



Clinical trial results:

A Randomized, Double-Blinded, Placebo-Controlled Trial to Investigate the Efficacy, Safety, and Tolerability of Efgartigimod PH20 SC in Adult Patients With Pemphigus (Vulgaris or Foliaceus) (ADDRESS)

Summary

EudraCT number	2020-002915-23
Trial protocol	DE FR HU BG ES GR IT
Global end of trial date	22 August 2023

Results information

Result version number	v1 (current)
This version publication date	30 August 2024
First version publication date	30 August 2024

Trial information

Trial identification

Sponsor protocol code	ARGX-113-1904
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04598451
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	argenx BV
Sponsor organisation address	Industriepark Zwijnaarde 7, Zwijnaarde (Ghent), Belgium, 9052
Public contact	Regulatory, argenx BV, 0032 93103400, regulatory@argenx.com
Scientific contact	Regulatory, argenx BV, 0032 93103400, 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	03 July 2024
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	22 August 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the efficacy of efgartigimod PH20 SC compared to placebo in the treatment of participants with pemphigus vulgaris

Protection of trial subjects:

The protocol, protocol amendments, ICFs, relevant supporting information, and participant recruitment information were approved by the IEC/IRB and regulatory agency before participants were enrolled. This study was conducted in accordance with the protocol and consensus ethical principles derived from international guidelines, including the Declaration of Helsinki, applicable ICH GCP guidelines, and applicable laws and regulations.

Participants or their legally authorized representative were required to sign a statement of informed consent that met the requirements of the local regulations, ICH guidelines, privacy and data protection requirements, where applicable, and the IRB/IEC or study center.

Background therapy:

All participants, regardless of treatment assignment, concomitantly received oral prednisone (or equivalent such as prednisolone) at 0.5 mg/kg qd as a starting dose. Except for oral prednisone (or equivalent), no other systemic pemphigus therapies (eg, immunosuppressants, IVIg, immunoadsorption, anti-CD20 biologics) were permitted during the trial. In addition to oral prednisone, 204 of 222 patients received concomitant therapy. Concomitant therapies were defined as any therapy or procedure that was started on or after the date of the first IMP dose.

Evidence for comparator:

Placebo

Actual start date of recruitment	12 October 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: 5
Country: Number of subjects enrolled	China: 35
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	Georgia: 7
Country: Number of subjects enrolled	India: 13
Country: Number of subjects enrolled	Japan: 11
Country: Number of subjects enrolled	Russian Federation: 15
Country: Number of subjects enrolled	Serbia: 1
Country: Number of subjects enrolled	Türkiye: 3
Country: Number of subjects enrolled	Ukraine: 20

Country: Number of subjects enrolled	United States: 14
Country: Number of subjects enrolled	Poland: 16
Country: Number of subjects enrolled	Romania: 3
Country: Number of subjects enrolled	Spain: 6
Country: Number of subjects enrolled	Bulgaria: 15
Country: Number of subjects enrolled	France: 11
Country: Number of subjects enrolled	Germany: 14
Country: Number of subjects enrolled	Greece: 12
Country: Number of subjects enrolled	Hungary: 7
Country: Number of subjects enrolled	Italy: 11
Worldwide total number of subjects	222
EEA total number of subjects	95

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)	190
From 65 to 84 years	32
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 82 study sites that enrolled participants in 20 countries. A total of 222 participants were randomized in a 2:1 ratio to receive IMP: 147 to the efgartigimod PH20 SC arm and 75 to the placebo arm. Overall, 190 participants with pemphigus vulgaris (PV) and 32 participants with pemphigus foliaceus (PF) were enrolled.

Pre-assignment

Screening details:

All participants were adults, aged from 18 years, with moderate-to-severe pemphigus vulgaris (PV) or with pemphigus foliaceus (PF). Enrolled participants were either those who are newly diagnosed or having flare.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	EFG PH20 SC - PV + PF

Arm description:

Patients randomized to receive weekly administrations of efgartigimod PH20 until CRmin (complete remission on minimal prednisone therapy) or end of treatment period or early roll-over to the open-label extension study ARGX-113-1905. All participants received concurrent oral prednisone (or equivalent) at a starting dosage of 0.5 mg/kg/day. The dose of prednisone was adjusted according to recommendations as per protocol.

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:

Efgartigimod PH20 SC 1000 mg once weekly for up to 30 weeks. All participants received concurrent oral prednisone (or equivalent) at a starting dosage of 0.5 mg/kg/day.

Arm title	PBO PH20 SC - PV + PF
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Arm description:

Patients randomized to receive weekly administrations of efgartigimod PH20 until CRmin (complete remission on minimal prednisone therapy) or end of treatment period or early roll-over to the open-label extension study ARGX-113-1905. All participants received concurrent oral prednisone (or equivalent) at a starting dosage of 0.5 mg/kg/day. The dose of prednisone was adjusted according to recommendations as per protocol.

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

Dosage and administration details:

Placebo PH20 SC once weekly for up to 30 weeks. All participants received concurrent oral prednisone

(or equivalent) at a starting dose of 0.5 mg/kg/day.

Number of subjects in period 1	EFG PH20 SC - PV + PF	PBO PH20 SC - PV + PF
Started	147	75
Completed	104	46
Not completed	43	29
Consent withdrawn by subject	3	7
Physician decision	4	1
Adverse event, non-fatal	3	2
Other	30	19
Requires prohibited medication	1	-
Lost to follow-up	2	-

Baseline characteristics

Reporting groups

Reporting group title	EFG PH20 SC - PV + PF
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Reporting group description:

Patients randomized to receive weekly administrations of efgartigimod PH20 until CRmin (complete remission on minimal prednisone therapy) or end of treatment period or early roll-over to the open-label extension study ARGX-113-1905. All participants received concurrent oral prednisone (or equivalent) at a starting dosage of 0.5 mg/kg/day. The dose of prednisone was adjusted according to recommendations as per protocol.

Reporting group title	PBO PH20 SC - PV + PF
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Reporting group description:

Patients randomized to receive weekly administrations of efgartigimod PH20 until CRmin (complete remission on minimal prednisone therapy) or end of treatment period or early roll-over to the open-label extension study ARGX-113-1905. All participants received concurrent oral prednisone (or equivalent) at a starting dosage of 0.5 mg/kg/day. The dose of prednisone was adjusted according to recommendations as per protocol.

Reporting group values	EFG PH20 SC - PV + PF	PBO PH20 SC - PV + PF	Total
Number of subjects	147	75	222
Age categorical Units: Subjects			
Adults (18-64 years)	129	61	190
From 65-84 years	18	14	32
Age continuous Units: years			
arithmetic mean	48.9	52.3	
standard deviation	± 12.55	± 13.37	-
Gender categorical Units: Subjects			
Female	73	42	115
Male	74	33	107

End points

End points reporting groups

Reporting group title	EFG PH20 SC - PV + PF
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Reporting group description:

Patients randomized to receive weekly administrations of efgartigimod PH20 until CRmin (complete remission on minimal prednisone therapy) or end of treatment period or early roll-over to the open-label extension study ARGX-113-1905. All participants received concurrent oral prednisone (or equivalent) at a starting dosage of 0.5 mg/kg/day. The dose of prednisone was adjusted according to recommendations as per protocol.

Reporting group title	PBO PH20 SC - PV + PF
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Reporting group description:

Patients randomized to receive weekly administrations of efgartigimod PH20 until CRmin (complete remission on minimal prednisone therapy) or end of treatment period or early roll-over to the open-label extension study ARGX-113-1905. All participants received concurrent oral prednisone (or equivalent) at a starting dosage of 0.5 mg/kg/day. The dose of prednisone was adjusted according to recommendations as per protocol.

Subject analysis set title	EFG PH20 SC - PV only
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Subject analysis set type	Sub-group analysis
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Subject analysis set description:

Randomized participants with pemphigus vulgaris who received at least part of a dose of efgartigimod PH20 SC. These participants also received prednisone with a starting dosage of 0.5 mg/kg/day. The dose of prednisone was adjusted per protocol.

Subject analysis set title	PBO PH20 SC - PV only
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Subject analysis set type	Sub-group analysis
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Subject analysis set description:

Randomized participants with pemphigus vulgaris who received at least part of a dose of placebo PH20 SC. These participants also received prednisone with a starting dosage of 0.5 mg/kg/day. The dose of prednisone was adjusted per protocol.

Primary: Proportion of PV participants who achieve Complete Remission on Minimal Therapy (CRmin) within 30 weeks

End point title	Proportion of PV participants who achieve Complete Remission on Minimal Therapy (CRmin) within 30 weeks
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End point description:

The primary efficacy endpoint is the proportion of participants with pemphigus vulgaris who had CRmin within 30 weeks, defined as the absence of new lesions and complete healing of established lesions while the participant was receiving prednisone at ≤ 10 mg/day for at least 8 weeks.

End point type	Primary
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End point timeframe:

From Baseline to Week 30

End point values	EFG PH20 SC - PV only	PBO PH20 SC - PV only		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	124	66		
Units: percent				
number (not applicable)	35.5	30.3		

Statistical analyses

Statistical analysis title	Statistical analysis
Comparison groups	EFG PH20 SC - PV only v PBO PH20 SC - PV only
Number of subjects included in analysis	190
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5956
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	2.41

Secondary: Proportion of participants with PV and PF who achieve CRmin within 30 weeks

End point title	Proportion of participants with PV and PF who achieve CRmin within 30 weeks
End point description:	
The secondary efficacy endpoint is the proportion of participants with pemphigus vulgaris and pemphigus foliaceus who had CRmin within 30 weeks, defined as the absence of new lesions and complete healing of established lesions while the participant was receiving prednisone at ≤ 10 mg/day for at least 8 weeks.	
End point type	Secondary
End point timeframe:	
From Baseline to Week 30	

End point values	EFG PH20 SC - PV + PF	PBO PH20 SC - PV + PF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	147	75		
Units: percent				
number (not applicable)	37.4	32.0		

Statistical analyses

Statistical analysis title	Statistical analysis
Comparison groups	EFG PH20 SC - PV + PF v PBO PH20 SC - PV + PF

Number of subjects included in analysis	222
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5785
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	2.25

Secondary: Normalized Cumulative Prednisone Dose During the Treatment Period in Participants With PV

End point title	Normalized Cumulative Prednisone Dose During the Treatment Period in Participants With PV
End point description:	
NCPD (mg/kg/day) is the average daily intake of all weight-adjusted prednisone doses received during the study, taking into account the number of days in study.	
End point type	Secondary
End point timeframe:	
From Baseline to Week 30	

End point values	EFG PH20 SC - PV only	PBO PH20 SC - PV only		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	124	66		
Units: mg/kg/day				
arithmetic mean (standard deviation)				
Mean (SD)	0.416 (± 0.215)	0.444 (± 0.232)		
LS-means (SE)	0.413 (± 0.021)	0.437 (± 0.027)		

Statistical analyses

Statistical analysis title	Statistical analysis
Comparison groups	EFG PH20 SC - PV only v PBO PH20 SC - PV only
Number of subjects included in analysis	190
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4662
Method	Analysis of Covariance
Parameter estimate	LS-mean difference
Point estimate	-0.024

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.09
upper limit	0.041

Secondary: Time to CR in participants with PV

End point title	Time to CR in participants with PV
End point description: Time to complete remission (absence of new lesions and complete healing of established lesions) in participants with pemphigus vulgaris.	
End point type	Secondary
End point timeframe: From Baseline to Week 30	

End point values	EFG PH20 SC - PV only	PBO PH20 SC - PV only		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	124	66		
Units: days				
median (confidence interval 95%)	106 (79 to 161)	120 (85 to 188)		

Statistical analyses

Statistical analysis title	Statistical analysis
Comparison groups	PBO PH20 SC - PV only v EFG PH20 SC - PV only
Number of subjects included in analysis	190
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7376
Method	Logrank
Parameter estimate	Cox proportional hazard ratio
Point estimate	1.025
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.696
upper limit	1.509

Secondary: Time to DC in participants with PV

End point title	Time to DC in participants with PV
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End point description:	
Time to disease control in participants with pemphigus vulgaris (Absence of new lesions and complete healing of established lesions).	
End point type	Secondary
End point timeframe:	
From Baseline to Week 30	

End point values	EFG PH20 SC - PV only	PBO PH20 SC - PV only		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	124	66		
Units: days				
median (confidence interval 95%)				
Median (95% CI), days	16 (15 to 21)	15 (8 to 17)		

Statistical analyses

Statistical analysis title	Statistical analysis
Comparison groups	PBO PH20 SC - PV only v EFG PH20 SC - PV only
Number of subjects included in analysis	190
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3949
Method	Logrank
Parameter estimate	Cox proportional hazard
Point estimate	0.874
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.635
upper limit	1.204

Secondary: Normalized Cumulative Prednisone Dose During the Treatment Period in Participants With Pemphigus (PV and PF)

End point title	Normalized Cumulative Prednisone Dose During the Treatment Period in Participants With Pemphigus (PV and PF)
End point description:	
NCPD (mg/kg/day) is the average daily intake of all weight-adjusted prednisone doses received during the study, taking into account the number of days in study.	
End point type	Secondary
End point timeframe:	
From Baseline to Week 30	

End point values	EFG PH20 SC - PV + PF	PBO PH20 SC - PV + PF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	147	75		
Units: mg/kg/day				
arithmetic mean (standard deviation)	0.403 (± 0.210)	0.431 (± 0.225)		

Statistical analyses

Statistical analysis title	Statistical analysis
Comparison groups	EFG PH20 SC - PV + PF v PBO PH20 SC - PV + PF
Number of subjects included in analysis	222
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4709
Method	Analysis of Covariance
Parameter estimate	LS-mean difference
Point estimate	-0.022
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.082
upper limit	0.038

Secondary: Time to CR in participants with PV and PF

End point title	Time to CR in participants with PV and PF
End point description:	
Time to complete remission (absence of new lesions and complete healing of established lesions) in participants with pemphigus vulgaris and pemphigus foliaceus.	
End point type	Secondary
End point timeframe:	
From Baseline to Week 30	

End point values	EFG PH20 SC - PV + PF	PBO PH20 SC - PV + PF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	147	75		
Units: days				
median (confidence interval 95%)	106 (84 to 142)	113 (81 to 149)		

Statistical analyses

Statistical analysis title	Statistical analysis
Comparison groups	EFG PH20 SC - PV + PF v PBO PH20 SC - PV + PF
Number of subjects included in analysis	222
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8863
Method	Logrank
Parameter estimate	Cox proportional hazard
Point estimate	0.967
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	1.377

Secondary: Time to DC in participants with PV and PF

End point title	Time to DC in participants with PV and PF
End point description: Time to disease control in participants with pemphigus vulgaris and foliaceus (Absence of new lesions and complete healing of established lesions).	
End point type	Secondary
End point timeframe: From Baseline to Week 30	

End point values	EFG PH20 SC - PV + PF	PBO PH20 SC - PV + PF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	147	75		
Units: days				
median (confidence interval 95%)	15 (15 to 17)	15 (9 to 16)		

Statistical analyses

Statistical analysis title	Statistical analysis
Comparison groups	EFG PH20 SC - PV + PF v PBO PH20 SC - PV + PF

Number of subjects included in analysis	222
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4778
Method	Logrank
Parameter estimate	Cox proportional hazard
Point estimate	0.898
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.668
upper limit	1.208

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The adverse events were collected during the treatment period (up to 30 weeks) and in the follow-up period (up to 8 weeks) for participants who did not roll over to the OLE study (ARGX-113-1905).

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	26.0
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Reporting groups

Reporting group title	EFG PH20 SC
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Reporting group description:

Patients randomized to receive weekly administrations of efgartigimod PH20 until CRmin (complete remission on minimal prednisone therapy) or end of treatment period or early roll-over to the open-label extension study ARGX-113-1905. All participants received concurrent oral prednisone (or equivalent) at a starting dosage of 0.5 mg/kg/day. The dose of prednisone was adjusted according to recommendations as per protocol.

Reporting group title	PBO PH20 SC
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Reporting group description:

Patients randomized to receive weekly administrations of efgartigimod PH20 until CRmin (complete remission on minimal prednisone therapy) or end of treatment period or early roll-over to the open-label extension study ARGX-113-1905. All participants received concurrent oral prednisone (or equivalent) at a starting dosage of 0.5 mg/kg/day. The dose of prednisone was adjusted according to recommendations as per protocol.

Serious adverse events	EFG PH20 SC	PBO PH20 SC	
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 147 (12.24%)	10 / 75 (13.33%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Superficial spreading melanoma stage unspecified			
subjects affected / exposed	0 / 147 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 147 (1.36%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			

Asthma	subjects affected / exposed	0 / 147 (0.00%)	1 / 75 (1.33%)	
	occurrences causally related to treatment / all	0 / 0	0 / 1	
	deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure	subjects affected / exposed	1 / 147 (0.68%)	0 / 75 (0.00%)	
	occurrences causally related to treatment / all	0 / 1	0 / 0	
	deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations				
Weight increased	subjects affected / exposed	1 / 147 (0.68%)	0 / 75 (0.00%)	
	occurrences causally related to treatment / all	0 / 1	0 / 0	
	deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications				
Spinal compression fracture	subjects affected / exposed	2 / 147 (1.36%)	0 / 75 (0.00%)	
	occurrences causally related to treatment / all	0 / 2	0 / 0	
	deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders				
Tachycardia	subjects affected / exposed	1 / 147 (0.68%)	0 / 75 (0.00%)	
	occurrences causally related to treatment / all	0 / 1	0 / 0	
	deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders				
Headache	subjects affected / exposed	0 / 147 (0.00%)	1 / 75 (1.33%)	
	occurrences causally related to treatment / all	0 / 0	0 / 1	
	deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders				
Anaemia	subjects affected / exposed	0 / 147 (0.00%)	1 / 75 (1.33%)	
	occurrences causally related to treatment / all	0 / 0	0 / 1	
	deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders				
Vision blurred				

subjects affected / exposed	1 / 147 (0.68%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastritis erosive			
subjects affected / exposed	0 / 147 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 147 (0.68%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 147 (0.68%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Drug eruption			
subjects affected / exposed	1 / 147 (0.68%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pemphigus			
subjects affected / exposed	1 / 147 (0.68%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Glomerulonephritis			
subjects affected / exposed	1 / 147 (0.68%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19			

subjects affected / exposed	2 / 147 (1.36%)	2 / 75 (2.67%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	1 / 147 (0.68%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	1 / 147 (0.68%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 147 (0.68%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin infection			
subjects affected / exposed	1 / 147 (0.68%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 147 (0.68%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	1 / 147 (0.68%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 147 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			

subjects affected / exposed	0 / 147 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoproteinaemia			
subjects affected / exposed	1 / 147 (0.68%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic syndrome			
subjects affected / exposed	0 / 147 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	EFG PH20 SC	PBO PH20 SC	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	113 / 147 (76.87%)	47 / 75 (62.67%)	
Investigations			
Blood lactate dehydrogenase increased			
subjects affected / exposed	10 / 147 (6.80%)	3 / 75 (4.00%)	
occurrences (all)	11	3	
Vascular disorders			
Hypertension			
subjects affected / exposed	21 / 147 (14.29%)	3 / 75 (4.00%)	
occurrences (all)	23	3	
Nervous system disorders			
Headache			
subjects affected / exposed	9 / 147 (6.12%)	2 / 75 (2.67%)	
occurrences (all)	16	5	
Blood and lymphatic system disorders			
Increased tendency to bruise			
subjects affected / exposed	5 / 147 (3.40%)	5 / 75 (6.67%)	
occurrences (all)	5	5	
General disorders and administration site conditions			

Injection site erythema subjects affected / exposed occurrences (all)	8 / 147 (5.44%) 34	1 / 75 (1.33%) 4	
Skin and subcutaneous tissue disorders Dermatitis acneiform subjects affected / exposed occurrences (all)	7 / 147 (4.76%) 7	6 / 75 (8.00%) 6	
Psychiatric disorders Depression subjects affected / exposed occurrences (all) Insomnia subjects affected / exposed occurrences (all)	9 / 147 (6.12%) 9 18 / 147 (12.24%) 19	3 / 75 (4.00%) 3 9 / 75 (12.00%) 10	
Renal and urinary disorders Leukocyturia subjects affected / exposed occurrences (all)	4 / 147 (2.72%) 9	4 / 75 (5.33%) 4	
Musculoskeletal and connective tissue disorders Myopathy subjects affected / exposed occurrences (all)	9 / 147 (6.12%) 9	8 / 75 (10.67%) 8	
Infections and infestations COVID-19 subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Oral candidiasis subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	17 / 147 (11.56%) 18 4 / 147 (2.72%) 6 6 / 147 (4.08%) 8 4 / 147 (2.72%) 8	3 / 75 (4.00%) 4 5 / 75 (6.67%) 6 6 / 75 (8.00%) 6 6 / 75 (8.00%) 14	
Metabolism and nutrition disorders			

Hypertriglyceridaemia subjects affected / exposed occurrences (all)	11 / 147 (7.48%) 19	2 / 75 (2.67%) 3	
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More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 February 2021	<p>Protocol, version 2.0</p> <p>A secondary objective and endpoint were added to measure the health impact of glucocorticoid use in participants with pemphigus.</p> <p>Training for self-administration and caregiver-supported administration were implemented to allow these types of administration in OLE study ARGX-113-1905.</p> <p>Assessments of vaccine-induced immunity in the context of efgartigimod treatment were added.</p> <p>The upper age limit of participants was removed.</p> <p>Changes to the contraceptive requirements based on new data about the IMP were implemented.</p> <p>Participants with specific cancers were allowed in the study if they were adequately treated before they started the study.</p> <p>It was clarified that dapsone use within 2 months of baseline was not exclusionary.</p> <p>A new criterion was added allowing the withdrawal of a participant from the study for whom a severe AE, SAE, or clinically significant change in a laboratory test parameter was reported.</p> <p>A transition in efgartigimod concentration from 165 mg/mL to 180 mg/mL was implemented to reduce the volume for each 1000-mg SC injection.</p> <p>Information on estimands and sensitivity analyses was added to align with the ICH guidelines.</p> <p>The prednisone dose escalation criteria were clarified.</p>
18 May 2021	<p>Protocol, version 3.0</p> <p>A requirement to assess direct immunofluorescence/histopathology at screening, if not available from medical history, was added.</p> <p>High-density lipoprotein cholesterol, total cholesterol, and triglycerides were added to the blood chemistry profile.</p> <p>Guidance was added that the investigator should not implement any deviation from the concurrent oral prednisone (or equivalent) regimen except for immediate safety concerns of the participant.</p> <p>Specialty tests (ie, apolipoprotein B, lipoprotein A, fibrinogen, von Willebrand factor, D-dimer, and proprotein convertase subtilisin/kexin type 9 serine protease) were added to further investigate the effect of the IMP on lipid metabolism.</p>
09 June 2022	<p>Protocol, version 4.0</p> <p>The sample size was increased due to (1) the geopolitical situation in Ukraine and impacted areas and (2) the additional analyses (including a supplementary landmark analysis of the primary endpoint performed at week 30) to align with feedback from regulatory interactions.</p> <p>The changes implemented in the Japan country-specific amendment (version 3.1 – Japan) were incorporated.</p> <p>Specialty tests (ie, apolipoprotein B, lipoprotein A, fibrinogen, von Willebrand factor, D-dimer, and proprotein convertase subtilisin/kexin type 9 serine protease) were removed because no relevant safety signals were observed in efgartigimod studies to date.</p> <p>Based on nonclinical teratogenicity and reproductive toxicity data, the inclusion and exclusion criteria were updated: 1) Female participants could stop their contraception method at the date of the last IMP dose; 2) Female participants could become pregnant immediately after the study.</p>

09 December 2022	<p>Protocol, version 5.0</p> <p>To limit the risk of unblinding and ensure data integrity in this double-blinded efgartigimod study, study sites were no longer provided with the real-time albumin and total protein results.</p> <p>The inclusion criteria were updated to allow male participants to donate sperm, in alignment with the general guidance for efgartigimod on sperm donation.</p> <p>The use of male contraception was no longer required until the end of the study but until the last dose of IMP.</p> <p>Relevant changes implemented in the Germany and China country-specific protocols, v4.1-Germany and v4.1-China, were included also in this protocol amendment.</p>
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Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported