



Clinical trial results:

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

Summary

EudraCT number	2020-000699-39
Trial protocol	FR BE AT NL IT ES
Global end of trial date	14 December 2023

Results information

Result version number	v1 (current)
This version publication date	31 August 2024
First version publication date	31 August 2024

Trial information

Trial identification

Sponsor protocol code	FGCL-3019-094
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04632940
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., FG3019-094DMDStudy@fibrogen.com
Scientific contact	Clinical Trial Information Desk, FibroGen, Inc., FG3019-094DMDStudy@fibrogen.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-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	14 December 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 December 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 administered every 2 weeks in ambulatory participants with Duchenne muscular dystrophy (DMD) (age 6 to <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 IEC requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 March 2021
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	Austria: 2
Country: Number of subjects enrolled	Belgium: 4
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	China: 17
Country: Number of subjects enrolled	France: 8
Country: Number of subjects enrolled	Italy: 7
Country: Number of subjects enrolled	Netherlands: 2
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	United States: 30
Worldwide total number of subjects	73
EEA total number of subjects	24

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)	69
Adolescents (12-17 years)	4
Adults (18-64 years)	0
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: a Double-blind (DB) period and an Open-label extension (OLE) period.

Period 1

Period 1 title	DB 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
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Arm title	Pamrevlumab
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Arm description:

Participants received pamrevlumab 35 milligrams (mg)/kilogram (kg) by intravenous (IV) infusion every 2 weeks + systemic deflazacort or equivalent potency of corticosteroids administered orally for up to 52 weeks in the DB period.

Arm type	Experimental
Investigational medicinal product name	Pamrevlumab
Investigational medicinal product code	FG-3019
Other name	
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
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Arm description:

Participants received placebo matched to pamrevlumab by IV infusion every 2 weeks + systemic deflazacort or equivalent potency of corticosteroids administered orally for up to 52 weeks in the DB period.

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	37	36
Received at least 1 dose of study drug	36	36
Completed	35	36
Not completed	2	0
Participant/Legal Guardian Decision	2	-

Period 2

Period 2 title	OLE Period (52 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 continued to receive the same dose of pamrevlumab for up to 52 weeks in the OLE period or until pamrevlumab was commercially available, or the sponsor decided to end the study, whichever occurred first.

Arm type	Experimental
Investigational medicinal product name	Pamrevlumab
Investigational medicinal product code	FG-3019
Other name	
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/Pamrevlumab
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Arm description:

Participants who received placebo in the DB period, received pamrevlumab 35 mg/kg by IV infusion every 2 weeks + systemic deflazacort or equivalent potency of corticosteroids administered orally for up to 52 weeks in the OLE period or until pamrevlumab was commercially available, or the sponsor decided to end the study, whichever occurred first.

Arm type	Placebo
Investigational medicinal product name	Pamrevlumab
Investigational medicinal product code	FG-3019
Other name	
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/Pamrevlumab
Started	34	35
Received at least 1 dose of study drug	34	34
Completed	0	0
Not completed	34	35
Physician decision	1	-
Adverse event, non-fatal	1	-
Sponsor Decision to Terminate Study	21	19
Other than specified	-	1
Lost to follow-up	-	1
Participant/Legal Guardian Decision	11	13
Entered into OLE but not treated	-	1

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: 2 participants who completed DB period, did not roll over into the OLE period.

Baseline characteristics

Reporting groups

Reporting group title	Pamrevlumab
Reporting group description:	
Participants received pamrevlumab 35 milligrams (mg)/kilogram (kg) by intravenous (IV) infusion every 2 weeks + systemic deflazacort or equivalent potency of corticosteroids administered orally for up to 52 weeks in the DB period.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo matched to pamrevlumab by IV infusion every 2 weeks + systemic deflazacort or equivalent potency of corticosteroids administered orally for up to 52 weeks in the DB period.	

Reporting group values	Pamrevlumab	Placebo	Total
Number of subjects	37	36	73
Age categorical Units: Subjects			

Age Continuous Units: years arithmetic mean standard deviation	9.1 ± 1.46	9.0 ± 1.56	-
Sex: Female, Male Units: participants			
Female	0	0	0
Male	37	36	73
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	5	6
Not Hispanic or Latino	34	28	62
Unknown or Not Reported	2	3	5
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	10	9	19
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	1	2
White	23	22	45
More than one race	0	0	0
Unknown or Not Reported	3	4	7

End points

End points reporting groups

Reporting group title	Pamrevlumab
Reporting group description: Participants received pamrevlumab 35 milligrams (mg)/kilogram (kg) by intravenous (IV) infusion every 2 weeks + systemic deflazacort or equivalent potency of corticosteroids administered orally for up to 52 weeks in the DB period.	
Reporting group title	Placebo
Reporting group description: Participants received placebo matched to pamrevlumab by IV infusion every 2 weeks + systemic deflazacort or equivalent potency of corticosteroids administered orally for up to 52 weeks in the DB period.	
Reporting group title	Pamrevlumab
Reporting group description: Participants continued to receive the same dose of pamrevlumab for up to 52 weeks in the OLE period or until pamrevlumab was commercially available, or the sponsor decided to end the study, whichever occurred first.	
Reporting group title	Placebo/Pamrevlumab
Reporting group description: Participants who received placebo in the DB period, received pamrevlumab 35 mg/kg by IV infusion every 2 weeks + systemic deflazacort or equivalent potency of corticosteroids administered orally for up to 52 weeks in the OLE period or until pamrevlumab was commercially available, or the sponsor decided to end the study, whichever occurred first.	

Primary: Change From Baseline in North Star Ambulatory Assessment (NSAA) Total Score at Week 52

End point title	Change From Baseline in North Star Ambulatory Assessment (NSAA) Total Score at Week 52
End point description: The NSAA consisted of 17 activities, each scored as 0 (activity could not be performed), 1 (modified method but achieved goal without physical assistance from another), or 2 (normal, achieved goal without assistance). The sum of these 17 scores was used to form a total score ranging from 0 (worst) to 34 (fully independent function). If fewer than 15 of the 17 activities were performed, the total score was considered missing. If 15 to 16 activities were performed, the total score was calculated by multiplying the sum of the scores in the x activities that were performed by 17/x. If an activity could not be performed due to disease progression/loss of ambulation, a score of 0 was assigned. Higher scores indicated better functioning. Least square (LS) mean and standard error (SE) were analyzed using a mixed model for repeated measure (MMRM). The ITT set included all randomized participants. 'Overall number of participants analyzed' = participants evaluable for this endpoint.	
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	36	36		
Units: units on a scale				
least squares mean (standard error)	-3.022 (\pm 0.5505)	-2.494 (\pm 0.6962)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Pamrevlumab v Placebo
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5553
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-0.528
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.308
upper limit	1.251
Variability estimate	Standard error of the mean
Dispersion value	0.8912

Secondary: Change From Baseline in 4-Stair Climb Velocity (4SCV) Assessment at Week 52

End point title	Change From Baseline in 4-Stair Climb Velocity (4SCV) Assessment at Week 52
End point description: The 4SCV (centimeters [cm]/second [sec]) was calculated as the ratio of the total height (cm) of stairs climbed divided by the number of seconds taken to complete the 4-stair climb. The ITT set included all randomized participants. Here, 'Overall number of participants analyzed' = participants evaluable for this endpoint.	
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	36	36		
Units: cm/sec				
arithmetic mean (standard deviation)	-1.858 (± 4.5459)	-3.797 (± 5.1899)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the 10-Meter Walk/Run Test at Week 52

End point title	Change From Baseline in the 10-Meter Walk/Run Test at Week 52
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End point description:

The time (in sec) required for a participant to run or walk a distance of 10 meters as quickly as possible was calculated as velocity (meters/sec). The ITT set included all randomized participants. Here, 'Overall number of participants analyzed' = participants evaluable for this endpoint.

End point type	Secondary
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End point timeframe:

Baseline, Week 52

End point values	Pamrevlumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	36		
Units: meters/sec				
arithmetic mean (standard deviation)	-0.176 (\pm 0.2193)	-0.196 (\pm 0.3552)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Time to Stand (TTSTAND) at Week 52

End point title	Change From Baseline in Time to Stand (TTSTAND) at Week 52
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End point description:

The time (in sec) required for a participant to stand from a supine position has been reported. A longer time taken reflected a worse outcome. The ITT set included all randomized participants. Here, 'Overall number of participants analyzed' = participants evaluable for this endpoint.

End point type	Secondary
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End point timeframe:

Baseline, Week 52

End point values	Pamrevlumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	31		
Units: sec				
arithmetic mean (standard deviation)	2.24 (\pm 3.353)	1.94 (\pm 3.688)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Loss of Ambulation (LoA) From Baseline to Week 52

End point title	Time to Loss of Ambulation (LoA) From Baseline to Week 52
End point description: Time (days) to LoA was defined as the number of days from randomization to the date of LoA, or all-cause death based on observed data, whichever occurred earlier during the on-study period. Median time (days) to LoA was calculated using Kaplan Meier Survival Estimates. The ITT set included all randomized participants. Here, '99999' signifies 'Due to insufficient number of participants with an event of LoA or death, median and 95% confidence interval (CI) could not be calculated.'	
End point type	Secondary
End point timeframe: Baseline to Week 52	

End point values	Pamrevlumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	36		
Units: days				
median (confidence interval 95%)	99999 (99999 to 99999)	99999 (99999 to 99999)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to Week 129

Adverse event reporting additional description:

As pre-specified, All-cause mortality data were collected and reported for all enrolled participants; and Serious and Non-serious adverse events data were collected and reported for all participants who received any dose of study medication.

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	DB Period: Pamrevlumab
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Reporting group description:

Participants received pamrevlumab 35 mg/kg by IV infusion every 2 weeks + systemic deflazacort or equivalent potency of corticosteroids administered orally for up to 52 weeks in the DB period.

Reporting group title	OLE Period: Pamrevlumab
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Reporting group description:

Participants received pamrevlumab 35 mg/kg by IV infusion every 2 weeks + systemic deflazacort or equivalent potency of corticosteroids administered orally for up to 52 weeks in the OLE period or until pamrevlumab was commercially available, or the sponsor decided to end the study, whichever occurred first.

Reporting group title	DB Period: Placebo
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Reporting group description:

Participants received placebo matched to pamrevlumab by IV infusion every 2 weeks + systemic deflazacort or equivalent potency of corticosteroids administered orally for up to 52 weeks in the DB period.

Serious adverse events	DB Period: Pamrevlumab	OLE Period: Pamrevlumab	DB Period: Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 36 (8.33%)	0 / 68 (0.00%)	1 / 36 (2.78%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Cardiac disorders			
Myocarditis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 68 (0.00%)	0 / 36 (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
Musculoskeletal and connective tissue disorders			
Knee deformity			

subjects affected / exposed	1 / 36 (2.78%)	0 / 68 (0.00%)	0 / 36 (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
Rhabdomyolysis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 68 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	1 / 36 (2.78%)	0 / 68 (0.00%)	0 / 36 (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

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

Non-serious adverse events	DB Period: Pamrevlumab	OLE Period: Pamrevlumab	DB Period: Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	35 / 36 (97.22%)	45 / 68 (66.18%)	33 / 36 (91.67%)
Investigations			
Blood pressure diastolic decreased			
subjects affected / exposed	2 / 36 (5.56%)	0 / 68 (0.00%)	0 / 36 (0.00%)
occurrences (all)	2	0	0
SARS-CoV-2 test positive			
subjects affected / exposed	2 / 36 (5.56%)	0 / 68 (0.00%)	1 / 36 (2.78%)
occurrences (all)	2	0	1
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	2 / 36 (5.56%)	1 / 68 (1.47%)	1 / 36 (2.78%)
occurrences (all)	3	1	1
Ligament sprain			
subjects affected / exposed	1 / 36 (2.78%)	1 / 68 (1.47%)	3 / 36 (8.33%)
occurrences (all)	1	1	3
Joint injury			
subjects affected / exposed	3 / 36 (8.33%)	0 / 68 (0.00%)	0 / 36 (0.00%)
occurrences (all)	3	0	0

Fall subjects affected / exposed occurrences (all)	7 / 36 (19.44%) 10	3 / 68 (4.41%) 3	2 / 36 (5.56%) 2
Vascular access site pain subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 68 (0.00%) 0	2 / 36 (5.56%) 2
Spinal compression fracture subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 68 (1.47%) 1	2 / 36 (5.56%) 2
Nervous system disorders Hypokinesia subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	0 / 68 (0.00%) 0	2 / 36 (5.56%) 2
Headache subjects affected / exposed occurrences (all)	14 / 36 (38.89%) 40	5 / 68 (7.35%) 6	5 / 36 (13.89%) 12
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	4 / 36 (11.11%) 6	2 / 68 (2.94%) 2	5 / 36 (13.89%) 5
Gait disturbance subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	0 / 68 (0.00%) 0	2 / 36 (5.56%) 2
Injection site bruising subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 68 (1.47%) 6	2 / 36 (5.56%) 13
Pyrexia subjects affected / exposed occurrences (all)	9 / 36 (25.00%) 16	10 / 68 (14.71%) 11	7 / 36 (19.44%) 8
Gastrointestinal disorders Abdominal discomfort subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	0 / 68 (0.00%) 0	2 / 36 (5.56%) 2
Abdominal pain subjects affected / exposed occurrences (all)	5 / 36 (13.89%) 6	2 / 68 (2.94%) 5	3 / 36 (8.33%) 5

Abdominal pain upper subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 2	3 / 68 (4.41%) 6	1 / 36 (2.78%) 1
Constipation subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	3 / 68 (4.41%) 3	2 / 36 (5.56%) 2
Diarrhoea subjects affected / exposed occurrences (all)	8 / 36 (22.22%) 12	6 / 68 (8.82%) 6	3 / 36 (8.33%) 7
Nausea subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 2	4 / 68 (5.88%) 6	3 / 36 (8.33%) 3
Vomiting subjects affected / exposed occurrences (all)	10 / 36 (27.78%) 10	12 / 68 (17.65%) 16	7 / 36 (19.44%) 11
Respiratory, thoracic and mediastinal disorders			
Cough subjects affected / exposed occurrences (all)	6 / 36 (16.67%) 6	10 / 68 (14.71%) 15	4 / 36 (11.11%) 4
Epistaxis subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 10	0 / 68 (0.00%) 0	3 / 36 (8.33%) 4
Nasal congestion subjects affected / exposed occurrences (all)	3 / 36 (8.33%) 3	1 / 68 (1.47%) 1	6 / 36 (16.67%) 10
Oropharyngeal pain subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 2	3 / 68 (4.41%) 3	6 / 36 (16.67%) 7
Rhinorrhoea subjects affected / exposed occurrences (all)	4 / 36 (11.11%) 6	4 / 68 (5.88%) 4	3 / 36 (8.33%) 8
Skin and subcutaneous tissue disorders			
Urticaria subjects affected / exposed occurrences (all)	3 / 36 (8.33%) 3	0 / 68 (0.00%) 0	0 / 36 (0.00%) 0
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	4 / 36 (11.11%)	1 / 68 (1.47%)	2 / 36 (5.56%)
occurrences (all)	5	1	2
Back pain			
subjects affected / exposed	4 / 36 (11.11%)	2 / 68 (2.94%)	2 / 36 (5.56%)
occurrences (all)	4	2	2
Myalgia			
subjects affected / exposed	2 / 36 (5.56%)	3 / 68 (4.41%)	1 / 36 (2.78%)
occurrences (all)	6	3	1
Musculoskeletal chest pain			
subjects affected / exposed	0 / 36 (0.00%)	1 / 68 (1.47%)	2 / 36 (5.56%)
occurrences (all)	0	1	2
Pain in extremity			
subjects affected / exposed	4 / 36 (11.11%)	3 / 68 (4.41%)	2 / 36 (5.56%)
occurrences (all)	4	5	3
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	2 / 36 (5.56%)	3 / 68 (4.41%)	1 / 36 (2.78%)
occurrences (all)	3	4	1
Ear infection			
subjects affected / exposed	1 / 36 (2.78%)	1 / 68 (1.47%)	4 / 36 (11.11%)
occurrences (all)	1	1	4
COVID-19			
subjects affected / exposed	16 / 36 (44.44%)	4 / 68 (5.88%)	8 / 36 (22.22%)
occurrences (all)	17	4	9
Influenza			
subjects affected / exposed	2 / 36 (5.56%)	4 / 68 (5.88%)	1 / 36 (2.78%)
occurrences (all)	2	4	1
Nasopharyngitis			
subjects affected / exposed	10 / 36 (27.78%)	11 / 68 (16.18%)	7 / 36 (19.44%)
occurrences (all)	18	17	12
Pharyngitis			
subjects affected / exposed	2 / 36 (5.56%)	0 / 68 (0.00%)	0 / 36 (0.00%)
occurrences (all)	2	0	0
Upper respiratory tract infection			

subjects affected / exposed	4 / 36 (11.11%)	6 / 68 (8.82%)	8 / 36 (22.22%)
occurrences (all)	4	11	10
Rhinitis			
subjects affected / exposed	3 / 36 (8.33%)	5 / 68 (7.35%)	3 / 36 (8.33%)
occurrences (all)	4	6	6

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 October 2020	<p>It included following changes: - The secondary endpoint of time to LoA was added to better assess the impact of pamrevlumab on LoA as a disease progression. - The exploratory endpoint of change in percent predicted forced vital capacity (ppFVC) and percent predicted peak expiratory flow (ppPEF) (assessed by spirometry) from baseline to Week 52 was added to assess the impact of pamrevlumab on pulmonary function. - The exploratory endpoint of change in left ventricular ejection fraction percentage (left ventricular ejection fraction percentage [LVEF%]; assessed by cardiac magnetic resonance imaging [MRI]) from baseline to Week 52 was added to assess the impact of pamrevlumab on cardiac fibrosis, as recommended by the European Medicines Agency (EMA). - The minimum distance requirement for Inclusion Criterion, ability to complete a certain distance during the 6-minute walking distance (6MWD), was changed from 330 meters to 270 meters to increase the population representatives and include a broad range of severities/disease progression rate. - The 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). - More benefit/risk statements were added to provide further information on the risk/benefit of studying pamrevlumab in ambulatory DMD. - The study drug administration time was updated from 24 to 48 hours to align with updated pamrevlumab stability information. - Genetic testing and electrocardiograms were removed. - Laboratory assessments and physical examinations were added to the OLE period. - The muscle fibrosis MRI assessment and endpoint were removed from the OLE period, as they were not a direct measure of participant function and were of uncertain clinical meaningfulness as a biomarker of disease progression.</p>
26 October 2020	<p>It included following changes: Inclusion criterion was changed to the average (of screening and Day 0) ppFVC above 45%, as opposed to an average ppFVC between 45% to 85%. This change was based on investigator feedback about forced vital capacity limit for ambulatory participants, especially with the shorter minimum distance for the 6MWD test implemented in Amendment 1.</p>
09 August 2021	<p>It included following changes: - Cardiac MRI was removed as an exploratory endpoint, as it was difficult to measure a meaningful result in this age group, and it was a worthwhile reduction in participant burden. - Acceptable ranges for central laboratory assessments and vaccination requirements were added to increase clarity and specificity related to eligibility. - The exclusion criterion for allergic reactions was expanded to include hypersensitivity to study drug, its components, or gadolinium-based contrast agents required for the MRI. - The recently approved Casimersen (amondys 45) was added to the prohibited medications list. - An exclusion criterion was added to include abnormal glomerular filtration rate (GFR) or evidence of acute kidney injury. - Time points for vital signs were corrected, and methods for temperature collection were defined. A physical examination was added at Week 36 during the OLE period. - Contraception methods were expanded to include condoms. - Clarification was added that the Duchenne Video Assessment (DVA) would not be conducted in Belgium.</p>

28 October 2022	It included following changes: - Bone fracture and height velocity safety assessments were added to align with the pediatric investigational plan. - The inclusion criterion requiring pneumococcal vaccination was changed from a requirement to a suggestion, as vaccine recommendations varied by country and depended on participant health status. - Removed exclusion criterion of hypersensitivity reaction to gadolinium-based contrast agents required for MRI acquisition as well as language pertaining to contrast MRI, as the cardiac MRI was removed in Amendment 3. Additionally, LVEF% was removed throughout the protocol, as it only pertained to the removed cardiac MRI. - The collection of specific DMD genetic mutation was added to support characterization of the most recent DMD mutation landscape and potentially evaluate possible relationships between participant genotype and clinical outcomes. - Clarification was added that the DVA would not be conducted in China. - Additional pharmacokinetic (PK), antidrug antibody (ADA), and antidrug antibody neutralizing antibody (ADA-NA) blood draws, along with immunogenic reaction blood draws, were added to meet regulatory recommendations for immunogenicity testing, and clarification was added for investigators to follow local guidance for allowable total blood volume.
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Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The OLE was discontinued due to study termination by the Sponsor.

Notes: