



Clinical trial results:

A Long-Term, Single-Arm, Open-Label, Multicenter, Phase 3 Follow-on Trial of ARGX-113-1704 to Evaluate the Safety and Tolerability of ARGX-113 in Patients with Myasthenia Gravis having Generalized Muscle Weakness

Summary

EudraCT number	2018-002133-37
Trial protocol	NL CZ DE DK BE HU IT
Global end of trial date	30 June 2022

Results information

Result version number	v1 (current)
This version publication date	07 July 2023
First version publication date	07 July 2023

Trial information

Trial identification

Sponsor protocol code	ARGX-113-1705
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03770403
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Argenx BVBA
Sponsor organisation address	Industriepark Zwijnaarde 7, Ghent, Belgium, 9052
Public contact	Regulatory Manager, argenx BV, argenx BVBA, regulatory@argenx.com
Scientific contact	Regulatory Manager, argenx BV, 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	30 June 2022
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	30 June 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the long-term safety and tolerability of efgartigimod in anti-acetylcholine receptor antibody (AChR-Ab) seropositive participants.

Protection of trial subjects:

This study was conducted according to the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use of Good Clinical Practice, the principles of the Declaration of Helsinki, and other applicable local ethical and legal requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 March 2019
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: 29
Country: Number of subjects enrolled	Belgium: 6
Country: Number of subjects enrolled	Czechia: 12
Country: Number of subjects enrolled	Denmark: 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: 3
Country: Number of subjects enrolled	Georgia: 19
Country: Number of subjects enrolled	Japan: 10
Country: Number of subjects enrolled	Russian Federation: 4
Country: Number of subjects enrolled	Serbia: 15
Country: Number of subjects enrolled	United States: 36
Worldwide total number of subjects	145
EEA total number of subjects	58

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)	124
From 65 to 84 years	21
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This Phase III, open-label study was a follow-on study of ARGX-113-1704 (NCT03669588) and was conducted in participants with myasthenia gravis having generalized muscle weakness at 51 investigational sites. This study was conducted in 2 sequential parts: Part A (1 year) and Part B (≤ 2 years).

Pre-assignment

Screening details:

Participants from ARGX-113-1704 who either completed that study or required retreatment that could not be completed during a treatment cycle in that study were included in this study to receive efgartigimod. A total of 151 participants rolled over to this study and 145 of them received at least 1 dose of study treatment.

Period 1

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

Arms

Arm title	Efgartigimod
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Arm description:

Participants were administered efgartigimod intravenous (IV) 10 milligrams/kilograms (mg/kg) over 1 hour every 7 days for 4 administrations per treatment period (TP) for 3 weeks in this study irrespective of whether they received efgartigimod or placebo in ARGX-113-1704. After the fourth infusion, participants entered an intertreatment period (ITP) of variable duration (minimum 4 weeks between treatment periods). Subsequent TPs were implemented according to clinical response.

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

Dosage and administration details:

Efgartigimod was available as a sterile, colorless concentrate for solution for IV administration. Participants were administered efgartigimod 10 mg/kg over 1 hour every 7 days for 4 administrations per TP for 3 weeks. The maximum permitted efgartigimod dose per infusion was 1200 mg.

Number of subjects in period 1	Efgartigimod
Started	145
Completed	28
Not completed	117
Physician decision	1
Consent withdrawn by subject	13
Study terminated by Sponsor	1
Adverse event, non-fatal	8
Death	5

Unspecified	88
Sponsor decision	1

Baseline characteristics

Reporting groups

Reporting group title	Efgartigimod
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Reporting group description:

Participants were administered efgartigimod intravenous (IV) 10 milligrams/kilograms (mg/kg) over 1 hour every 7 days for 4 administrations per treatment period (TP) for 3 weeks in this study irrespective of whether they received efgartigimod or placebo in ARGX-113-1704. After the fourth infusion, participants entered an intertreatment period (ITP) of variable duration (minimum 4 weeks between treatment periods). Subsequent TPs were implemented according to clinical response.

Reporting group values	Efgartigimod	Total	
Number of subjects	145	145	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	47.0 ± 14.76	-	
Gender categorical Units: Subjects			
Female	103	103	
Male	42	42	
Race Units: Subjects			
American Indian or Alaska Native	2	2	
Asian	11	11	
Black or African American	5	5	
White	126	126	
Multiple	1	1	
Ethnicity Units: Subjects			
Japanese	10	10	
Hispanic or Latino	9	9	
Not Hispanic or Latino	126	126	
AChR-Ab status Units: Subjects			
AChR-Ab seropositive	111	111	
AChR-Ab seronegative	34	34	

End points

End points reporting groups

Reporting group title	Efgartigimod
Reporting group description:	
Participants were administered efgartigimod intravenous (IV) 10 milligrams/kilograms (mg/kg) over 1 hour every 7 days for 4 administrations per treatment period (TP) for 3 weeks in this study irrespective of whether they received efgartigimod or placebo in ARGX-113-1704. After the fourth infusion, participants entered an intertreatment period (ITP) of variable duration (minimum 4 weeks between treatment periods). Subsequent TPs were implemented according to clinical response.	

Primary: Number of Participants With Treatment-Emergent Adverse Events (TEAEs), Treatment-Emergent Serious AEs, TEAEs Leading to Study Drug Discontinuation and Fatal TEAEs in AChR-Positive Participants

End point title	Number of Participants With Treatment-Emergent Adverse Events (TEAEs), Treatment-Emergent Serious AEs, TEAEs Leading to Study Drug Discontinuation and Fatal TEAEs in AChR-Positive Participants ^[1]
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End point description:

An AE was any untoward medical occurrence in a clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. Any clinically significant abnormal laboratory test results (hematology, clinical chemistry, or urinalysis) or other safety assessments (electrocardiogram [ECG], radiological scans, vital signs measurements) were collected as AEs. All AEs starting on or after first dosing were considered as TEAEs. A serious AE (SAE) was any AE that resulted in death, was life-threatening, required inpatient hospitalization, resulted in persistent or significant disability/incapacity, was a congenital abnormality, or was medically significant. The Safety Analysis set consisted of all participants who rolled over from ARGX-113-1704 and received ≥ 1 dose or part of a dose of EFG in this study. Only those participants with AChR-positive status are included in this analysis.

End point type	Primary
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End point timeframe:

TEAEs were collected from the start of first administered study treatment (Day 1) up to end of follow-up, approximately up to 3 years

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analysis was prespecified for this endpoint.

End point values	Efgartigimod			
Subject group type	Reporting group			
Number of subjects analysed	111			
Units: Count of Participants				
number (not applicable)				
TEAE	92			
Treatment-emergent SAE	28			
TEAEs leading to study drug discontinuation	10			
Fatal TEAE	4			

Statistical analyses

Secondary: Number of Participants With TEAEs, Treatment-Emergent SAEs, TEAEs Leading to Study Drug Discontinuation and Fatal TEAEs in the Overall Population

End point title	Number of Participants With TEAEs, Treatment-Emergent SAEs, TEAEs Leading to Study Drug Discontinuation and Fatal TEAEs in the Overall Population
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End point description:

Overall Population included both AChR-Ab seropositive and AChR-Ab seronegative participants. An AE was any untoward medical occurrence in a clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. Any clinically significant abnormal laboratory test results (hematology, clinical chemistry, or urinalysis) or other safety assessments (ECG, radiological scans, vital signs measurements) were collected as AEs. All AEs starting on or after first dosing were considered as TEAEs. An SAE was any AE that resulted in death, was life-threatening, required inpatient hospitalization, resulted in persistent or significant disability/incapacity, was a congenital abnormality, or was medically significant. The Safety Analysis set consisted of all participants who rolled over from ARGX-113-1704 and received ≥ 1 dose or part of a dose of EFG in this study.

End point type	Secondary
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End point timeframe:

TEAEs were collected from the start of first administered study treatment (Day 1) up to end of follow-up, approximately up to 3 years

End point values	Efgartigimod			
Subject group type	Reporting group			
Number of subjects analysed	145			
Units: count of participants				
number (not applicable)				
TEAE	124			
Treatment-emergent SAE	36			
TEAEs leading to study drug discontinuation	12			
Fatal TEAE	5			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

TEAEs were collected from the start of first administered study treatment (Day 1) up to end of follow-up, approximately up to 3 years

Adverse event reporting additional description:

The Safety Analysis set consisted of all participants who rolled over from ARGX-113-1704 and received ≥ 1 dose or part of a dose of efgartigimod in this study.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	24.1
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Reporting groups

Reporting group title	Efgartigimod
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Reporting group description:

Participants were administered efgartigimod IV 10 mg/kg over 1 hour every 7 days for 4 administrations per TP for 3 weeks in this study irrespective of whether they received efgartigimod or placebo in ARGX-113-1704. After the fourth infusion, participants entered an ITP of variable duration (minimum 4 weeks between treatment periods). Subsequent TPs were implemented according to clinical response.

Serious adverse events	Efgartigimod		
Total subjects affected by serious adverse events			
subjects affected / exposed	36 / 145 (24.83%)		
number of deaths (all causes)	5		
number of deaths resulting from adverse events	5		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatocellular carcinoma			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lung neoplasm malignant			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pancreatic carcinoma metastatic			

subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Prostate cancer			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Squamous cell carcinoma of the vulva			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Uterine leiomyoma			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Shock			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Shoulder arthroplasty			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal decompression			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal operation			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	2 / 145 (1.38%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Asthma			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonitis aspiration			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary mass			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
SARS-CoV-2 test positive			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Infusion related reaction			

subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal compression fracture			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Arrhythmia			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac failure congestive			
subjects affected / exposed	2 / 145 (1.38%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Defect conduction intraventricular			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebral venous sinus thrombosis			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myasthenia gravis			

subjects affected / exposed	7 / 145 (4.83%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 0		
Myasthenia gravis crisis			
subjects affected / exposed	2 / 145 (1.38%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Stupor			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Retinal detachment			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Irritable bowel syndrome			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			

subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bladder neck obstruction			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
COVID-19			
subjects affected / exposed	2 / 145 (1.38%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
COVID-19 pneumonia			
subjects affected / exposed	2 / 145 (1.38%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Dysentery			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	2 / 145 (1.38%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pneumonia escherichia			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pseudomonal sepsis			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Septic shock			

subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Urinary tract infection			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Type 1 diabetes mellitus			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Efgartigimod		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	83 / 145 (57.24%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	8 / 145 (5.52%)		
occurrences (all)	10		
Nervous system disorders			
Headache			
subjects affected / exposed	36 / 145 (24.83%)		
occurrences (all)	103		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	11 / 145 (7.59%)		
occurrences (all)	11		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	13 / 145 (8.97%)		
occurrences (all)	18		
Nausea			

subjects affected / exposed occurrences (all)	9 / 145 (6.21%) 13		
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all)	8 / 145 (5.52%) 8		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	12 / 145 (8.28%) 15		
Infections and infestations COVID-19 subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	16 / 145 (11.03%) 16 20 / 145 (13.79%) 24 12 / 145 (8.28%) 18		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 August 2019	Clarified that there needs to be a serious safety risk in order to have the participant discontinued. Updated exclusion criteria and schedule of activities to align with ARGX-113-1705. For participant safety, allowed vaccines to be administered according to common clinical practice and reduce the risk of confusing vaccination-related AEs (such as fever) with infusion-related AEs. Clarified that participants should not start treatment with a new standard of care. Clarified that in Quantitative Myasthenia Gravis evaluation, the rater can be a trained person instead of a physician. Updated criteria for AE of special interest and clarified that all SAEs will be followed up until resolution. Updated ethical conduct to align with protocol of ARGX-113-1704 The Netherlands-specific amendment version 1.1. upon request of the Ethics Committee of The Netherlands.
18 December 2019	An additional 2 years (defined as part B) were added to the study to provide participants uninterrupted access to EFG until it was available either commercially or through another participant program. Redefined endpoint definitions. Changes in methodology and investigational plan. Endpoints were streamlined to reflect what would be summarized and labels added to clarify what would be analyzed in Part A and Part B of the trial. Corrected to reflect that changes from the treatment period baseline of the first cycle would be summarized (instead of changes from study entry baseline) as participants might start the study with an intertreatment period. Modified the endpoint definition and clarified tertiary endpoints. Given the long-time frame of the extension and the option of unscheduled visits being carried out at the request of the investigator, the more flexible option of working with a local laboratory was chosen over the central laboratory structure.
19 January 2021	Updated benefit-risk assessment based on emerging data and consistency with investigator brochure version 9.0. Clarified that participants who completed ≥ 1 cycle of treatment and ≥ 1 year of ARGX-113-1705 and had started Part B were given the option to enroll in ARGX-113-2002 to receive EFG co-formulated with recombinant human hyaluronidase PH20 subcutaneously. Provided end of trial instructions. Exclusion criteria removed. Guidance on contraception was updated following results of nonclinical reproductive toxicity studies. Instructions were added to collect vaccination history. The ECG assessment was added to Part B to comply with the data safety monitoring board recommendation to monitor QT interval corrected by Fridericia abnormalities that could arise due to the accumulation of EFG. An additional change was made to allow for testing of participants who exhibited symptoms of Coronavirus disease-2019 (COVID-19) infection. Even in countries where COVID-19 safety measures were stopped according to local regulations, COVID-19 testing was continued and the results were sent to the sponsor for filing.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported