EU Clinical Trials Register

Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled, Multicenter Phase 3 Trial to Evaluate the Efficacy, Safety and Tolerability of ARGX-113 in Patients with Myasthenia Gravis Having Generalized Muscle Weakness (ADAPT)

Summary

EudraCT number	2018-002132-25
Trial protocol	NL DK FR CZ DE HU BE IT
Global end of trial date	06 April 2020

Results information

Result version number	v1 (current)
This version publication date	22 April 2021
First version publication date	22 April 2021

Trial information

Trial identification

Sponsor protocol code	ARGX-113-1704

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03669588
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	argenx BVBA
Sponsor organisation address	Industriepark Zwijnaarde 7, Zwijnaarde, Belgium, 9052
Public contact	Regulatory Manager, argenx BVBA, regulatory@argenx.com
Scientific contact	Regulatory Manager, argenx BVBA, 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	06 April 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 April 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of ARGX-113 (efgartigimod) as assessed by the percentage of Myasthenia Gravis Activities of Daily Living (MG-ADL) responders after the first treatment cycle (TC) in the acetylcholine receptor (AChR)-antibody (Ab) seropositive (AChR-Ab seropositive) population.

The study included both AChR-Ab seropositive and seronegative patients. AChR-Ab seronegative patients were patients in whom AChR-Ab was undetectable in serum during the screening period, using a radioimmunoassay.

Protection of trial subjects:

This study was conducted according to the International Conference on Harmonisation of Good Clinical Practice, the principles of the Declaration of Helsinki, and other applicable local ethical and legal requirements.

Background therapy:

Patients were required to be on a stable dose of standard of care (SoC) (concomitant generalized myasthenia gravis [gMG] treatment) prior to screening. Concomitant gMG treatment was limited to acetylcholinesterase inhibitors, steroids and nonsteroidal immunosuppressive drugs (NSIDs).

Evidence for comparator: -

Actual start date of recruitment	22 August 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Poland: 30
Country: Number of subjects enrolled	Belgium: 6
Country: Number of subjects enrolled	Czechia: 13
Country: Number of subjects enrolled	Denmark: 1
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Hungary: 1
Country: Number of subjects enrolled	Italy: 6
Country: Number of subjects enrolled	Canada: 4
Country: Number of subjects enrolled	Japan: 15
Country: Number of subjects enrolled	Russian Federation: 6
Country: Number of subjects enrolled	Serbia: 19
Country: Number of subjects enrolled	United States: 40

Country: Number of subjects enrolled	Georgia: 22
Worldwide total number of subjects	167
EEA total number of subjects	61

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)	142
From 65 to 84 years	25
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study was conducted in gMG patients at 56 sites worldwide. Patients were randomized 1:1 within each stratum (Japanese/non-Japanese, AChR-Ab status and SoC) to receive ARGX-113 intravenous (IV) 10 milligrams/kilogram (mg/kg) or placebo, in addition to SoC. Patients completing the study were eligible to roll over into a follow-up study ARGX-113-1705.

Pre-assignment

Screening details:

Total study duration was up to 28 weeks, including a 2-week screening period, an initial 8-week TC and intertreatment cycle (ITC) of variable length depending on the patient. Patients had to be on a stable dose of SoC and not have received immunoglobulins by IV, subcutaneous or intramuscular route, or plasma exchange, < 1 month prior to screening.

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	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	ARGX-113

Arm description:

Patients received ARGX-113 IV 10 mg/kg administered as a 1-hour infusion every 7 days for 4 infusions (Days 1, 8, 15, and 22) in each cycle.
Each 8-week TC comprised a 3-week treatment period and a 5-week follow-up period. At the end of each TC, patients entered the ITC period consisting of visits every 2 weeks. At each ITC visit, retreatment criteria were evaluated to determine if the patient was eligible to enter the next cycle for retreatment, based on clinical response as measured by the MG-ADL scale.

Arm type	Experimental
Investigational medicinal product name	ARGX-113
Investigational medicinal product code	
Other name	Efgartigimod
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

ARGX-113 was provided as a 20 mg/milliliter (mL) sterile, colorless and clear concentrate solution for IV administration. Appropriate dilutions in a 0.9% saline solution were made on site prior to administration. For each administration, patients were administered a dose of 10 mg/kg of body weight in a total volume of 125 mL, infused over 1 hour. The maximum permitted ARGX-113 dose per infusion was 1200 mg.

Arm title	Placebo

Arm description:

Patients received matching placebo administered as a 1-hour infusion every 7 days for 4 infusions (Days 1, 8, 15, and 22) in each cycle.
Each 8-week TC comprised a 3-week treatment period and a 5-week follow-up period. At the end of each TC, patients entered the ITC period consisting of visits every 2 weeks. At each ITC visit, retreatment criteria were evaluated to determine if the patient was eligible to enter the next cycle for retreatment, based on clinical response as measured by the MG-ADL scale.

Arm type	Placebo

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Matched placebo was provided as a sterile, colorless and clear concentrate solution for IV administration. Appropriate dilutions in a 0.9% saline solution were made on site prior to administration. For each administration, patients were administered a total volume of 125 mL, infused over 1 hour.

Number of subjects in period 1	ARGX-113	Placebo
Started	84	83
Completed	80	76
Not completed	4	7
Consent withdrawn by subject	1	4
Physician decision	-	1
Adverse event, non-fatal	1	-
Sponsor decision	1	1
Rescue therapy needed	-	1
Protocol deviation	1	-

Baseline characteristics

Reporting groups

Reporting group title	ARGX-113

Reporting group description:

Patients received ARGX-113 IV 10 mg/kg administered as a 1-hour infusion every 7 days for 4 infusions (Days 1, 8, 15, and 22) in each cycle.
Each 8-week TC comprised a 3-week treatment period and a 5-week follow-up period. At the end of each TC, patients entered the ITC period consisting of visits every 2 weeks. At each ITC visit, retreatment criteria were evaluated to determine if the patient was eligible to enter the next cycle for retreatment, based on clinical response as measured by the MG-ADL scale.

Reporting group title	Placebo

Reporting group description:

Patients received matching placebo administered as a 1-hour infusion every 7 days for 4 infusions (Days 1, 8, 15, and 22) in each cycle.
Each 8-week TC comprised a 3-week treatment period and a 5-week follow-up period. At the end of each TC, patients entered the ITC period consisting of visits every 2 weeks. At each ITC visit, retreatment criteria were evaluated to determine if the patient was eligible to enter the next cycle for retreatment, based on clinical response as measured by the MG-ADL scale.

Reporting group values	ARGX-113	Placebo	Total
Number of subjects	84	83	167
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	73	69	142
From 65-84 years	11	14	25
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	45.9	48.2	
standard deviation	± 14.41	± 14.97	-
Gender categorical			
Units: Subjects			
Female	63	55	118
Male	21	28	49
Race			
Units: Subjects			
American Indian or Alaska native	2	0	2
Asian	9	7	16
Black or African American	3	3	6
White	69	72	141
Multiple	1	0	1
Not reported	0	1	1
Ethnicity, Customized			

Units: Subjects			
Japanese	8	7	15
Hispanic or Latino	7	2	9
Not Hispanic or Latino	69	73	142
Not reported	0	1	1
Concomitant gMG treatment Units: Subjects			
NSIDs	51	51	102
No NSIDs	33	32	65
AChR-Ab status Units: Subjects			
Positive	65	64	129
Negative	19	19	38

End points

End points reporting groups

Reporting group title	ARGX-113

Reporting group description:

Patients received ARGX-113 IV 10 mg/kg administered as a 1-hour infusion every 7 days for 4 infusions (Days 1, 8, 15, and 22) in each cycle.
Each 8-week TC comprised a 3-week treatment period and a 5-week follow-up period. At the end of each TC, patients entered the ITC period consisting of visits every 2 weeks. At each ITC visit, retreatment criteria were evaluated to determine if the patient was eligible to enter the next cycle for retreatment, based on clinical response as measured by the MG-ADL scale.

Reporting group title	Placebo

Reporting group description:

Patients received matching placebo administered as a 1-hour infusion every 7 days for 4 infusions (Days 1, 8, 15, and 22) in each cycle.
Each 8-week TC comprised a 3-week treatment period and a 5-week follow-up period. At the end of each TC, patients entered the ITC period consisting of visits every 2 weeks. At each ITC visit, retreatment criteria were evaluated to determine if the patient was eligible to enter the next cycle for retreatment, based on clinical response as measured by the MG-ADL scale.

Primary: Percentage of MG-ADL Responders During Cycle 1 (C1); Analyzed in the AChR-Ab Seropositive Population

End point title	Percentage of MG-ADL Responders During Cycle 1 (C1); Analyzed in the AChR-Ab Seropositive Population

End point description:

The MG-ADL is an 8-item patient-reported scale to assess MG symptoms and their effects on daily activities. The scale comprises 2 items on daily life activities and 6 items on symptoms. The MG-ADL total score range is 0-24, with higher scores indicative of greater disease severity.
A patient was considered an MG-ADL responder during C1 if there was a reduction of ≥2 points on the MG-ADL total score (compared to baseline of C1 [C1B]) for ≥4 consecutive weeks with the first reduction occurring no later than 1 week after the last infusion of investigational medicinal product (IMP) in C1.
Analysis was performed in the AChR-Ab seropositive population using the modified intention-to-treat (mITT) analysis set which included all randomized patients with a value for the MG-ADL total score at baseline and at least 1 postbaseline timepoint.

End point type	Primary

End point timeframe:

Baseline up to Day 63 (end of TC1)

End point values	ARGX-113	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	64		
Units: percentage of patients				
number (not applicable)	67.7	29.7		

Statistical analyses

Statistical analysis title	Comparison of ARGX-113 versus (vs) Placebo

Statistical analysis description:

MG-ADL responders after the first TC:
2-sided exact test (using logistic regression) at the 2-sided 5% significance level in the AChR-Ab seropositive population, stratified by Japanese vs non-Japanese and NSID vs no NSID as concomitant gMG treatment, with cycle baseline MG-ADL total score as covariate.
The treatment effect was presented as the odds ratio. An odds ratio of more than 1 represents a higher response rate for ARGX-113 compared to placebo.

Comparison groups	ARGX-113 v Placebo
Number of subjects included in analysis	129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.951
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.213
upper limit	11.528

Secondary: Percentage of Quantitative Myasthenia Gravis (QMG) Responders During C1; Analyzed in the AChR-Ab Seropositive Population

End point title	Percentage of Quantitative Myasthenia Gravis (QMG) Responders During C1; Analyzed in the AChR-Ab Seropositive Population

End point description:

The QMG scale quantifies disease severity based on impairments of body functions and structures as defined by the International Classification of Disability and Health. The QMG scale consists of 13 items that measure endurance or fatigability, and accounts for fluctuations in disease state. The QMG total score range is 0-39, with higher scores indicative of greater disease severity.
A patient was considered a QMG responder during C1 if there was a reduction of ≥3-points on the QMG total score (compared to C1B) for ≥4 consecutive weeks with the first reduction occurring no later than 1 week after the last infusion of IMP in C1.
Analysis was performed in the AChR-Ab seropositive population using the mITT analysis set which included all randomized patients with a value for the MG-ADL total score at baseline and at least 1 postbaseline timepoint.

End point type	Secondary

End point timeframe:

Baseline up to Day 63 (end of TC1)

End point values	ARGX-113	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	64		
Units: percentage of patients				
number (not applicable)	63.1	14.1		

Statistical analyses

Statistical analysis title	Comparison of ARGX-113 vs Placebo

Statistical analysis description:

QMG responders after the first TC:
2-sided exact test (using logistic regression) at the 2-sided 5% significance level in the AChR-Ab seropositive population, stratified by Japanese vs non-Japanese and NSID vs no NSID as concomitant gMG treatment, with cycle baseline QMG total score as covariate.
The treatment effect was presented as the odds ratio. An odds ratio of more than 1 represents a higher response rate for ARGX-113 compared to placebo.

Comparison groups	ARGX-113 v Placebo
Number of subjects included in analysis	129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	10.842
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.179
upper limit	31.2

Secondary: Percentage of MG-ADL Responders During C1; Analyzed in the Overall Population

End point title	Percentage of MG-ADL Responders During C1; Analyzed in the Overall Population

End point description:

The percentage of MG-ADL responders during C1 in the overall population is reported for this secondary end point; percentage of MG-ADL responders during C1 in the AChR-Ab seropositive population is reported previously as a primary end point.
Analysis was performed in the overall population (including both AChR-Ab seropositive and seronegative patients) using the mITT analysis set which included all randomized patients with a value for the MG-ADL total score at baseline and at least 1 postbaseline timepoint.

End point type	Secondary

End point timeframe:

Baseline up to Day 63 (end of TC1)

End point values	ARGX-113	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	84	83		
Units: percentage of patients				
number (not applicable)	67.9	37.3		

Statistical analyses

Statistical analysis title	Comparison of ARGX-113 vs Placebo

Statistical analysis description:

MG-ADL responders after the first TC:
2-sided exact test (using logistic regression) at the 2-sided 5% significance level in the overall population, stratified by AChR-Ab status (seropositive vs seronegative), Japanese vs non-Japanese and NSID vs no NSID as concomitant gMG treatment, with cycle baseline MG-ADL total score as covariate. The treatment effect was presented as the odds ratio. An odds ratio of more than 1 represents a higher response rate for ARGX-113 compared to placebo.

Comparison groups	ARGX-113 v Placebo
Number of subjects included in analysis	167
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.699
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.854
upper limit	7.578

Secondary: Percentage of Time That Patients Had a Clinically Meaningful Improvement (CMI) in MG-ADL Total Score up to and Including Day 126; Analyzed in the AChR-Ab Seropositive Population

End point title	Percentage of Time That Patients Had a Clinically Meaningful Improvement (CMI) in MG-ADL Total Score up to and Including Day 126; Analyzed in the AChR-Ab Seropositive Population

End point description:

An MG-ADL CMI was defined as a reduction of ≥2 points on the total MG-ADL score compared to study entry baseline (SEB).
Analysis was performed in the AChR-Ab seropositive population using the mITT analysis set which included all randomized patients with a value for the MG-ADL total score at baseline and at least 1 postbaseline timepoint.

End point type	Secondary

End point timeframe:

Baseline up to Day 126

End point values	ARGX-113	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	64		
Units: percentage of time (in days)				
least squares mean (standard error)	48.714 (± 6.163)	26.649 (± 6.316)		

Statistical analyses

Statistical analysis title	Comparison of ARGX-113 vs Placebo

Statistical analysis description:

Percentage of time patients had a CMI in MG-ADL total score up to and including Day 126:
Analysis of covariance (ANCOVA) in the AChR-Ab seropositive population with treatment, baseline MG-ADL total score, Japanese vs non-Japanese, and NSID vs no NSID as concomitant gMG treatment as the covariates.

Comparison groups	ARGX-113 v Placebo
Number of subjects included in analysis	129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0001
Method	ANCOVA
Parameter estimate	Least square means difference
Point estimate	22.065
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.949
upper limit	33.181
Variability estimate	Standard error of the mean
Dispersion value	5.616

Secondary: Time From Week 4 to Qualify for Retreatment; Analyzed in the AChR-Ab Seropositive Population

End point title	Time From Week 4 to Qualify for Retreatment; Analyzed in the AChR-Ab Seropositive Population

End point description:

Time to qualify for retreatment was defined as time from the Week 4 assessment until the first visit with a <2-point reduction compared to SEB in the MG-ADL total score and MG-ADL total score ≥5 points with >50% of the total score attributable to nonocular symptoms.
Analysis was performed in the AChR-Ab seropositive population using the mITT analysis set which included all randomized patients with a value for the MG-ADL total score at baseline and at least 1 postbaseline timepoint.

End point type	Secondary

End point timeframe:

Week 4 up to Day 182 (end of study [EoS])

End point values	ARGX-113	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	64		
Units: days				
median (confidence interval 95%)	35.0 (29.0 to 43.0)	8.0 (1.0 to 30.0)		

Statistical analyses

Statistical analysis title	Comparison of ARGX-113 vs Placebo

Statistical analysis description:

Time from Week 4 to qualify for retreatment:
Analysis was performed in the AChR-Ab seropositive population and the p-value was calculated using the log-rank test, stratified by Japanese vs non-Japanese and NSID vs no NSID as concomitant gMG treatment.

Comparison groups	Placebo v ARGX-113
Number of subjects included in analysis	129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2604
Method	Logrank

Secondary: Percentage of Early MG-ADL Responders During C1; Analyzed in the AChR-Ab Seropositive Population

End point title	Percentage of Early MG-ADL Responders During C1; Analyzed in the AChR-Ab Seropositive Population

End point description:

A patient was considered an early MG-ADL responder during C1 if there was a reduction of ≥2 points on the MG-ADL total score (compared to C1B) for ≥4 consecutive weeks with the first reduction occurring no later than Week 2 (ie, after 1 or maximum 2 infusions of IMP in C1).
Analysis was performed in the AChR-Ab seropositive population using the mITT analysis set which included all randomized patients with a value for the MG-ADL total score at baseline and at least 1 postbaseline timepoint.

End point type	Secondary

End point timeframe:

Baseline up to Day 63 (end of TC1)

End point values	ARGX-113	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	64		
Units: percentage of patients				
number (not applicable)	56.9	25.0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events were monitored from first administration of IMP on Day 1 until the EoS (up to a maximum of approximately 182 days).

Adverse event reporting additional description:

The safety analysis set included patients in the randomized population who received at least a partial dose of IMP.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	ARGX-113

Reporting group description:

Patients received ARGX-113 IV 10 mg/kg administered as a 1-hour infusion every 7 days for 4 infusions (Days 1, 8, 15, and 22) in each cycle.

Reporting group title	Placebo

Reporting group description:

Patients received matching placebo administered as a 1-hour infusion every 7 days for 4 infusions (Days 1, 8, 15, and 22) in each cycle.

Serious adverse events	ARGX-113	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 84 (4.76%)	7 / 83 (8.43%)	
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)			
Rectal adenocarcinoma			
subjects affected / exposed	1 / 84 (1.19%)	0 / 83 (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			
Procedural pain			
subjects affected / exposed	0 / 84 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			

subjects affected / exposed	0 / 84 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 84 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			
subjects affected / exposed	0 / 84 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Myasthenia gravis			
subjects affected / exposed	1 / 84 (1.19%)	2 / 83 (2.41%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myasthenia gravis crisis			
subjects affected / exposed	0 / 84 (0.00%)	1 / 83 (1.20%)	
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			
Thrombocytosis			
subjects affected / exposed	1 / 84 (1.19%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Therapeutic product ineffective			
subjects affected / exposed	0 / 84 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			

	ARGX-113	Placebo	
subjects affected / exposed	1 / 84 (1.19%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Spinal ligament ossification			
subjects affected / exposed	0 / 84 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	0 / 84 (0.00%)	1 / 83 (1.20%)	
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	ARGX-113	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	49 / 84 (58.33%)	48 / 83 (57.83%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 84 (3.57%)	6 / 83 (7.23%)	
occurrences (all)	4	6	
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 84 (3.57%)	5 / 83 (6.02%)	
occurrences (all)	5	5	
Headache			
subjects affected / exposed	24 / 84 (28.57%)	23 / 83 (27.71%)	
occurrences (all)	40	39	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	6 / 84 (7.14%)	9 / 83 (10.84%)	
occurrences (all)	6	14	
Nausea			

subjects affected / exposed	7 / 84 (8.33%)	9 / 83 (10.84%)
occurrences (all)	7	15

Respiratory, thoracic and mediastinal disorders		
Cough		
subjects affected / exposed	3 / 84 (3.57%)	5 / 83 (6.02%)
occurrences (all)	3	5
Oropharyngeal pain		
subjects affected / exposed	3 / 84 (3.57%)	7 / 83 (8.43%)
occurrences (all)	3	7

Musculoskeletal and connective tissue disorders		
Myalgia		
subjects affected / exposed	5 / 84 (5.95%)	1 / 83 (1.20%)
occurrences (all)	6	3

Infections and infestations		
Bronchitis		
subjects affected / exposed	5 / 84 (5.95%)	2 / 83 (2.41%)
occurrences (all)	6	2
Nasopharyngitis		
subjects affected / exposed	10 / 84 (11.90%)	15 / 83 (18.07%)
occurrences (all)	12	17
Upper respiratory tract infection		
subjects affected / exposed	9 / 84 (10.71%)	4 / 83 (4.82%)
occurrences (all)	11	4
Urinary tract infection		
subjects affected / exposed	8 / 84 (9.52%)	4 / 83 (4.82%)
occurrences (all)	9	4

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 November 2018	Changes encompassed by this amendment included updates for clarification or to apply minor corrections.
11 July 2019	Changes encompassed by this amendment included updates for clarification or to apply minor corrections. A new section for Adverse Events of Special Interest was added.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

 None reported