentration (Ctrough) in the Overall Population

End point title	Serum Efgartigimod Trough Concentration (Ctrough) in the Overall Population[11]

End point description:

All pharmacokinetic (PK) samples were collected predose, on the day of IMP administration.

PK Analysis Set: Safety analysis set excluding placebo participants and including participants with at least one serum post dose PK measurement.

End point type	Secondary

End point timeframe:

Predose on Weeks 1, 2, 3, 17, 19, 21, 23, and 24

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: Data collection was pre-specified for the Efgartigimod arm only.

End point values	Efgartigimod PH20 SC			
Subject group type	Reporting group			
Number of subjects analysed	135			
Units: µg/mL				
arithmetic mean (standard deviation)				
Week 1 (N = 135)	13.2 (± 6.46)			
Week 2 (N = 133)	16.6 (± 8.17)			
Week 3 (N = 126)	17.0 (± 7.95)			
Week 17 (N = 89)	15.1 (± 8.54)			
Week 19 (N = 91)	15.4 (± 7.43)			
Week 21 (N = 78)	15.1 (± 8.86)			
Week 23 (N = 88)	14.9 (± 7.79)			
Week 24 (N = 91)	14.7 (± 8.10)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change From Baseline in Total IgG in the Overall Population

End point title	Percentage Change From Baseline in Total IgG in the Overall Population

End point description:

Samples were collected predose, on the day of IMP administration.

Pharmacodynamic (PD) Analysis Set: Safety analysis set including participants with at least one serum post dose PD measurement.

End point type	Secondary

End point timeframe:

Baseline and Weeks 1, 2, 3, 17, 19, 21, 23, and 24

End point values	Efgartigimod PH20 SC	Placebo PH20 SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	133	67		
Units: percentage of total IgG				
arithmetic mean (standard deviation)				
Week 1 (N = 133, 67)	-33.64 (± 26.018)	0.60 (± 14.065)		
Week 2 (N = 132, 64)	-50.68 (± 34.973)	10.31 (± 44.858)		
Week 3 (N = 131, 64)	-56.80 (± 39.133)	4.97 (± 28.484)		
Week 17 (N = 96, 45)	-64.76 (± 11.478)	1.27 (± 16.749)		
Week 19 (N = 98, 51)	-60.98 (± 26.460)	9.28 (± 44.989)		
Week 21 (N = 89, 49)	-62.38 (± 15.176)	4.62 (± 25.406)		
Week 23 (N = 92, 49)	-62.45 (± 20.286)	2.45 (± 21.271)		
Week 24 (N = 102, 55)	-61.97 (± 18.200)	-0.36 (± 17.408)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Antiplatelet Antibodies in the Overall

Population

End point title	Number of Participants With Antiplatelet Antibodies in the Overall Population

End point description:

The antiplatelet antibody was positive if optical density value >0.129.

PD Analysis Set: Safety analysis set including participants with at least one serum post dose PD measurement and tested positive for antiplatelet antibodies at Baseline.

End point type	Secondary

End point timeframe:

Weeks 7, 15, 23, and 24

End point values	Efgartigimod PH20 SC	Placebo PH20 SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	16		
Units: participants				
Week 7 (N = 36, 14)	20	10		
Week 15 (N = 33, 16)	18	10		
Week 23 (N = 28, 14)	17	9		
Week 24 (N = 32, 13)	19	8		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 35 weeks

Adverse event reporting additional description:

The total number of participants affected by other (not including serious) adverse events (AEs) include participants who experienced other AEs under the frequency threshold of 5%.

SAF: All participants who received at least 1 dose or part of a dose.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Efgartigimod PH20 SC

Reporting group description:

Participants receiving efgartigimod PH20 SC treatment.

Reporting group title	Placebo PH20 SC

Reporting group description:

Participants receiving placebo PH20 SC treatment.

Serious adverse events	Efgartigimod PH20 SC	Placebo PH20 SC	
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 137 (10.22%)	10 / 70 (14.29%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	1	0	
Reproductive system and breast disorders			
Heavy menstrual bleeding			
subjects affected / exposed	1 / 137 (0.73%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intermenstrual bleeding			
subjects affected / exposed	1 / 137 (0.73%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Epistaxis			

subjects affected / exposed	0 / 137 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Haemoglobin decreased			
subjects affected / exposed	1 / 137 (0.73%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased			
subjects affected / exposed	0 / 137 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	0 / 137 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	1 / 137 (0.73%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Headache			
subjects affected / exposed	2 / 137 (1.46%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Immune thrombocytopenia			
subjects affected / exposed	1 / 137 (0.73%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			

subjects affected / exposed	1 / 137 (0.73%)	2 / 70 (2.86%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Amaurosis fugax			
subjects affected / exposed	1 / 137 (0.73%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vitreous haemorrhage			
subjects affected / exposed	1 / 137 (0.73%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 137 (0.73%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematochezia			
subjects affected / exposed	1 / 137 (0.73%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia strangulated			
subjects affected / exposed	0 / 137 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	1 / 137 (0.73%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 137 (0.73%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 137 (0.00%)	2 / 70 (2.86%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Autoimmune thyroiditis			
subjects affected / exposed	0 / 137 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Osteonecrosis			
subjects affected / exposed	0 / 137 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Arthritis infective			
subjects affected / exposed	0 / 137 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	3 / 137 (2.19%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	1 / 137 (0.73%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis aseptic			
subjects affected / exposed	1 / 137 (0.73%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			

subjects affected / exposed	1 / 137 (0.73%)	0 / 70 (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	Placebo PH20 SC	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	130 / 137 (94.89%)	65 / 70 (92.86%)	
Vascular disorders			
Haematoma			
subjects affected / exposed	7 / 137 (5.11%)	3 / 70 (4.29%)	
occurrences (all)	10	3	
Hypertension			
subjects affected / exposed	7 / 137 (5.11%)	4 / 70 (5.71%)	
occurrences (all)	16	5	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	8 / 137 (5.84%)	0 / 70 (0.00%)	
occurrences (all)	9	0	
Injection site bruising			
subjects affected / exposed	13 / 137 (9.49%)	2 / 70 (2.86%)	
occurrences (all)	23	3	
Injection site erythema			
subjects affected / exposed	9 / 137 (6.57%)	2 / 70 (2.86%)	
occurrences (all)	31	6	
Injection site haemorrhage			
subjects affected / exposed	14 / 137 (10.22%)	14 / 70 (20.00%)	
occurrences (all)	17	26	
Injection site pain			
subjects affected / exposed	8 / 137 (5.84%)	2 / 70 (2.86%)	
occurrences (all)	43	2	
Injection site rash			
subjects affected / exposed	7 / 137 (5.11%)	1 / 70 (1.43%)	
occurrences (all)	12	1	

Injection site reaction			
subjects affected / exposed	10 / 137 (7.30%)	1 / 70 (1.43%)	
occurrences (all)	28	1	
Vessel puncture site haemorrhage			
subjects affected / exposed	3 / 137 (2.19%)	5 / 70 (7.14%)	
occurrences (all)	3	6	
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	20 / 137 (14.60%)	15 / 70 (21.43%)	
occurrences (all)	50	38	
Investigations			
Blood urine present			
subjects affected / exposed	43 / 137 (31.39%)	20 / 70 (28.57%)	
occurrences (all)	77	34	
C-reactive protein increased			
subjects affected / exposed	3 / 137 (2.19%)	8 / 70 (11.43%)	
occurrences (all)	3	12	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	22 / 137 (16.06%)	12 / 70 (17.14%)	
occurrences (all)	102	43	
Nervous system disorders			
Dizziness			
subjects affected / exposed	8 / 137 (5.84%)	3 / 70 (4.29%)	
occurrences (all)	10	3	
Headache			
subjects affected / exposed	16 / 137 (11.68%)	7 / 70 (10.00%)	
occurrences (all)	23	9	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	10 / 137 (7.30%)	6 / 70 (8.57%)	
occurrences (all)	10	13	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	7 / 137 (5.11%)	1 / 70 (1.43%)	
occurrences (all)	8	1	
Dyspepsia			

subjects affected / exposed	3 / 137 (2.19%)	5 / 70 (7.14%)	
occurrences (all)	4	8	
Gingival bleeding			
subjects affected / exposed	14 / 137 (10.22%)	10 / 70 (14.29%)	
occurrences (all)	17	25	
Mouth haemorrhage			
subjects affected / exposed	19 / 137 (13.87%)	6 / 70 (8.57%)	
occurrences (all)	37	16	
Oral blood blister			
subjects affected / exposed	10 / 137 (7.30%)	1 / 70 (1.43%)	
occurrences (all)	19	2	
Skin and subcutaneous tissue disorders			
Ecchymosis			
subjects affected / exposed	34 / 137 (24.82%)	20 / 70 (28.57%)	
occurrences (all)	88	83	
Petechiae			
subjects affected / exposed	34 / 137 (24.82%)	19 / 70 (27.14%)	
occurrences (all)	77	40	
Purpura			
subjects affected / exposed	15 / 137 (10.95%)	11 / 70 (15.71%)	
occurrences (all)	56	38	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	32 / 137 (23.36%)	23 / 70 (32.86%)	
occurrences (all)	47	43	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 137 (2.19%)	4 / 70 (5.71%)	
occurrences (all)	4	4	
Infections and infestations			
COVID-19			
subjects affected / exposed	18 / 137 (13.14%)	6 / 70 (8.57%)	
occurrences (all)	18	6	
Upper respiratory tract infection			
subjects affected / exposed	12 / 137 (8.76%)	6 / 70 (8.57%)	
occurrences (all)	15	8	

Urinary tract infection subjects affected / exposed occurrences (all)	8 / 137 (5.84%) 11	6 / 70 (8.57%) 10	
Metabolism and nutrition disorders Hyperuricaemia subjects affected / exposed occurrences (all)	7 / 137 (5.11%) 9	3 / 70 (4.29%) 4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 January 2021	- IgG subtype levels were removed from the PD secondary endpoint. - Which participants should complete the EoT visit was updated. - The inclusion criteria were updated for the requirement of mean platelet count of <30 × 10^9/L to require at least 3 documented qualifying counts where at least 2 of the qualifying counts must be taken during the screening period. If the third count is not available from the 3 preceding months, this third platelet count could be obtained during the screening period. - The contraception requirements were updated due to final reproductive toxicity study results, which did not indicate a risk to male or female fertility or embryo-fetal developmental toxicity. - The primary endpoint analysis was updated per the United States Food and Drug Administration recommendations. A supportive analysis was also added. - Additional details on prior ITP procedures and therapies were specified per the United States Food and Drug Administration recommendations.
16 July 2021	- Caregiver-related requirements were clarified. - An eligibility evaluation requirement was added for participants rolling over to study ARGX-113-2005 who had an SAE during ARGX-113-2004. - A disease-specific measure of health-related QoL for use in adults with ITP was added. - The following parameters were added to be tested at baseline and visit 14 for safety purposes: apolipoprotein B, lipoprotein A, fibrinogen, von Willebrand factor, D-dimer, PCSK9. - The inclusion criteria were updated to make an exception for the age of consent in certain countries with higher legal age. - The exclusion criteria were updated to exclude participants with active clinically significant bleeding of an organ or internal mucosal bleeding, other than expected in ITP, that warrants emergent treatment or therapeutic procedure. - The exclusion criteria were updated to exclude participants with an estimated high risk of clinically significant bleeding of an organ or internal mucosal bleeding, other than expected in ITP, that warrants emergent treatment or therapeutic procedure. - Baseline platelet count category was added to the analysis model for consistency with the primary endpoint analysis approach (Cochran-Mantel- Haenszel test). - Added suspected transmission of any infectious agent as an SAE per EMA guidelines.
15 July 2022	- The sample size was changed to approximately 180 participants with chronic ITP. - The hierarchical order for testing the third and fourth key secondary efficacy endpoints was updated. - The statistical method was modified for analysis of the key secondary efficacy endpoint “incidence and severity of the WHO-classified bleeding events in the overall population". - Contraception requirements and the required time period for collecting pregnancy information were updated. - It was specified that the baseline visit in ARGX-113-2005 would occur 7 days after the ARGX-113-2004 end of trial (EoT) visit for ARGX-113-2004 participants who met the criteria to transition to an every-other-week IMP dosing regimen based on their platelet counts at the EoT visit. - The clinical chemistry parameters apolipoprotein B, lipoprotein A, fibrinogen, von Willebrand factor, D-dimer, and PCSK9 were removed. - Updated safety reporting processes to align with the sponsor’s current practices.

17 February 2023	- The exclusion criterion and washout period for serious thromboembolic events were updated. The prohibited period for any major thrombotic or embolic event (eg, myocardial infarction, stroke, deep venous thrombosis, pulmonary embolism) was revised from within 12 months to within 5 years before randomization. - Language was added to clarify that any participant developing a new or recurrent malignancy except basal cell carcinoma would discontinue study treatment regardless of the relationship to IMP. - The collection time of PK/PD/anti-drug antibody samples was revised from within 2 hours to within the same day before IMP administration. - The contraception requirement for male participants was removed. - An efficacy objective was added to compare efgartigimod PH20 SC to placebo PH20 SC in IWG response and initial response, measuring the proportions of participants with an IWG response, an IWG complete response, and an initial response. - Anti-CD20 therapy (eg, rituximab) with a washout of 6 months before randomization was added. - The age of consent inclusion criterion was revised to state that participants should be at least the local legal age of consent for clinical studies when signing the informed consent form. - The follow-up time after IMP administration was revised from 15 to 30 minutes. - Language was added describing blinding procedures for albumin and urine total protein (quantitative) values per DSMB recommendations.
06 April 2023	The substantiality assessment was revised from referring to Article 2 §2 (13) of Regulation No 536/2014 of the European Parliament and the Council of the European Union to Article 10(a) of Directive 2001/20/EC of the European Parliament and the Council of the European Union.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported