Clinical trial results:
A Phase 3, Randomized, Double-Blind Trial of Pamrevlumab (FG 3019) or Placebo in Combination with Systemic Corticosteroids in Subjects with Non-Ambulatory Duchenne Muscular Dystrophy (DMD)

Summary

EudraCT number	2020-000698-26
Trial protocol	FR AT CZ NL BE GB IT ES
Global end of trial date	17 August 2023

Results information

Result version number	v1 (current)
This version publication date	06 March 2024
First version publication date	06 March 2024

Trial information

Trial identification

Sponsor protocol code	FGCL-3019-093

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04371666
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	FibroGen, Inc.
Sponsor organisation address	409 Illinois Street, San Francisco, United States, CA 94158
Public contact	Clinical Trial Information Desk, FibroGen, Inc., FG3019-093DMDStudy@fibrogen.com
Scientific contact	Clinical Trial Information Desk, FibroGen, Inc., FG3019-093DMDStudy@fibrogen.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002979-PIP01-21
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	17 August 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 August 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective of this trial was to evaluate the efficacy and safety of pamrevlumab versus placebo in combination with systemic corticosteroids in participants with DMD (non-ambulatory, aged ≥12 years).

Protection of trial subjects:

This study was conducted in accordance with the Declaration of Helsinki, Good Clinical Practice (GCP), the International Council for Harmonisation (ICH) E6 Guidance for GCP, any other applicable local health and regulatory requirements, and Ethics Committee (EC) requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 July 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	United States: 51
Country: Number of subjects enrolled	France: 8
Country: Number of subjects enrolled	Italy: 10
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	Switzerland: 1
Country: Number of subjects enrolled	Austria: 1
Country: Number of subjects enrolled	New Zealand: 1
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Czechia: 5
Country: Number of subjects enrolled	China: 12
Worldwide total number of subjects	98
EEA total number of subjects	31

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)	77
Adults (18-64 years)	21
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study included 2 periods: Double-blind (DB) Treatment Period and Open-label Extension (OLE) Period.

Period 1

Period 1 title	DB Treatment Period (52 Weeks)
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	Pamrevlumab

Arm description:

Participants received pamrevlumab intravenously (IV) every 2 weeks for up to 52 weeks in the DB treatment period. After completing Week 52 of the DB treatment period, participants in the OLE period then moved to Week 2 of the OLE period and received pamrevlumab IV every 2 weeks.

Arm type	Experimental
Investigational medicinal product name	Pamrevlumab
Investigational medicinal product code	
Other name	FG-3019
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pamrevlumab was administered per dose and schedule specified in the arm description.

Arm title	Placebo

Arm description:

Participants received placebo matched to pamrevlumab IV every 2 weeks for up to 52 weeks in the DB treatment period. After completing Week 52 of the DB treatment period, participants in the OLE period then moved to Week 2 of the OLE period and received pamrevlumab IV every 2 weeks.

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

Dosage and administration details:

Placebo matched to pamrevlumab was administered per schedule specified in the arm description.

Number of subjects in period 1	Pamrevlumab	Placebo
Started	49	49
Received at least 1 dose of study drug	48	49
Completed	44	46
Not completed	5	3
Adverse event, non-fatal	3	1
Other than specified	1	-
Participant/Legal Guardian Decision	1	2

Period 2

Period 2 title	OLE (Maximum Exposure: 93.4 Weeks)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Pamrevlumab

Arm description:

Participants received pamrevlumab IV every 2 weeks for up to 52 weeks in the DB treatment period. After completing Week 52 of the DB treatment period, participants in the OLE period then moved to Week 2 of the OLE period and received pamrevlumab IV every 2 weeks.

Arm type	Experimental
Investigational medicinal product name	Pamrevlumab
Investigational medicinal product code	
Other name	FG-3019
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pamrevlumab was administered per dose and schedule specified in the arm description.

Arm title	Placebo

Arm description:

Participants received placebo matched to pamrevlumab IV every 2 weeks for up to 52 weeks in the DB treatment period. After completing Week 52 of the DB treatment period, participants in the OLE period then moved to Week 2 of the OLE period and received pamrevlumab IV every 2 weeks.

Arm type	Placebo
Investigational medicinal product name	Pamrevlumab
Investigational medicinal product code	
Other name	FG-3019
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pamrevlumab was administered per dose and schedule specified in the arm description.

Number of subjects in period 2[1]	Pamrevlumab	Placebo
Started	43	43
Received at least 1 dose of study drug	43	43
Completed	0	0
Not completed	43	43
Sponsor Decision to Terminate Study	40	41
Other than specified	1	-
Participant/Legal Guardian Decision	2	2

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: 4 participants who completed the DB Treatment Period did not enter in to the OLE period.

Baseline characteristics

Reporting groups	
Reporting group title	Pamrevlumab
Reporting group description:	
Participants received pamrevlumab intravenously (IV) every 2 weeks for up to 52 weeks in the DB treatment period. After completing Week 52 of the DB treatment period, participants in the OLE period then moved to Week 2 of the OLE period and received pamrevlumab IV every 2 weeks.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo matched to pamrevlumab IV every 2 weeks for up to 52 weeks in the DB treatment period. After completing Week 52 of the DB treatment period, participants in the OLE period then moved to Week 2 of the OLE period and received pamrevlumab IV every 2 weeks.	

Reporting group values	Pamrevlumab	Placebo	Total
Number of subjects	49	49	98
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	15.6	15.5	
standard deviation	± 2.74	± 2.42	-
Sex: Female, Male Units: participants			
Female	0	0	0
Male	49	49	98
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	6	9	15
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	2	2
White	42	35	77
More than one race	1	3	4
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	2	4	6
Not Hispanic or Latino	44	41	85
Unknown or Not Reported	3	4	7

End points

End points reporting groups

Reporting group title	Pamrevlumab
Reporting group description:	
Participants received pamrevlumab intravenously (IV) every 2 weeks for up to 52 weeks in the DB treatment period. After completing Week 52 of the DB treatment period, participants in the OLE period then moved to Week 2 of the OLE period and received pamrevlumab IV every 2 weeks.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo matched to pamrevlumab IV every 2 weeks for up to 52 weeks in the DB treatment period. After completing Week 52 of the DB treatment period, participants in the OLE period then moved to Week 2 of the OLE period and received pamrevlumab IV every 2 weeks.	
Reporting group title	Pamrevlumab
Reporting group description:	
Participants received pamrevlumab IV every 2 weeks for up to 52 weeks in the DB treatment period. After completing Week 52 of the DB treatment period, participants in the OLE period then moved to Week 2 of the OLE period and received pamrevlumab IV every 2 weeks.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo matched to pamrevlumab IV every 2 weeks for up to 52 weeks in the DB treatment period. After completing Week 52 of the DB treatment period, participants in the OLE period then moved to Week 2 of the OLE period and received pamrevlumab IV every 2 weeks.	

Primary: Change From Baseline in the Total Score of Performance of Upper Limb (PUL) 2.0 Version at Week 52

End point title	Change From Baseline in the Total Score of Performance of Upper Limb (PUL) 2.0 Version at Week 52
End point description:	
The PUL module is an observer-administered performance battery of upper extremity mobility tasks for the shoulder (upper, 6 items, 12 points), elbow (middle, 9 items, 17 points) and wrist/hand (distal, 7 items, 13 points). Higher scores indicate higher level of function. Total score ranges from 0-42 points and is the sum of the scores for the 3 subscales. Analysis was done using a random coefficient model (RCM), which included fixed effects of time (as a continuous variable), treatment, and treatment-by-time interaction, with baseline ordinal PUL entry score as covariate. The modified intent-to-treat (mITT) population included all randomized participants with a PUL Entry score ≥2 (excluding PUL entry scores of 1) at baseline. Here, 'Overall number of participants analyzed' = participants evaluable for specified outcome measure.	
End point type	Primary
End point timeframe:	
Baseline, Week 52	

End point values	Pamrevlumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	40		
Units: units on a scale				
least squares mean (standard error)	-2.036 (± 0.4471)	-2.119 (± 0.3367)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Pamrevlumab v Placebo
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8802 [1]
Method	Random coefficient model
Parameter estimate	Least square (LS) Mean Difference
Point estimate	0.083
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.01
upper limit	1.176
Variability estimate	Standard error of the mean
Dispersion value	0.5494

Notes:

[1] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline in Percent Predicted Forced Vital Capacity (ppFVC) at Week 52, Assessed by Spirometry

End point title	Change From Baseline in Percent Predicted Forced Vital Capacity (ppFVC) at Week 52, Assessed by Spirometry

End point description:

FVC is a standard pulmonary function test used to quantify respiratory muscle weakness. FVC was the volume of air that can forcibly be blown out after full inspiration in the upright position, measured in liters. Predicted FVC is based on a formula using sex, age and height of a person, and is an estimate of healthy lung capacity. Percent of predicted FVC = (observed value)/(predicted value) * 100%. Analysis was done using an RCM, which included fixed effects of time (as a continuous variable), treatment, and treatment-by-time interaction, with baseline value as covariate. The mITT population included all randomized participants with a PUL Entry score ≥2 (excluding PUL entry scores of 1) at baseline. Here, 'Overall number of participants analyzed' = participants evaluable for specified outcome measure.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Pamrevlumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	40		
Units: percentage of predicted FVC				
least squares mean (standard error)	-8.349 (± 1.5760)	-5.989 (± 1.2233)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Grip Strength of the Hands at Week 52, Assessed by Hand Held Myometry (HHM)

End point title	Change From Baseline in the Grip Strength of the Hands at Week 52, Assessed by Hand Held Myometry (HHM)

End point description:

The HHM was used to measure distal upper arm strength (grip strength). Data has been presented by dominant and non-dominant hand. Grip Strength was analyzed using a MMRM with fixed effects for treatment, visit (as a factor), treatment-by-visit interaction, and covariates (baseline values). The mITT population included all randomized participants with a PUL Entry score ≥2 (excluding PUL entry scores of 1) at baseline. Here, 'Overall number of participants analyzed' = participants evaluable for specified outcome measure. 'n' = participants evaluable for specified category.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Pamrevlumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	39		
Units: newton				
least squares mean (standard error)				
Grip Strength by Dominant Hand (n=37,39)	-7.570 (± 2.0989)	-0.072 (± 2.2065)		
Grip Strength by Nondominant Hand (n=36,39)	-7.627 (± 1.8893)	-0.012 (± 1.8546)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Left Ventricular Ejection Fraction percentage (LVEF %) at Week 52, Assessed by Magnetic Resonance Imaging (MRI)

End point title	Change From Baseline in Left Ventricular Ejection Fraction percentage (LVEF %) at Week 52, Assessed by Magnetic Resonance Imaging (MRI)

End point description:

LVEF% is an important measure of cardiac function. LVEF is a fraction of blood (in percent) pumped out

of the left ventricle of the heart (the main pumping chamber). The LVEF% was analyzed using an analysis of covariance (ANCOVA) model with treatment and baseline value. The mITT population included all randomized participants with a PUL Entry score ≥2 (excluding PUL entry scores of 1) at baseline. Here, 'Overall number of participants analyzed' = participants evaluable for specified outcome measure.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Pamrevlumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	37		
Units: percentage of LVEF				
least squares mean (standard error)	-0.499 (± 0.9750)	-1.114 (± 0.9204)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Percent Predicted Peak Expiratory Flow (ppPEF) at Week 52, Assessed by Spirometry

End point title	Change From Baseline in Percent Predicted Peak Expiratory Flow (ppPEF) at Week 52, Assessed by Spirometry

End point description:

The ppPEF is a measure of the maximal or peak flow produced during an exhalation with maximal effort and, as such, is the most effort-dependent measure of lung function. The ppFEV1 was analyzed using an RCM including fixed effects of time, treatment, and treatment-by-time interaction, with baseline as covariate. The ITT set included all randomized participants. Here, 'Overall number of participants analyzed' = participants evaluable for specified outcome measure.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Pamrevlumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	47		
Units: percentage of predicted PEF				
least squares mean (standard error)	-4.921 (± 2.3086)	-4.516 (± 1.7663)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

DB treatment period: From first dose of study drug up to 61 weeks
OLE period: From first dose of study drug up to study termination by Sponsor and safety follow-up (up to approximately 102 weeks)

Adverse event reporting additional description:

The safety analysis set included all participants who received any dose of study medication.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	DB Period: Placebo

Reporting group description:

Participants received placebo matched to pamrevlumab IV every 2 weeks for up to 52 weeks in the DB treatment period.

Reporting group title	OLE Period: Pamrevlumab

Reporting group description:

After completing Week 52 of the DB treatment period, participants in the OLE period then moved to Week 2 of the OLE period and received pamrevlumab IV every 2 weeks.

Reporting group title	DB Period: Pamrevlumab

Reporting group description:

Participants received pamrevlumab IV every 2 weeks for up to 52 weeks in the DB treatment period.

Serious adverse events	DB Period: Placebo	OLE Period: Pamrevlumab	DB Period: Pamrevlumab
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 49 (12.24%)	5 / 86 (5.81%)	8 / 48 (16.67%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Fracture			
subjects affected / exposed	0 / 49 (0.00%)	0 / 86 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	3 / 49 (6.12%)	2 / 86 (2.33%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			

subjects affected / exposed	0 / 49 (0.00%)	0 / 86 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle fracture			
subjects affected / exposed	0 / 49 (0.00%)	1 / 86 (1.16%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 49 (0.00%)	0 / 86 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Myocarditis			
subjects affected / exposed	1 / 49 (2.04%)	0 / 86 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Loss of consciousness			
subjects affected / exposed	0 / 49 (0.00%)	0 / 86 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 49 (0.00%)	0 / 86 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Food allergy			
subjects affected / exposed	0 / 49 (0.00%)	0 / 86 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Testicular necrosis			

subjects affected / exposed	0 / 49 (0.00%)	0 / 86 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Testicular torsion			
subjects affected / exposed	0 / 49 (0.00%)	0 / 86 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 49 (0.00%)	1 / 86 (1.16%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 49 (0.00%)	0 / 86 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	1 / 49 (2.04%)	0 / 86 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 49 (0.00%)	0 / 86 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 49 (0.00%)	1 / 86 (1.16%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 49 (2.04%)	1 / 86 (1.16%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

COVID-19			
subjects affected / exposed	1 / 49 (2.04%)	0 / 86 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	1 / 49 (2.04%)	0 / 86 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection			
subjects affected / exposed	0 / 49 (0.00%)	1 / 86 (1.16%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	DB Period: Placebo	OLE Period: Pamrevlumab	DB Period: Pamrevlumab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	44 / 49 (89.80%)	53 / 86 (61.63%)	42 / 48 (87.50%)
Investigations			
Heart rate increased			
subjects affected / exposed	0 / 49 (0.00%)	0 / 86 (0.00%)	3 / 48 (6.25%)
occurrences (all)	0	0	7
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	2 / 49 (4.08%)	4 / 86 (4.65%)	4 / 48 (8.33%)
occurrences (all)	4	4	4
Limb injury			
subjects affected / exposed	0 / 49 (0.00%)	3 / 86 (3.49%)	4 / 48 (8.33%)
occurrences (all)	0	3	4
Vascular access site bruising			
subjects affected / exposed	4 / 49 (8.16%)	1 / 86 (1.16%)	3 / 48 (6.25%)
occurrences (all)	4	1	3
Ligament sprain			
subjects affected / exposed	3 / 49 (6.12%)	0 / 86 (0.00%)	0 / 48 (0.00%)
occurrences (all)	3	0	0

Femur fracture			
subjects affected / exposed	3 / 49 (6.12%)	1 / 86 (1.16%)	1 / 48 (2.08%)
occurrences (all)	3	1	1
Vascular disorders			
Flushing			
subjects affected / exposed	2 / 49 (4.08%)	3 / 86 (3.49%)	3 / 48 (6.25%)
occurrences (all)	2	3	3
Cardiac disorders			
Cardiomyopathy			
subjects affected / exposed	5 / 49 (10.20%)	0 / 86 (0.00%)	1 / 48 (2.08%)
occurrences (all)	5	0	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 49 (4.08%)	1 / 86 (1.16%)	4 / 48 (8.33%)
occurrences (all)	2	3	4
Headache			
subjects affected / exposed	10 / 49 (20.41%)	24 / 86 (27.91%)	25 / 48 (52.08%)
occurrences (all)	20	50	65
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	4 / 49 (8.16%)	14 / 86 (16.28%)	12 / 48 (25.00%)
occurrences (all)	4	15	14
Pain			
subjects affected / exposed	0 / 49 (0.00%)	0 / 86 (0.00%)	4 / 48 (8.33%)
occurrences (all)	0	0	10
Eye disorders			
Cataract			
subjects affected / exposed	0 / 49 (0.00%)	0 / 86 (0.00%)	3 / 48 (6.25%)
occurrences (all)	0	0	3
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	4 / 49 (8.16%)	4 / 86 (4.65%)	5 / 48 (10.42%)
occurrences (all)	4	4	8
Nausea			
subjects affected / exposed	3 / 49 (6.12%)	5 / 86 (5.81%)	8 / 48 (16.67%)
occurrences (all)	3	8	13
Vomiting			

subjects affected / exposed	5 / 49 (10.20%)	5 / 86 (5.81%)	10 / 48 (20.83%)
occurrences (all)	6	8	15
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 49 (8.16%)	6 / 86 (6.98%)	2 / 48 (4.17%)
occurrences (all)	4	6	4
Rhinorrhoea			
subjects affected / exposed	3 / 49 (6.12%)	0 / 86 (0.00%)	1 / 48 (2.08%)
occurrences (all)	3	0	1
Oropharyngeal pain			
subjects affected / exposed	3 / 49 (6.12%)	1 / 86 (1.16%)	3 / 48 (6.25%)
occurrences (all)	3	1	3
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	5 / 49 (10.20%)	0 / 86 (0.00%)	4 / 48 (8.33%)
occurrences (all)	5	0	4
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	3 / 49 (6.12%)	3 / 86 (3.49%)	2 / 48 (4.17%)
occurrences (all)	3	3	2
Arthralgia			
subjects affected / exposed	4 / 49 (8.16%)	2 / 86 (2.33%)	2 / 48 (4.17%)
occurrences (all)	4	2	2
Back pain			
subjects affected / exposed	3 / 49 (6.12%)	9 / 86 (10.47%)	7 / 48 (14.58%)
occurrences (all)	4	11	7
Osteoporosis			
subjects affected / exposed	1 / 49 (2.04%)	6 / 86 (6.98%)	1 / 48 (2.08%)
occurrences (all)	1	6	1
Myalgia			
subjects affected / exposed	0 / 49 (0.00%)	5 / 86 (5.81%)	1 / 48 (2.08%)
occurrences (all)	0	5	2
Infections and infestations			
Rhinitis			
subjects affected / exposed	4 / 49 (8.16%)	4 / 86 (4.65%)	1 / 48 (2.08%)
occurrences (all)	5	4	1

Upper respiratory tract infection			
subjects affected / exposed	3 / 49 (6.12%)	2 / 86 (2.33%)	6 / 48 (12.50%)
occurrences (all)	3	3	6
Nasopharyngitis			
subjects affected / exposed	8 / 49 (16.33%)	8 / 86 (9.30%)	3 / 48 (6.25%)
occurrences (all)	9	15	8
COVID-19			
subjects affected / exposed	19 / 49 (38.78%)	10 / 86 (11.63%)	19 / 48 (39.58%)
occurrences (all)	19	10	20

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 April 2020	It included following changes: - Muscle fibrosis MRI assessment was removed from inclusion criteria, and the fibrosis MRI assessment was added as an exploratory endpoint, per Food and Drug Administration (FDA) feedback.
15 September 2020	It included following changes: - Safety follow-up was extended to 60 days (+ 3 days) after the last infusion to align with 5 times the half-life of pamrevlumab (12.2 days). - Clarification was added that participants already on an approved DMD therapy should not discontinue that therapy to be eligible for the study. - Study drug administration window was extended from 24 to 48 hours to align with updated pamrevlumab stability information. - Electrocardiograms (ECGs) were removed to align with DMD standard of care. - Basophils were added to include all components of the lab testing panel. - Pulmonary function test (PFT) inclusion criteria were clarified. - Criteria for participants to continue into the OLE period were clarified. - Muscle fibrosis MRI assessment and fibrosis endpoint were removed from the OLE period.
26 October 2020	It included following changes: - Per investigator feedback, Inclusion Criterion was changed to average (of Screening and Day 0) ppFVC between 45 and 85, inclusive, to mitigate risk and safeguard the wellbeing of the DMD participants, who could have potentially suffered from exhaustion with the original ppFVC requirements.
09 July 2021	It included following changes: - Participation requirements for cardiac MRI, pneumonia and influenza vaccinations, and acceptable ranges for central laboratory assessments were clarified. - Inclusion Criterion was changed to remove the requirement for cardiomyopathy diagnosis. - The exclusion criterion for allergic reactions was expanded to include hypersensitivity to the study drug components or the gadolinium-based contrast agents required for the MRI. - Casimersen (amondys 45) was added to the prohibited concomitant medications, due to its recent drug approval. - Cardiac and pulmonary assessment exclusion criteria were expanded to exclude participants with abnormal glomerular filtration rate (GFR) or acute kidney injury. - Clarification was added to state that pamrevlumab would be permanently discontinued in the case of a serious or life-threatening allergic reaction. - Instruction was added for participants to speak to the study doctor and assess if an unscheduled visit is required after any adverse reaction during an home health care (HHC) visit. - Guidance regarding the time separation between study drug and COVID-19 vaccination was added. - Guidance regarding visit modality (in-person vs remote) and visit scheduling was added to align with FDA/European Medicines Agency (EMA) guidance regarding the COVID-19 pandemic and the resulting need for flexibility for visits and assessments. • Contraception requirements were added to include permitted methods, such as condoms and abstinence. • Clarification was added that subjects who discontinue from the Double-blind Treatment period were not eligible for OLE participation. • AE reporting and AE definition were updated to reflect International Council for Harmonisation (ICH) E2A standard language.

01 November 2022	It included following changes: - Bone fracture safety assessments were added to align with the pediatric investigational plan. - Secondary endpoints were rearranged to align with the revised analysis plan. - The exploratory endpoint of summarizing the subscores of the 3 regional dimensions of the PUL was added. - Withdrawal criteria were updated to include a description for participants discontinuing infusions. • Additional pharmacokinetics (PK), anti-drug antibodies (ADA), antidrug antibody neutralizing antibody (ADA-NA), and immunogenic reaction blood draws were added to increase the scope of specialty lab testing.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported